



IRB STANDARD OPERATING PROCEDURES

Table of Contents

I. PROTECTION OF HUMAN SUBJECTS	12
I.1. Ethical Principles that Govern Research	12
I.1.a. The Nuremberg Code	12
I.1.b. The Declaration of Helsinki	12
I.1.c. The Belmont Report.....	12
I.2. Mandate to Protect Human Subjects	13
I.2.a. Functions of the HRPP	14
I.2.a.1. Quality Assurance	14
I.2.a.2. Vetting Investigators.....	15
I.2.a.3. Grants and Contracts Department.....	15
I.2.a.4. Finance	16
I.2.a.5. BRANY Institute for Research Education.....	16
II. INSTITUTIONAL REVIEW BOARD ADMINISTRATION	17
II.1. Purpose of the IRB	17
II.2. Definition and Scope	19
II.2.a. Definition of Terms.....	19
II.2.b. BRANY IRB Definition of Human Subject Research	22
II.2.c. Exemptions.....	24
II.2.c.1. Procedures.....	27
II.3. Institutional Review Board Membership	28
II.3.a. IRB Membership Requirements	28
II.3.b. Selection of IRB Members	28
II.3.b.1. Member Responsibilities.....	29
II.3.c. Appointment of IRB Chairpersons.....	29
II.3.d. Length of Service.....	30
II.3.e. Evaluation of IRB Chairpersons	30
II.3.f. Evaluation of IRB Members	30
II.3.g. IRB Chairperson’s Responsibilities	31
II.3.g.1. Vice-Chair Responsibilities	312
II.3.h. Consultants.....	32
II.3.i. Guests	33



IRB STANDARD OPERATING PROCEDURES

II.3.j.	IRB Committees.....	33
II.3.k.	Initial Training, Continuing Education, and Professional Development of IRB Members.....	34
II.4.	Institutional Review Board Administrative Staff.....	35
II.4.a.	Resource Allocation.....	35
II.4.b.	Reporting Lines and Supervision	36
II.4.c.	IRB Staff Responsibilities.....	36
II.4.d.	Initial Training, Continuing Education, and Professional Development of IRB Staff.....	37
II.4.e.	Interactions with Affiliated IRBs.....	37
II.5.	Record Keeping and Required Documentation	38
II.5.a.	Record Retention.....	38
II.5.b.	Access to IRB Records.....	38
II.5.c.	IRB Records	39
II.5.d.	IRB Membership Roster.....	40
II.5.e.	Education and Training Records.....	40
II.5.f.	IRB Correspondence	41
II.5.g.	Electronic Research Protocol Tracking System.....	41
II.5.h.	IRB Minutes	42
II.5.i.	Creation, Review, Maintenance, Revision and Archive of BRANY IRB Standard Operating Procedures (SOPs)	43
II.5.j.	Quorum Requirements.....	44
II.5.k.	Voting	45
II.6.	Principal Investigator (PI) Responsibilities.....	45
II.6.a.	Investigator (and Key Personnel) Human Subject Protection Education Requirement.....	50
II.6.b.	Remedial or Additional Training	51
II.6.c.	Change of Principal Investigator	51
II.6.c.1.	Planned Changes of PI.....	51
II.6.c.2.	Unplanned Changes of PI.....	51
II.6.c.3.	Change of PI Submission Process	52
II.7.	Responsibilities of the Research Staff.....	53
II.8.	Sponsor Responsibilities	53
II.9.	On Site Quality Assurance Auditing and Compliance Reporting.....	57
II.9.a.	Organization and Responsibilities	57
II.9.a.1.	The QA Group.....	57



IRB STANDARD OPERATING PROCEDURES

II.9.b. Audits	57
II.9.b.1. Auditing Process	57
II.9.b.2. Selection of Trials to be Audited	58
II.9.b.3. Reports.....	60
II.9.c. Post Auditing Activities.....	60
II.10. Quality Improvement Activities to Monitor Institutional Review Board Functions and HRPP Effectiveness	60
II.10.a. Review of Standard Operating Procedures (SOPs)	61
II.10.b. Review of IRB Meeting Minutes	61
II.10.c. Review of IRB Member Files.....	61
II.10.d. Review of IRB Member Composition	61
II.10.e. Review of Protocol-Specific IRB Records	62
II.10.f. Institutional Review Board – Peer Review.....	62
II.10.g. Accreditation.....	62
II.10.h. Community Outreach.....	63
II.11. Responsibilities of the Institutional Official (IO).....	63
II.12. Reporting of Research Concerns	63
II.12.a. Complaints/Concerns from Research Subjects and/or Family Members of Subjects.....	64
II.12.b. Research Staff Complaints/Concerns	64
II.12.c. Complaints/Concerns From IRB Members.....	65
II.12.d. Complaints/Concerns From Investigators	65
II.12.e. Processing Complaints	65
III. THE SUBSTANCE OF IRB REVIEW.....	67
III.1. Actions Taken by the IRB.....	67
III.1.a. Appeal of IRB Decision.....	68
III.1.b. Types of IRB Review	69
III.1.b.1. Initial Review by the Convened IRB.....	69
III.1.b.2. Primary and Secondary Reviewer System.....	71
III.1.c. Continuing Review	72
III.1.c.1. Continuing Reviewer’s Responsibilities	73
III.1.c.2. Study Termination	76
III.1.c.3. Short Term Continuation and Reinstatement.....	76
III.1.c.4. Reinstatement of a Terminated or Lapsed Research Project.....	77
III.1.d. Expedited Review of Research	77



IRB STANDARD OPERATING PROCEDURES

III.1.d.1. Categories of new and continuing research that may be reviewed by the IRB through an Expedited Review Procedure.....	78
III.1.d.2. Documentation for Expedited Review	81
III.1.d.3. Expedited Review of Minor Changes in Previously Approved Research	82
III.1.d.4. Expedited Review of Additional Investigators for Previously Approved Studies	82
III.1.e. Modifications to Previously Approved Research	83
III.1.f. Amendments	84
III.1.f.1. Amendment Review	84
III.1.f.2. Amendment Approval/Rejection	85
III.1.g. Full Board Review (More Than Minor Modifications to Previously Approved Research).....	86
III.1.h. Administrative Reviews.....	87
III.1.i. Review of Reports of Unanticipated Problems Involving Risks to Subjects or Others.....	88
III.1.i.1. Processing reports of unanticipated problems involving risks to subjects or others.....	90
III.1.j. Serious Adverse Events (SAEs) (ON-SITE adverse events).....	93
III.1.j.1. Definitions of AE and SAE	93
III.1.j.2. Reporting Procedures for SAEs.....	94
III.1.j.3. External Adverse Events	96
III.1.j.4. Possible Actions of IRB after Review of SAEs.....	97
III.1.k. Deviations.....	98
III.1.k.1. Procedure for Reporting Protocol Deviations to BRANY IRB.....	99
III.1.k.2. Procedure for Requesting Approval of Protocol Exceptions from BRANY IRB	101
III.1.l. Reports of Non-Compliance.....	101
III.1.l.1. Investigation and Processing of Allegations of Non-compliance.	103
III.1.m. Suspension/Termination of IRB Approval.....	105
III.1.m.1. Suspension of IRB Approval.....	106
III.1.m.2. Termination of IRB Approval.....	107
III.1.n. Institutional Review Board Review and Approval Considerations.....	107
III.1.n.1. Levels of Risk.....	107
III.1.n.2. Risks minimized	109



IRB STANDARD OPERATING PROCEDURES

III.1.n.3. Risks Reasonable Relative to Anticipated Benefits and to the Importance of the Knowledge to be Gained	109
III.1.n.4. Equitable Selection of Subjects	110
III.1.n.5. Evaluation of Staff Available to Conduct Research	110
III.1.n.6. Review of Plans for Data and Safety Monitoring	111
III.1.n.7. Review of Interim Analysis Reports, Data Monitoring Committee (DMC), Data and Safety Monitoring Board (DSMB) Reports	111
III.1.n.8. Local Research Context	111
III.1.n.9. Privacy of Subjects and Confidentiality of Data.....	112
III.1.n.10. Research Using Data or Tissue Banks (also called Repositories)	114
III.1.n.11. Recruitment of Subjects	115
III.1.n.12. Guidelines for Pre-Screening Subjects for Recruitment	115
III.1.n.13. Telephone Screening	116
III.1.n.14. Pre-Screening Through Centralized Phone Banks	116
III.1.n.15. Retaining Information Obtained From Pre-Screening	117
III.1.n.16. HIPAA Waivers for Recruitment Purposes	117
III.1.n.17. Family Members.....	117
III.1.n.18. Physician-to-Physician Referrals	118
III.1.o. Reporting Procedures for Unanticipated Problems Involving Risks to Subjects or Others, Non-Compliance, or Suspension or Termination of IRB Approval.....	118
III.1.p. Reporting and Procedures for AAHRPP Accreditation	120
III.2. Advertising.....	121
III.2.a. Information Required on an Advertisement for Recruitment.....	121
III.2.b. Submission of Advertisements to the IRB	122
III.2.c. Listing of Clinical Trials on the Internet and/or Public Registries	122
III.3. Payment to Research Subjects.....	122
III.3.a. Justifying External Factors	123
III.3.b. Review of Compensation for Reasonableness.....	123
III.3.c. Compensation in Pediatric Research	123
III.4. Certificates of Confidentiality	123
III.5. Compliance with All Applicable State and Local Law	124
III.6. Emergency Use of a Test Article Without IRB Review	125
III.7. Emergency Use of a Test Article Without Informed Consent	126



IRB STANDARD OPERATING PROCEDURES

III.8. Exception From Informed Consent (EFIC) for Planned Emergency Research	127
III.8.a. Requirements	128
III.8.b. Implementation of IRB requirements in accordance with 21CFR50.24(a)(7)	132
III.8.c. References	135
III.9. Additional Committee Review for IRB Approved Projects	135
III.9.a. The New York Harbor Health Care System (VA Institutions)	135
III.9.b. The Health and Hospitals Cooperation (HHC) Public Hospitals	135
III.9.c. BioSafety Committee	135
III.9.d. NCI Designated Centers	135
III.9.e. GCRC	135
III.9.f. Radiation Safety	135
III.9.g. Pharmacy Committee	136
III.9.h. Cooperative Research Projects	136
III.9.i. Multi-Center Research	136
III.9.i.1. Designation of BRANY IRB	136
III.9.i.2. Responsibilities for a Lead Investigator in a Multi-Center Study	136
IV. INFORMED CONSENT	138
IV.1. Investigations Involving Human Subjects and Informed Consent	138
IV.1.a. Informed Consent	138
IV.1.b. IRB's Responsibilities	138
IV.1.c. Consent Monitoring	138
IV.1.d. Principal Investigator's Responsibilities	139
IV.1.d.1. Re-Consent	140
IV.1.d.1.1. Re-consent due to modifications	140
IV.1.e. General Issues in Informed Consent Documents and Process	140
IV.1.f. Consent Form Criteria	141
IV.1.g. Documentation of Informed Consent	143
IV.1.h. Waiver of Documentation of Consent	143
IV.1.i. Basic Elements of Informed Consent	144
IV.1.j. Additional Elements of Informed Consent	144
IV.2. Waiver or Alteration of Informed Consent Requirements	146
IV.2.a. Minimal Risk Research	146
IV.2.b. The FDA's Requirements for Waiver of Informed Consent	146



IRB STANDARD OPERATING PROCEDURES

IV.2.c. Waiver of Informed Consent for Department of Defense Supported Research.....	1467
IV.3. Criteria for Obtaining Informed Consent.....	147
IV.3.a. Categories of Investigational Research that are Exempt from Subject Consent.....	147
IV.3.b. Limited English Proficient Subjects	148
IV.3.c. When Investigator Anticipates a Limited English Proficient Population	149
IV.3.d. When Investigator Encounters a Non-English Speaking Subject Whose Primary Language Was Not Anticipated (e.g., rarely-encountered foreign languages) ..	149
IV.3.d.1. Ongoing Translation For All Limited English Proficient Subjects Enrolled in Research	150
IV.3.e. Illiterate Subjects	150
IV.3.f. Consent Issues for Phase I studies.....	150
IV.4. Health Insurance Portability and Accountability Act of 1996 (HIPAA)	150
V. SPECIAL CONSIDERATIONS IN IRB REVIEW	152
V.1. Potentially Vulnerable Subject Groups	152
V.1.a. Elements to Consider in Reviewing Research Involving Vulnerable Subjects ..	152
V.1.b. Research Involving Children – Special Considerations	153
V.1.b.1. Definition of Terms Relevant to This Area of Research.....	153
V.1.b.2. Degrees of Risk.....	154
V.1.b.3. Children Who Are Wards of the State or Other Agency, Institution or Entity	156
V.1.b.4. Justification of Exclusion of Children	157
V.1.b.5. Requirements for Permission by Parents or Guardians and for Assent by Children	157
V.1.b.6. Obtaining Assent	158
V.1.b.7. Waiver of Assent	160
V.1.b.8. Documentation of Assent.....	160
V.1.b.9. Proposed Reimbursement for Child Subjects	160
V.1.b.10.Emancipated Minors.....	160
V.1.c. Research Involving Pregnant Women, Fetuses and Neonates	161
V.1.c.1. Definition of Terms Relevant to This Area of Research.....	161
V.1.c.2. Research Involving Pregnant Women or Fetuses.....	161
V.1.c.3. Research Involving Neonates.....	163
V.1.c.3.1. Neonates of Uncertain Viability and Nonviable Neonates	163



IRB STANDARD OPERATING PROCEDURES

V.1.c.3.2. Neonates of Uncertain Viability.....	163
V.1.c.3.3. Nonviable Neonates	164
V.1.c.3.4. Viable neonates.....	164
V.1.c.4. Research Involving, After Delivery, the Placenta, the Dead Fetus or Fetal Material.....	165
V.1.c.4.1. Dead Fetus, Fetal Material or the Placenta.....	165
V.1.c.5. Obtaining Consent from Women in Labor.....	165
V.1.c.5.1. Obtaining Consent in Advance	165
V.1.c.5.2. Not Obtaining Consent in Advance.....	165
V.1.d. Prisoners	166
V.1.d.1. Subjects Who Become Prisoners After Enrollment in Research	169
V.1.e. Research Involving Psychiatric Populations.....	169
V.1.e.1. Definition of Terms Relevant to This Area of Research.....	169
V.1.e.2. Physician’s Responsibilities.....	171
V.1.e.3. Specially Trained Psychiatric In-Patients	171
V.1.f. Surrogate Consent with Subjects Incompetent or Unable to Give Consent or Emancipated Minors who are not Children.....	171
V.1.f.1. Individuals Who May Serve As Surrogates.....	171
V.1.f.2. Assessment of Capacity	172
V.1.f.3. Assessment of Clinical Suitability	173
V.1.f.4. Enrollment	173
V.1.f.5. Monitoring and Home Monitors.....	174
V.1.g. Use of Waiting Periods	174
V.1.h. Subject Advocate.....	174
V.1.i. Withdrawing Drugs from Subjects.....	174
V.1.i.1. Content of the Consent Form for Withdrawal From Therapeutic Medication.....	175
V.2. Requirements for HIV Testing/Consent Form.....	175
V.3. HIV Counseling	176
V.4. Release of HIV Information Form.....	176
V.5. Genetic Research and Tissue Banking	176
V.5.a. Definitions.....	177
V.5.b. Issues in Genetic Research	178
V.5.c. Disclosure of Results of Genetic Tests	178



IRB STANDARD OPERATING PROCEDURES

V.5.d. Family History Research.....	178
V.5.e. Types of Studies.....	179
V.5.f. Types of Samples.....	179
V.5.g. Research Using Properly Collected Samples.....	179
V.5.h. Retrospective Studies of Existing Samples.....	180
VI. CONFLICTS OF INTEREST	181
VI.1. Managing Conflicts of Interest.....	181
VI.1.a. Definitions.....	181
VI.1.b. Reporting of Financial Interests	183
VI.1.c. IRB Meetings	185
VI.1.d. Review of Conflicts	185
VI.1.e. IRB Chairpersons and Members/Other Conflicts.....	186
VI.1.f. Institutional Officials.....	187
VI.1.g. The Organization	187
VI.1.h. Organization Officials.....	187
VI.1.i. IRB Conflict of Interest in Research Policy.....	188
VI.1.j. Nature of Disclosure to Subjects.....	188
VI.1.k. Additional Measures	189
VI.1.l. Required Education	190
VI.1.m. Monitoring, Enforcement, and Reporting.....	190
VI.1.n. Providing for Protection of Privacy of Individual's Financial Information Except as Needed to Manage Conflict of Interest.....	190
VI.1.o. Violations of the Policy.....	190
VII. THE HIPAA PRIVACY RULE	192
VII.1. HIPAA Privacy Rule and the "Common Rule"	192
VII.2. The Role of the BRANY IRB	192
VII.2.a. Definitions.....	192
VII.3. Access to Information	193
VII.3.a. Reviews Preparatory to Research.....	193
VII.3.b. Use and Disclosure of Information	194
VII.3.c. Use and Disclosure With Authorization of the Subject	194
VII.3.d. Authorization.....	194
VII.3.d.1. Core Elements of an Authorization	194
VII.3.d.2. Required Statements in an Authorization.....	195
VII.3.e. Waiver of Authorization.....	196



IRB STANDARD OPERATING PROCEDURES

VII.3.f. De-Identification (Safe Harbor)	196
VII.3.g. Statistical Method of De-identification	198
VII.3.h. Limited Data Set	198
VII.3.i. Research on Decedents' Information	199
VII.4. Safeguarding Confidentiality	199
VIII. INVESTIGATIONAL DRUGS, DEVICES, AND BIOLOGICS.....	201
VIII.1. Investigational Drugs, Devices, and Biologics	201
VIII.1.a. FDA Requirements in Relation to 45 CFR 46	201
VIII.1.b. Research Involving Investigational FDA Regulated Test Articles.....	202
VIII.2. Protocols Involving the Investigational Use of Marketed Products	2043
VIII.3. Investigators also Serving as Sponsors	204
VIII.4. Gene Transfer Research.....	205
VIII.5. IRB Review of Medical Devices.....	206
VIII.5.a. Definitions and IRB Determinations.....	206
VIII.5.a.1. Significant Risk Device	206
VIII.5.a.2. Non-Significant Risk Device.....	206
VIII.5.a.3. IRB's Role in Classification of Devices.....	206
VIII.5.a.4. IRB Determinations.....	207
VIII.5.a.4.1. Study Involves a SR Device	2079
VIII.5.a.4.2. Study Involves a NSR Device.....	209
VIII.5.a.4.3. Study Involves Device Equivalent to Marketed Device	209
APPENDIX	210



IRB STANDARD OPERATING PROCEDURES

I. Protection of Human Subjects

I.1. Ethical Principles that Govern Research

Many of the basic ethical principles that guide research that involves human subjects are described in The Nuremberg Code, The Declaration of Helsinki and The Belmont Report. Copies of these documents are attached as [Appendix 1](#), [Appendix 2](#), and [Appendix 3](#).

I.1.a. The Nuremberg Code

The modern history of human subject protections began with the discovery of numerous atrocities that were committed during World War II by Nazi physicians who conducted war-related human research experiments. The Nuremberg Military Tribunal published *The Nuremberg Code* in 1949. This code delineates the ten principles that were developed for judging the “research” practices of the Nazi doctors. *The Nuremberg Code* is significant because it addressed the need to require the voluntary consent of a human subject and the requirement that any individual who initiates, directs, or engages in an experiment must bear personal responsibility for ensuring the quality of consent.

I.1.b. The Declaration of Helsinki:

In 1964 the World Medical Association published the Declaration of Helsinki: Recommendations Guiding Medical Doctors in Biomedical Research Involving Human Subjects. This document expressed similar principles to The Nuremberg Code and expanded upon them. Importantly, The Declaration of Helsinki additionally called for prior approval and ongoing monitoring of research by independent ethical review committees. This document was revised in 1975, 1983, 1989, 1996, 2000, 2002 and 2004.

I.1.c. The Belmont Report

Based upon revelations in the early 1970s about the 40 year USPHS study of untreated syphilis in the Negro male at Tuskegee and the recognition of other ethically questionable research in this country, federal legislation in 1974 called for the development of regulations to protect human subjects and for a National Commission to examine ethical issues related to human subject research. The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research was established and in 1979 the Commission published *The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subject Research*. This document defined the ethical principles and guidelines for the protection of human subjects and, most significantly, stated the following three basic ethical principles that continue to represent the gold standard for human subject research:

- (a) Respect for persons (which is applied by obtaining informed consent, by consideration of privacy and confidentiality and by providing additional protections for vulnerable populations);



IRB STANDARD OPERATING PROCEDURES

- (b) Beneficence: maximizing benefits while minimizing risks, and consideration of both; and
- (c) Justice: equitable selection of subjects.

An additional important section of *The Belmont Report* was a description of the boundaries between research and clinical practice and, therefore, the following is quoted directly from the Report:

“It is important to distinguish between biomedical and behavioral research, on the one hand, and the practice of accepted therapy on the other, in order to know what activities ought to undergo review for the protection of human subjects of research. The distinction between research and practice is blurred partly because both often occur together (as in research designed to evaluate a therapy) and partly because notable departures from standard practice are often called “experimental” when the terms “experimental” and “research “ are not carefully defined.

For the most part, the term “practice” refers to interventions that are designed solely to enhance the well being of an individual patient or client and that have a reasonable expectation of success. The purpose of medical or behavioral practice is to provide diagnosis, preventive treatment or therapy to particular individuals. By contrast, the term “research” designates an activity designed to test a hypothesis, permit conclusions to be drawn, and thereby to develop or contribute to generalizable knowledge (expressed, for example, in theories, principles, and statements of relationships). Research is usually described in a formal protocol that sets forth an objective and a set of procedures designed to reach that objective.

When a clinician departs in a significant way from standard or accepted practice, the innovation does not, in and of itself, constitute research. The fact that a procedure is “experimental” in the sense of new, untested or different does not automatically place it in the category of research. Radically new procedures of this description should, however, be made the object of formal research at an early stage in order to determine whether they are safe and effective. Thus, it is the responsibility of medical practice committees, for example, to insist that a major innovation be incorporated into a formal research project.

Research and practice may be carried on together when research is designed to evaluate the safety and efficacy of a therapy. This need not cause any confusion regarding whether or not the activity requires review; the general rule is that if there is any element of research activity, that activity should undergo review for the protection of human subjects.”

I.2. Mandate to Protect Human Subjects

All research reviewed by the Biomedical Research Alliance of New York Institutional Review Board must be conducted in an ethical manner: in accordance with *The Nuremberg Code*, *The Declaration of Helsinki* and *The Belmont Report*. In addition, all research reviewed by



IRB STANDARD OPERATING PROCEDURES

BRANY IRB must be in compliance with Federal regulation, FDA's Good Clinical Practice (GCP) guidelines, applicable state and local regulation, BRANY policies and the BRANY IRB's written Assurance to the Department of Health and Human Services (DHHS) in the form of a Federal Wide Assurance (FWA). Such Assurance shall be reviewed and updated as necessary. On an ongoing basis, BRANY IRB will also refer to and incorporate into its policies and practices applicable guidance and determinations issued by regulatory agencies (e.g., FDA and OHRP).

BRANY's Human Research Protection Program (HRPP) exists to protect the rights and welfare of subjects who participate in research programs facilitated by the Biomedical Research Alliance of New York. The HRPP must ensure that research involving human subjects is conducted in accordance with federal, state, institutional requirements and BRANY policies. Additionally, the HRPP oversees the review and conduct of research via the BRANY Institutional Review Board. The IRB is an integral part of the HRPP.

BRANY allocates sufficient resources to support the BRANY's HRPP and the BRANY IRB, including adequate meeting and office space, and staff for conducting IRB business. Office equipment and supplies, including technical support, file cabinets, computers, internet access, and copy machines will be made available to the HRPP and BRANY IRB staff. The resources provided for the HRPP are reviewed by the BRANY Board of Directors and BRANY Senior Management during the annual budget review process.

The HRPP Committee meets quarterly to review resources needed for the HRPP, review projects undertaken by the HRPP, evaluate community outreach activities, evaluate quality improvement activities and review issues that have evolved. Review of resources needed, includes but is not limited to: space, personnel, HRPP education program, legal counsel, conflict of interest, quality improvement plan, and community outreach.

The HRPP Committee with representatives from the following BRANY departments: IRB, Grants and Contracts, and Quality Assurance will meet quarterly, or at such times as the committee may otherwise direct. The Institutional Official will chair such meetings. Minutes will be recorded. Additional members may be added at the discretion of the Committee. The Committee is responsible for oversight of BRANY's policies regarding Human Research Protections.

I.2.a.Functions of the HRPP

To accomplish its goals, functions of the HRPP will be performed by various components of the BRANY organization in addition to the BRANY IRB.

I.2.a.1. Quality Assurance

In addition to the IRB's function in protecting human subjects in accordance with applicable regulations, the Quality Assurance department is responsible for auditing trials to ensure compliance with applicable regulations, BRANY policy and IRB requirements, in addition to supporting compliance with FDA's GCP guidelines. Quality Assurance staff provides detailed audit reports and attends IRB meetings to apprise the IRB of audit results. Auditing policies and procedures are maintained separately by the BRANY QA Division. Section II.9 and II.10 of this manual describe



IRB STANDARD OPERATING PROCEDURES

IRB policy and procedures relating to the processing of QA reports. The QA SOPs also sets forth the manner in which studies shall be selected for auditing, but the HRPP may direct an audit at its discretion notwithstanding any other process for selection of audited sites.

I.2.a.2. Vetting Investigators

BRANY conducts an in depth interview of the prospective investigator and their staff. This process includes the completion of an Investigator Database Information Form (See [Appendix 35](#).) that details past experience, past inspections, GCP training, and licensure.

An Internet search is also conducted to check licensure and disciplinary actions of the potential investigator. For example:

- (a) www.fda.gov/foi/nidpoe/default.html
- (b) <http://www.fda.gov/foi/warning.htm>
- (c) http://www.fda.gov/ora/compliance_ref/debar/default.htm
- (d) http://www.fda.gov/ora/compliance_ref/bimo/asurlist.htm
- (e) http://www.fda.gov/ora/compliance_ref/bimo/disqlist.htm
- (f) http://www.fda.gov/ora/compliance_ref/bimo/restlist.htm

When applicable, representatives of the Investigator's Institution are consulted for additional information about Investigators past performance.

I.2.a.3. Grants and Contracts Department

As part of the contract negotiation process, the Grants and Contracts department is responsible for ensuring that suitable provisions for the protection of subject privacy and safety are included in the Clinical Trial Agreement between the organization and the Study Sponsor and/or CRO. In that effort, Sponsors are asked to warrant that (i) any investigational materials have been designed, developed and produced in accordance with recognized industry and other regulatory standards; (ii) Sponsor has used its best efforts to obtain and provide all available information on the Safety and efficacy of the Product; and (iii) Sponsor has an effective investigational new drug application (IND) or investigational device exemption (IDE) on file with the U.S. Food and Drug Administration (FDA). The clinical trial contracts require Sponsors to report to the Institution findings detected during the study that could affect the safety of participants or their willingness to continue participation, influence the conduct of the study, or alter the IRB's approval to continue the study. Further, if participant safety or medical care is directly affected by study results, Sponsor shall ensure that those results are communicated to research participants. Sponsor shall



IRB STANDARD OPERATING PROCEDURES

communicate findings to the institution/investigator, who will then inform the IRB prior to communicating the findings to the research participants.

For device trials, the sponsor will be asked to provide documentation in support of the institution's billing department's compliance with section 731(b) of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (MMA) regarding Coverage of Routine Costs associated with Certain Clinical Trials of Category A Devices.

Other provisions and warranties obtained from the Sponsors by the Grants and Contracts department include: the ability for the investigator to deviate from the protocol and/or terminate the study for subject health and safety without penalty; subject injury remediation and compensation; insurance requirements; limitations on the use of patient health information and adherence to federal and state laws and regulations related to such information, including HIPAA; and registration of studies in compliance with the requirements of the International Committee of Medical Journal Editors. Also, Sponsors must agree to allow publication of study results without editorial control except for the timing of publication and removal of confidential information.

Additionally, the staff in the Grants and Contracts department will ensure consistency between the terms of the clinical trial agreement and the consent document (for example, Subject Injury/Compensation for Injury text).

I.2.a.4. Finance

The organization's Finance Department is responsible for the IRB's budget process. At least annually, the organization's CFO meets with Department Directors/Managers, including the Director of the IRB, to prepare a departmental budget. Together they analyze the prior year's budget, assess the organization's assumptions for growth, and review various financial reports such as balance sheets, profit and loss statements as well as other key performance indicators. Several factors are taken into account when planning the departmental budget including staffing needs, equipment including phones and computers, space, and supplies. This exercise ensures that the proper resources are allocated to ensure that the Human Research Protection Program and the IRB can carry out their functions effectively.

I.2.a.5. BRANY Institute for Research Education

BRANY Institute for Research Education offers several educational programs to aid research professionals in the clinical field by promoting Good Clinical Practice. All BRANY staff members are required to complete modules 1-3 of the Fundamentals of Clinical Research Course, which focus on significant events in human research, study designs and clinical trial startup. For information on educational program offerings, please refer to the BRANY website at www.brany.com.



IRB STANDARD OPERATING PROCEDURES

II. Institutional Review Board Administration

II.1. Purpose of the IRB

The mission of the BRANY IRB is to protect the rights and ensure the welfare of all human research subjects. In taking on this responsibility, the BRANY IRB ensures that human subject research is conducted ethically and in compliance with applicable Federal, State, local and institutional requirements by performing prospective and continuing review of all human subject research conducted under its auspices. The BRANY IRB has provided written assurance to the Department of Health and Human Services in the form of its Federal Wide Assurance (FWA # 00000337). Such assurance requires the BRANY IRB to comply with the requirements of 45 CFR46. BRANY's FWA will be updated as necessary, but at least every 36 months (3 years), even if no changes have occurred, in order to maintain an active FWA, and to avoid restriction, suspension, or termination of the BRANY's FWA for the protection of human subjects.

The BRANY IRB is a division of the Biomedical Research Alliance of New York LLC (BRANY), an organization founded by the following institutions: Montefiore Medical Center, Mount Sinai School of Medicine, NYU School of Medicine, North Shore – Long Island Jewish Health System, and St. Vincents Catholic Medical Centers. The BRANY IRB has been appointed by its owner institutions to review and monitor research involving human subjects to ensure that the rights and welfare of those who participate as subjects in research are protected. The Management Committee (Board of Directors) of BRANY has appointed an Institutional Official (IO) with the authority to oversee BRANY's Human Research Protection Program, including the BRANY IRB and clinical trials under its purview, and to effect changes and take action(s) as necessary to ensure protection of human subjects. The IO reports to the Management Committee. The Management Committee is composed of the Deans and/or CEOs of the owner institutions. The BRANY IRB may also function as a Central IRB for multi-center clinical trials. In accordance with Federal regulations (45 CFR 46.109, and 21 CFR 56.109) the IRB has the authority to approve, require modification in (to secure approval) or disapprove research involving human subjects. The IRB has the authority to suspend or terminate approval of research not being conducted in accordance with the IRB's requirements or that has been associated with unexpected serious harm to subjects. The IRB has the authority to observe or have a third party observe the consent process and the conduct of the research. The charge to the IRB is as follows:

- (a) To hold regularly scheduled meetings in order to review all research proposals involving human subjects.
- (b) To approve, require modification in or disapprove research activities that involve human subjects.
- (c) To ensure that information given to subjects as part of informed consent is in accord with the guidelines of the Department of Health and Human Services (DHHS).
- (d) To ensure that risks to research subjects are minimized, that any risks are reasonable in relation to anticipated benefits, and that selection of subjects is



IRB STANDARD OPERATING PROCEDURES

equitable, and that informed consent will be obtained and documented (where applicable).

- (e) To notify investigators and the institution, in writing, of its decision to approve or disapprove proposed research, and if disapproved, to suggest modifications that are required to secure approval.
- (f) To conduct continuing review, at least annually, of research involving human subjects.
- (g) To certify to the Department of Health and Human Services that an application has been reviewed and approved by the IRB.
- (h) To report to the appropriate institutional officials and the Office for Human Research Protections, Department of Health and Human Services, any serious or continuing non-compliance by investigators with the requirements and determinations of the IRB.
- (i) To periodically report on the activities of this committee to the BRANY Board of Directors.
- (j) To implement policies and procedures as needed to ensure the proper protection of human subjects.

No individual or group of individuals may inappropriately try to influence the deliberations and decisions of the BRANY IRB. Any IRB member may report any attempt to influence the decision of the BRANY IRB to the Institutional Official or the Director of the BRANY IRB. The IO, the Director and/or the BRANY Quality Assurance department will investigate such allegations. The results of the investigation will be documented. A response to the allegations will be prepared along with a corrective action plan, if needed, to ensure that there is no undue influence on the IRB members or on the committee's actions and determinations.

If the BRANY IRB does not approve a research project, no BRANY Official, or Officials (Institutional Official or Institution Liaison) of the organization where the research is taking place may override the BRANY IRB's decision. Research that is approved by BRANY IRB may be subject to further approval or disapproval by the local Institutional Official (if one exists) from the organization where the research is taking place and the BRANY Institutional Official.

The BRANY IRB is able to review research for institutions/investigators that have no requirement to use a local IRB. Local IRB's may also chose to have the BRANY IRB review and oversee research by designating the BRANY IRB as an IRB for the institution. Institutions with a Federalwide Assurance (FWA) must add the BRANY IRB as one of the IRBs of record. Institutions can decide on a study-by-study basis to designate the BRANY IRB by implementing a written agreement.

Research activities should not commence at any organization until IRB approval is received and any other approvals that may be required are in place.



IRB STANDARD OPERATING PROCEDURES

II.2. Definition and Scope

II.2.a. Definition of Terms

(Additional terms are defined in the glossary attached as [Appendix 4](#))

Human Subjects Research Subject to FDA Regulation:

Under FDA regulations, individuals are considered “**subjects**” when they become a participant in research, either as a recipient of the test article or as a control (21 CFR 50.3(g), 21 CFR 56.103(e), 21 CFR 312.3(b)). If the research involves a medical device, individuals are considered “subjects” when they participate in an investigation, either as an individual on whom or on whose specimen an investigational device is used or as a control (21 CFR 812.3(p)).

Under FDA regulations “**research**” means an activity involves an FDA regulated test article (use of a drug, other than the use of a marketed drug in the course of medical practice). The drug is either not approved by the FDA for marketing or it is not used in the course of medical practice. (For this policy “drug” means (i) an article recognized in the official United States Pharmacopoeia, official Homoeopathic Pharmacopoeia of the United States, or official National Formulary, or any supplement to any of them, (ii) an article intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in humans or other animals, (iii) an article (other than food) intended to affect the structure or any function of the body of humans or other animals, or (iv) an article intended for use as a component of any article specified in the above items.)

Activities are human research subject to FDA regulations when they meet the FDA definition of “research” (21 CFR 50.3(c), 21 CFR 56.103(c), 21 CFR 312.3(b), or 21 CFR 812.3(h)) and involve a “subject” as defined in FDA regulations (21 CFR 50.3(g), 21 CFR 56.103(e), 21 CFR 312.3(b), or 21 CFR 812.3(p))

Under FDA regulations activities are “research” when they involve:

- (a) Use of a drug other than the use of an approved drug in the course of medical practice (21 CFR 312.3(b))
- (b) Use of a medical device other than the use of an approved medical device in the course of medical practice (Food, Drug and Cosmetic Act §530(g)(3)(a)(i))
- (c) Gathering data that will be submitted to or held for inspection by FDA in support of a FDA marketing permit for a food, including a dietary supplement that bears a nutrient content claim or a health claim, an infant formula, a food or color additive, a drug for human use, a medical device for human use, a biological product for human use, or an electronic product. (21 CFR 50.1(a), or 21 CFR 56.101(a))

In the above criteria “approved” means “approved by the FDA for marketing.”



IRB STANDARD OPERATING PROCEDURES

Under FDA regulations, individuals are considered “subjects” when they become a participant in research, either as a recipient of the test article or as a control (21 CFR 50.3(g), 21 CFR 56.103(e), 21 CFR 312.3(b)). If the research involves a medical device, individuals are considered “subjects” when they participate in an investigation, either as an individual on whom or on whose specimen an investigational device is used or as a control (21 CFR 812.3(p)).

Human Subjects Research Subject to DHHS Regulation or other Common Rule Regulations

Activities are human subject research subject to DHHS regulations when they meet the DHHS definition of “research” (45 CFR 46.102(d)) and involve a “subject” as defined in DHHS regulations (45 CFR 46.102(f)).

“Human Subject” Under the DHHS regulations **“human subject”** means a living individual about whom an investigator (whether professional or student) conducting research obtains (1) data through intervention or interaction with the individual (e.g. Physical procedures performed on those individuals, Manipulation of those individuals, Manipulation of those individuals’ environments, Communication with those individuals, Interpersonal contact with those individuals) or (2) identifiable private information (e.g. the information is about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, or the individual has provided the information for specific purposes and can reasonably expect that the information will not be made public (for example, a medical record)).

“Human Subject Research” under the DHHS regulations means **an activity that is a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge.** (If the activity is NOT a systematic investigation designed to develop or contribute to generalizable knowledge, the activity does not meet the definition of human subject research under the DHHS regulations. However, it may meet the definition of human subject research under the FDA definition.)

Under DHHS regulations activities are **“research”** when they are a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge (45 CFR 46.102(d)).

“Generalizable knowledge” means that (1) conclusions are drawn from particular instances, and (2) the information from the investigation is to be disseminated. Activities that meet this definition may be funded or unfunded, or may be conducted as a component of another program not usually considered research. For example, demonstration and service programs may include evaluation components, which constitute research activities under this definition.



IRB STANDARD OPERATING PROCEDURES

“Systematic investigation” means an activity that involves a prospective research plan that incorporates data collection, either quantitative or qualitative, and data analysis to answer a research question.

Under DHHS regulations **“subjects”** means a living individual about whom an investigator (whether professional or student) conducting research obtains (1) data through intervention or interaction with the individual, or (2) identifiable private information (45 CFR 46.102(f)).

Intervention includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject’s environment that are performed for research purposes (45 CFR 46.102(f)).

Interaction includes communication or interpersonal contact between investigator and subject (45 CFR 46.102(f)).

“Private information” includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record). Private information must be individually identifiable (i.e. the identity of the subject is or may be readily ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects (45 CFR 46.102(f)).

“Minimal Risk” means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

For research subject to the requirements of the **Department of Defense**, the definition of the minimal risk based on the phrase “ordinarily encountered in daily life or during the performance of routine physical or physiological examinations or tests” must not be interpreted to include the inherent risks certain categories of human subjects face in their everyday life. For example, the risks imposed in research involving human subjects focused on a special population should not be evaluated against the inherent risks encountered in their work environment (e.g., emergency responder, pilot, soldier in a combat zone) or having a medical condition (e.g., frequent medical tests or constant pain).

“Legally Authorized Representative” means an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject’s participation in the procedure(s) involved in the research.

“Research” see above.

“Clinical Investigation” means any experiment that involves a test article and one or more human subjects and that either is subject to requirement for prior submission to the Food and Drug Administration, or need not meet the



IRB STANDARD OPERATING PROCEDURES

requirements for prior submission to the FDA but the results of which are intended to be submitted later to, or held for inspection by, the FDA as part of an application for a research or marketing permit.

“**Test Article**” means any drug for human use, a biological product for human use, medical device for human use, electronic product, or any other article subject to regulation by the FDA.

“**Behavioral Research**” means the scientific investigation or inquiry into the actions or reactions of persons under specific circumstances or to specific relationships.

“**Experimental Subject**” is a term that relates specifically to research that is subject to the Department of Defense requirements. Experimental subjects are a subset of human subjects, and in the context of **Department of Defense** supported research, an **experimental subject** is the recipient of an intervention or interaction for research purposes, when the primary purpose of the intervention or interaction is obtaining data regarding the effect of the intervention or interaction.

“**Research involving a human being as an experimental subject**” means an activity, for research purposes, where there is an intervention or interaction with a living individual for the primary purpose of obtaining data regarding the effect of the intervention or interaction. For research that is subject to **Department of Defense** requirements, consideration must be given to whether the activity meets this definition. Research involving a human being as an experimental subject is a subset of research involving human subjects (see Department of Defense Instruction 3216.02 section E2.1.3).

Research involving a human being as an experimental subject that also proposes to request a waiver of the requirement to obtain consent is subject to addition approval by the Department of Defense component involved in the research (see Department of Defense Instruction 3216.02 section 4.2.2).

II.2.b. BRANY IRB Definition of Human Subject Research

An activity is human research if it is any one of the following:

- (1) Human subjects research subject to FDA regulation;
- (2) Human subjects research subject to DHHS regulations;
- (3) Human subjects research subject to other applicable law; or
- (4) Human subjects research subject to local policies and procedures.

Activities that meet this definition of research should be reviewed by an IRB. The Investigator is responsible for making the determination of what constitutes research with human subjects. If there is a question, Investigators may choose to submit a project for an official IRB determination on whether an activity constitutes human subject



IRB STANDARD OPERATING PROCEDURES

research using the “Checklist – Human Research” ([Appendix 9](#)), The submission must include the form, as well as a description of the proposed activity and any additional supporting information to assist in making the determination. The IRB Chair or the IRB Director will review the submission to confirm that the determinations made by the Investigator are in accordance with the definitions of human subject research described above, and the IRB’s determination will be communicated to the Investigator in writing. For example, quality improvement, public health, program evaluation, innovative medical care and classroom exercises may represent activities that involve human research. Investigators may refer to OHRP’s Human Subject Regulations Decision Charts for additional guidance for categorizing proposed research (available online at:<http://www.hhs.gov/ohrp/policy/checklists/decisioncharts.html>). NOTE: Activities that are not human subject research under the DHHS regulations as described at the above URL might be considered human subject research under the FDA regulations.

Activities and Entities Covered by These Procedures

An institution/investigator is considered to be engaged in human subjects research when its employees or agents:

- (1) obtain data about living individuals for research purposes through intervention or interaction with them, or
- (2) obtain individually identifiable private information for research purposes (45 CFR 46.102(d),(f))
<http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#46.102>

Employees and agents, including students, are individuals performing institutionally designated activities and acting on behalf of the institution or exercising institutional authority or responsibility.

An institution is automatically considered to be engaged in human subjects research whenever it receives a direct DHHS award to support such research, even if agents or employees of another institution will perform all of the human subjects activities. For example, when the direct awardee institution subcontracts all human subjects activities to another institution the direct awardee institution would still be considered engaged in the research. In such cases, the awardee institution bears the ultimate responsibility for protecting subjects involved in the research conducted under the award. Institutions will also be considered engaged in human subjects research when its employees or agents intervene for research purposes with any human subjects of the research by performing invasive or noninvasive procedures, by manipulating the research environment, and/or by obtaining for research purposes identifiable private information or identifiable biological specimens from any source for the research.

In general, simply informing potential subjects about a research study is not considered engagement in research. Also, providing written information about a research study, including how to contact the investigators for information and enrollment, and seeking and obtaining prospective subjects’ permission for investigators to contact them are not considered engagement in research. However, seeking or obtaining informed consent from a research participant is considered engagement in research. Additionally,



IRB STANDARD OPERATING PROCEDURES

institutions that permit use of their facilities for intervention or interaction with subjects by investigators from another institution are generally not considered engaged in the research.

Access <http://www.hhs.gov/ohrp/policy/engage08.html> for other specific examples of engagement in human subject research.

The BRANY IRB is located in New York. New York State law does not distinguish between living and deceased individuals in its definition of human subject. The BRANY IRB will seek guidance from legal counsel regarding individual state requirements when reviewing research taking place in states other than New York. In addition to compliance with Federal regulations governing human subject research, the BRANY IRB requires investigators and institutions to comply with State and local laws that may provide additional protections for human subjects. This policy will not supersede State or local laws that are applicable to human subject protections.

II.2.c. Exemptions

The BRANY IRB will consider research that appears to qualify for exemption from IRB review under the federal regulations for researchers not obligated to seek exemptions from their institutional or other IRB with appropriate jurisdiction. Investigators cannot independently classify research as exempt from IRB review. The BRANY IRB will make the final determination of exempt status.

It is important to note that exemption from IRB review **does not** include exemption from HIPAA requirements when the research involves a covered entity's protected health information. Appropriate steps must be taken to ensure research that is determined to be exempt from IRB review is conducted in accordance with HIPAA requirements.

BRANY IRB will make a determination of exempt status when, in accordance with federal regulations at 45 CFR 46.101(b), 45 CFR 46.401(b), and 21 CFR 56.104 (d), the research falls into one of the following categories:

- (1) Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as (i) research on regular and special education instructional strategies, or (ii) research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.
- (2) Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, unless all the following are true:
 - (i) information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and
 - (ii) any disclosure of the human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability or



IRB STANDARD OPERATING PROCEDURES

be damaging to the subjects' financial standing, employability, or reputation. (See exception to this category at "Important Note Regarding Applicability of Categories of Exempt Research" below.)

- (3) Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior that is not exempt under paragraph (b)(2) of this section, if:
 - (i) the human subjects are elected or appointed public officials or candidates for public office; or
 - (ii) federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.

- (4) Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects. NOTE: The data must exist at the time the research was proposed.

- (5) Research and demonstration projects which are conducted by or subject to the approval of Department or Agency heads, and which are designed to study, evaluate, or otherwise examine:
 - (i) Public benefit or service programs;
 - (a) the program under study must deliver a public benefit (e.g., financial or medical benefits as provided under the Social Security Act) or service (e.g., social, supportive, or nutrition services as provided under the Older Americans Act);
 - (b) the research or demonstration project must be conducted pursuant to specific federal statutory authority;
 - (c) there must be no statutory requirement that the project be reviewed by an Institutional Review Board (IRB); and
 - (d) the project must not involve significant physical invasions or intrusions upon the privacy of participants (see 12/97 OPRR Guidance at <http://www.hhs.gov/ohrp/policy/exmpt-pb.html>). This exemption is for projects conducted by or subject to approval of Federal agencies, and is most appropriately invoked with authorization or concurrence by the funding agency.
 - (ii) Procedures for obtaining benefits or services under those programs;
 - (iii) Possible changes in or alternatives to those programs or procedures; or
 - (iv) Possible changes in methods or levels of payment for benefits or services under those programs.



IRB STANDARD OPERATING PROCEDURES

- (6) Taste and food quality evaluation and consumer acceptance studies, (i) if wholesome foods without additives are consumed or (ii) if a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.
- (7) Any investigation which commenced before July 27, 1981 and was subject to requirements for IRB review under FDA regulations before that date, provided that the investigation remains subject to review of an IRB which meets the FDA requirements in effect before July 27, 1981.
- (8) Any investigation commenced before July 27, 1981 and was not otherwise subject to requirements for IRB review under Food and Drug Administration regulations before that date.
- (9) Emergency use of a test article, provided that such emergency use is reported to the IRB within 5 working days. Any subsequent use of the test article at the institution is subject to IRB review.

Important Note Regarding Applicability of Categories of Exempt Research

- BRANY IRB will not make determinations of exempt status for research involving prisoners.
- The exemption for research involving survey or interview procedures or observation of public behavior does not apply to research involving children, EXCEPT for research involving observations of public behavior when the investigator(s) do not participate in the activities being observed.
- For categories #1-#5 above, exempt status does not apply when the research is FDA-regulated.
- For categories #7-9 above, exempt status does not apply when the research is DHHS-regulated

When considering requests for exemption, the IRB may also impose additional requirements as needed to assure the protection of the rights and welfare of research subjects. In the interest of human subject protection, the IRB may deem that the project requires IRB review. For example, the IRB may require review of research involving human tissue/specimens (including autopsy material) and the review of all patient records for research purposes even though they may not constitute the definition of human subjects.



IRB STANDARD OPERATING PROCEDURES

II.2.c.1. Procedures

If an investigator wishes to apply for exempt status from the BRANY IRB, he or she must submit a completed [Application for Determination of Exempt Status \(Appendix 27\)](#), unless reporting the emergency use of a test article, which must be submitted via the [“Emergency Use Notification Form” \(Appendix 39\)](#).

The application will be forwarded promptly to the BRANY IRB Chairperson for review. The Chair will evaluate whether the research conforms to one of the categories above, as well as consider the ethical principles of respect for persons, beneficence and autonomy. To ensure that subjects are protected for exempt research, the Chair will also consider whether the research presents no more than minimal risk to participants, whether informed consent will be sought from subjects, whether selection of subjects is equitable, and whether there are adequate provisions to maintain the confidentiality of data and to protect subject privacy. If necessary, the Chair will seek expert opinion regarding the proposed research and conformity to the applicable regulations. The following determinations may result:

If the project qualifies for exempt status, the researcher will promptly receive written notification indicating the exemption and the specific category under which the research qualifies as exempt, as well as any additional requirements that may have been imposed by the Chairperson to protect the rights and welfare of research subjects.

If the project does not qualify for exempt status, the researcher will receive a written notification requesting the project be submitted to the IRB for review with a completed [Research Application \(Appendix 11\)](#). See section III.1.d. for information pertaining to submission of projects for expedited and full board review.

HIPAA considerations must be taken into account for all research, including that which may be classified as exempt from IRB review. Researchers who receive an exempt status determination, but whose research involves protected health information must still submit a HIPAA authorization form (or a request for waiver of HIPAA authorization), or, if applicable, appropriate forms for research using a limited data set (data use agreement) (See [Appendix 11 – addendum to the Research Application](#))

While research that has been determined to be exempt from IRB review is not subject to continuing review, the Principal Investigator must notify IRB of any changes in the protocol (e.g., study design, procedures, etc.), as such changes may call for IRB review. Additionally any complaints or concerns that arise from the research should also be reported to the IRB (see Section II.12.).

Exemption decisions will be reported to the committee via the agendas and minutes of subsequent meetings of the convened IRB.



IRB STANDARD OPERATING PROCEDURES

II.3. Institutional Review Board Membership

II.3.a. IRB Membership Requirements

The BRANY IRB must satisfy the following federal requirements (45 CFR 46. 107, 38 CFR 16. 107 and 21 CFR 56. 107):

- (1) The IRB will have at least five members;
- (2) IRB members will possess varying professional backgrounds to promote complete and adequate review of research activities commonly conducted by BRANY affiliates;
- (3) IRB members will be sufficiently diverse relative to race, gender, cultural background, and sensitivity to community attitudes so as to promote respect for the IRB's advice and counsel in safeguarding the rights and welfare of human subjects through its diversity, experience, and expertise;
- (4) IRB members will include persons able to ascertain the acceptability of proposed research in terms of institutional commitments, regulations, applicable law, and standards of professional conduct and practice;
- (5) The IRB will not consist entirely of members of one profession;
- (6) The IRB will include at least one member whose primary concerns are in scientific areas;
- (7) The IRB will have at least one member whose primary concerns are in non-scientific areas. Non-scientist members represent the general perspective of participants. This person must always be present to have a quorum; and
- (8) The IRB will include at least one member who is not otherwise affiliated with BRANY and who is not part of the immediate family of a person who is affiliated with BRANY.
- (9) For **classified research** subject to the requirements of the **Department of Defense**, at least one non-affiliated member shall be a non-Federal employee.
 - The IRB shall determine whether the potential human subjects need access to classified information to make a valid, informed consent decision.

II.3.b. Selection of IRB Members

The IRB Chairperson(s), subsequent to review of the candidate's credentials, shall appoint the primary and alternate members of the IRB committee, with concurrence by the Institutional Official. The selection process of IRB members involves assessments on several different levels. An IRB member should have an interest in the regulations relevant to the ethical issues concerning human subjects research. Diversity also plays



IRB STANDARD OPERATING PROCEDURES

a role when considering committee membership, and it is desirable to include people of different race, gender, cultural background, and sensitivity to community attitudes to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects. Members may include physicians, specialists (e.g. pediatricians, psychiatrists, oncologists, cardiologists, etc.), registered nurses, pharmacists, other professionals, and community members.

The IRB shall have the appropriate expertise to properly judge the adequacy of information to be presented to subjects. The IRB will invite individuals with competence in special areas to assist in the review of issues that require expertise beyond or in addition to that available on the IRB. These individuals will not vote with the IRB, or be counted toward a quorum.

II.3.b.1. Member Responsibilities

Responsibilities of BRANY IRB members will include:

- (1) Regular attendance at IRB meetings.
- (2) Review of IRB meeting agendas and assignments (see section III.1.b.1.1. for details on reviewer assignments) prior to the IRB meeting.
- (3) Disclose potential conflicts of interests prior to reviewing items submitted to the IRB. IRB members will recuse themselves from the IRB meetings if a potential conflict of interest may exist for an item under review.
- (4) Review of IRB meeting minutes.
- (5) Serve as expedited reviewer as designated by the Chairperson.
- (6) Return all reviewer correspondence, including reviewer checklists and any additional comments, to the BRANY IRB office within 2 days of the IRB meeting.
- (7) Devote sufficient time to IRB activities to ensure a qualitative and substantive review.

Any IRB member may report any attempt to influence the decision of the BRANY IRB to the Institutional Official or the Director of the BRANY IRB. The Institutional Official, the Director, and/or the BRANY Quality Assurance department will investigate such allegations, and the results of the investigation will be documented. A response to the allegations will be prepared along with a corrective action plan, if needed, to ensure that there is no undue influence on the IRB members or on the committee's actions and determinations.

II.3.c. Appointment of IRB Chairpersons

The committee shall have a Chairperson (or Co-Chairpersons) appointed by the Institutional Official. The Chairperson is expected to have the background and



IRB STANDARD OPERATING PROCEDURES

reputation that engenders respect of the IRB members, the IRB staff, investigators, research coordinators and BRANY administrative staff. It is expected that the Chairpersons will have the requisite leadership, management and interpersonal skills that allow them to be role models as well as fair and impartial leaders of the IRB. The Chairperson is also expected to have an in-depth understanding of the ethical issues, institutional policies, and federal, state and local regulations that are applicable to research reviewed by the IRB.

II.3.d. Length of Service

The IRB members, including the Chairperson(s), will be appointed for an initial term of two (2) years. At the end of the two-year term, the member's term will be automatically renewed for an additional two years, unless:

- The member voluntarily forfeits his or her membership
- The member fails to fulfill his or her obligations as an IRB member, including preparation, presentation and documentation of assignments, in the opinion of the Chairperson(s), the Institutional Official, or the IRB administration
- The member has poor attendance at IRB meetings

II.3.e. Evaluation of IRB Chairpersons

The Chairperson's performance will be evaluated at the end of each two-year term. IRB administrative staff will provide the "Anonymous Chairperson Evaluation Form" ([Appendix 37](#)) to the IRB members to complete. The evaluation form captures key information that will assist in determining if the Chair is effective in his/her role. The IRB Director will tabulate the results and provide a report to the Institutional Official, and together they will determine whether a change in the appointment of the Chairperson is warranted. If the Chairperson fails to adequately fulfill the responsibilities of his or her office, or if circumstances arise that in the opinion of the Institutional Official warrant the Chairperson's removal, the Institutional Official may designate another Chairperson. The appointment process may be activated at any time to fill vacancy and/or to ensure the effective operation of the IRB. The IRB Director will provide the Chairperson with feedback in the form of a report incorporating the anonymous evaluation results and any resulting outcome of the Director's consultation with the Institutional Official.

II.3.f. Evaluation of IRB Members

The performance of IRB members will be evaluated biannually. IRB administrative staff will provide the IRB members with the "IRB Member Self-Evaluation Form" ([Appendix 53](#)). The evaluation form captures key information that will assist in determining if the member is effective in his/her role. The IRB Director or designee will tabulate the results and provide a report to the IRB Chairperson(s) to evaluate. Together, they will determine whether a change in the membership is warranted based on the evaluation, and will provide feedback to the IRB members. If the IRB member fails to adequately fulfill membership responsibilities, or if circumstances arise that in the opinion of the Chairperson(s) or IRB administrative team, warrant the IRB member's removal, the



IRB STANDARD OPERATING PROCEDURES

member will be removed from the IRB. The appointment process may be activated at any time to fill vacancy and/or to ensure the effective operation of the IRB.

II.3.g. IRB Chairperson's Responsibilities

- (1) Schedules interim or special meetings as needed.
- (2) May suspend or terminate research or enrollment of new subjects in studies when issues of non-compliance appear to place subjects at risk.
- (3) May require study modifications including suspension of enrollment when risks or complications arise that significantly endanger the subjects until discussion by the full board.
- (4) Designates members of the IRB that may conduct reviews on behalf of the IRB using the expedited procedure. This designation will be made on the New Member Application form by the Chairperson based on review of the member's credentials, including experience and scientific background. Designated IRB members for the purposes of expedited review may include only scientific members.
- (5) Assigns members to act as reviewers of projects or other matters that come to the board, or delegate this task to the IRB administrative staff
- (6) The IRB administrative staff will consult with the Chairperson with regard to the development and implementation of all IRB policies as well as the ongoing education program of the IRB.
- (7) When applicable, the Chairperson will seek counsel from the IRB's legal advisor.
- (8) The Chairperson will represent the BRANY IRB in discussions with federal, state or local authorities.
- (9) The Chairperson will have primary responsibility for directing the IRB administrative staff to ensure that the operation of the IRB is in compliance with all applicable regulatory requirements.
- (10) The Chairperson will have primary responsibility for conducting IRB meetings. If the Chairperson anticipates being absent for a scheduled IRB meeting, the Chairperson, along with the IRB administrative staff, will select another member to run the meeting. This may include a designated alternate Chairperson, a designated Vice-Chair, or other members of the IRB.
- (11) The Chairperson will assist the IRB administrative staff in drafting letters from the IRB to investigators regarding IRB decisions.



IRB STANDARD OPERATING PROCEDURES

- (12) The Chairperson will work with IRB members, institutional officials, and investigators to ensure that the rights and welfare of research subjects are adequately protected.
- (13) The Chairperson will work with IRB administration to observe and evaluate whether IRB members meet their obligations to ensure adequate protection of human subjects.
- (14) The Chairperson or a designee will be responsible for reviewing research that can be categorized as “Expedited” (see Section III.1.d.), adverse events, and advertisements.
- (15) The Chairperson will review the meeting minutes to ensure that they reflect the discussions and deliberations of projects reviewed at a convened meeting and that they adequately summarize any other issues considered at the meeting.
- (16) The Chairperson or designee(s) will compose official IRB correspondence.

II.3.g.1. Vice-Chair Responsibilities

The Vice-Chair will serve as member of the IRB and is subject to the same responsibilities and requirements indicated throughout this policy for all IRB Members.

Additionally, the Vice-Chair will serve as the Chairperson in the absence of the Chairperson, or alternate Chairperson. In this capacity, the Vice-Chair will have the same responsibilities as the IRB Chairperson as noted in Section II.3.g. above.

II.3.h. Consultants

On an as-needed basis the IRB Chairperson or Committee Members will request review by or additional information from a consultant, and/or IRB Staff may make a determination to invite individuals with expertise in special areas to assist in the review of issues that require knowledge beyond or in addition to that available on the IRB. These individuals may not vote with the IRB (45 CFR 46.107 and 21 CFR 56.107), and will not count toward a quorum. Prior to each meeting, IRB staff will survey the IRB members to ascertain whether a consultant will be required.

Consultants will be asked to evaluate the research proposal for scientific and scholarly merit, protection of rights and welfare of the subjects, and other specific issues as requested by the IRB. Consultants should also consider the research design, statistical power, equitable participant selection process, and risk/benefit analysis. The consultant may be invited to attend the Committee meeting for questions and clarification of issues.

Use of consultants, as well as the, consultant’s commentary (i.e. Addendum Checklist – Consultant Review – [Appendix 7](#) and the Reviewer Checklist [Appendix 6](#)), will be documented in the IRB file and minutes. All individuals who are asked to serve as consultants will be provided with the BRANY Conflict of Interest Policies to determine if they have a conflict prior to consulting. If a conflict exists another consultant will be



IRB STANDARD OPERATING PROCEDURES

selected. Consultants will be advised that all materials provided and all meeting discussions are considered confidential. Consultants will be asked to complete a checklist documenting consideration of the items described in the paragraph above, as well as any response to specific issues raised by the IRB that are not captured via the checklist.

II.3.i. Guests

Guests may attend the IRB meetings at the discretion of the IRB Director. Guests are individuals with a particular interest in the IRB and do not attend meetings regularly. Guests do not count toward quorum. Guests are advised that meeting discussions are confidential. Guests cannot be present during the vote on projects for which they have a potential or actual interest.

Although IRB administrative staff regularly attends IRB meetings, they will also be considered guests and will be named as guests in the meeting minutes.

II.3.j. IRB Committees

The BRANY IRB is scheduled to meet approximately twice a week. In addition, the IRB shall convene whenever deemed necessary by the Chairpersons, or IRB administrative staff. Initial reviews and continuing reviews shall be conducted at the convened meeting, except when eligible for expedited review, as detailed in Section III.1.d.

As the volume and complexity of IRB submissions grow additional committees may be formed to ensure that all IRB reviews continue to be timely and thorough. Such determination will be made by BRANY IRB administration in conjunction with the IRB Chairperson(s) and Institutional Official, and will also be based on the types of research reviewed, whether the IRB's reviews are thorough and timely, and the time IRB members devote to IRB activities, given other responsibilities. Additional committees may be formed and added to BRANY's Federal Wide Assurance (FWA) as needed. In the event a new committee or committees are activated, they shall function in accordance with the process contained herein.

The committee membership shall include representation from various disciplines, but must include representation from the following specialties: Pediatrics, Psychiatry, Oncology, and Internal Medicine. In the event changes in membership cause any committee to lack a member from one of the aforementioned specialties, the Chairperson(s) and Institutional Official shall attempt to fill the vacancy as quickly as possible. The committee may still review studies in these areas, but shall consult with outside specialists if necessary. BRANY recognizes that IRB members with a variety of backgrounds may possess the necessary expertise to review research protocols, but that in some instances the use of outside consultants may be necessary. In the event a reviewer does not possess the necessary expertise to conduct an independent review, the reviewer shall consult with outside experts as needed. If the reviewer does not have access to someone with the requisite expertise, the IRB Director or administrative staff shall assist the reviewer in locating a consultant. The composition of the IRBs membership will be evaluated periodically by the IRB Director in conjunction with the Chairperson(s) and the Institutional Official to ensure the committee has suitable



IRB STANDARD OPERATING PROCEDURES

representation. If changes are made to the membership, OHRP will be informed and the membership roster will be revised to reflect the changes.

Alternates may serve in place of primary members as follows:

- Non-scientific alternate members may replace only non-scientific primary members.
- Scientific alternate members with a medical degree (e.g., MD, DO) may replace scientific primary members with a medical degree.
- Scientific alternate members with a pharmacy degree may replace scientific primary members with a pharmacy degree.
- Scientific alternate members that do not have a medical or pharmacy degree will be designated to replace a specific primary scientific member, as indicated on the IRB roster.

Alternate members' qualifications will be comparable to the primary member they replace. Alternate members will receive and review the same material as the primary member that was replaced. The minutes will reflect which alternate members are present at each meeting. The IRB member roster shall identify the primary member or class of primary members for whom each alternate member may substitute.

Ad hoc substitutes are not permissible as members of the IRB. Ad hoc substitutes may attend as consultants and gather information for an absent member, but they may not be counted toward the quorum or participate in either the deliberation or the voting with the board.

II.3.k. Initial Training, Continuing Education, and Professional Development of IRB Members

All new members of the IRB will receive a package of reference material that includes copies of the IRB Guide Book, the BRANY IRB Standard Operating Procedures, *The Belmont Report*, *The Nuremberg Code*, *The Declaration of Helsinki*, 45 CFR 46, FDA Information Sheets, applicable FDA regulations (e.g., 21 CFR 11, 50, 54, 56, 312, 812), International Conference on Harmonization Guidelines for Good Clinical Practice, OHRP Guidelines on Genetic testing, and NIH Guidelines on Research using Recombinant DNA. All members will be required to sign a confidentiality agreement in the form attached hereto as [Appendix 24](#) (or similar form).

As part of the member training process, new IRB members will be required to attend three (3) meetings of the IRB before they are added to the member roster, and before they are assigned to review projects. Continuing education will also be provided to all IRB members, in part, by regular distribution of informational material at the IRB meetings. This material may include copies of "IRB Ethics and Human Research," "Human Research Compliance Insider," "Clinical Trials Advisor," "IRB Advisor," copies of various published articles in peer reviewed journals that are relevant to IRB function and deliberations, information received from the American Association of Medical Colleges



IRB STANDARD OPERATING PROCEDURES

(AAMC) and any other information that the leadership or an IRB member believes would be beneficial to the education of the IRB membership.

All members of the IRB will complete the educational module on the OHRP website (see OHRP Web site at: <http://ohrp-ed.od.nih.gov/CBTs/Assurance/login.asp>) and provide evidence of training in human subject protections (e.g. the NIH Office of Extramural Research online training module at <http://phrp.nihtraining.com/users/login.php>). Additionally, IRB members will complete any additional educational requirements for DoD supported research. Initial and continuing education regarding current DoD requirements will be provided to IRB members by the IRB Director or a designee at a convened IRB meeting with each DoD supported research project submitted for review. Specific requirements contained within the DoD regulations will be reviewed with the IRB members at the meetings when a DoD supported research project is submitted for review.

Under the direction of the IRB Director, the BRANY IRB administrative staff will conduct ongoing review and maintenance of committee membership, including:

- ensuring the membership continues to meet the criteria posed by applicable regulations
- ensuring the membership remains adequate for the types of research reviewed by BRANY IRB
- ensuring the memberships' credentials remain up-to-date and compliant with this policy;
- implementation of any updates to the member roster registered with OHRP;
- further development of procedures for vetting of IRB member candidates;
- further development of procedures for evaluation of IRB members, including: addressing concerns and complaints about IRB members; review of IRB member performance (e.g., contributions during IRB meetings; ability to perform a substantive and meaningful review; accuracy and completeness required documentation).

II.4. Institutional Review Board Administrative Staff

II.4.a. Resource Allocation

BRANY allocates sufficient resources to support the IRB's review and record keeping responsibilities and places a strong emphasis on careful, timely and thorough handling of all IRB functions. Resource allocation is adjusted to meet the needs of the IRB as needed, however a formal evaluation of resources is conducted each year in conjunction with annual budget preparations. Resource allocation considerations also include the volume, complexity and types of research reviewed. BRANY has made a commitment to provide meeting space and staff to support functions of the BRANY IRB, including review and recording keeping duties (45 CFR 46.103(b)(2)). Additionally, private office



IRB STANDARD OPERATING PROCEDURES

space will be available to the Director of the IRB so matters of a sensitive nature may be addressed privately.

II.4.b. Reporting Lines and Supervision

The IRB administrative staff will be supervised by and report to the Director of the IRB. The Director of the IRB shall be supervised by the IRB Chairperson(s) concerning human subject protections and other IRB matters, and a senior administrative officer concerning organizational and administrative matters.

II.4.c. IRB Staff Responsibilities

- (1) With the assistance of the IRB Chairperson, the IRB staff will assign a primary and secondary reviewer with the appropriate expertise to review each new protocol, and appropriate reviewers for other items on the agenda. These reviewers may be committee members or outside consultants when necessary. IRB Committee members or IRB staff may request a written review from a consultant when additional expertise is required for a particular project. Consultants may also be invited to attend the meeting in person. Prior to each meeting, IRB staff surveys the IRB members to ascertain whether a consultant will be required (See policy II.3.f. regarding consultants).
- (2) Transmit copies of the protocol, protocol summary (when applicable), investigator brochure (when applicable), informed consent form, all required IRB forms and any ancillary materials to the assigned reviewers.
- (3) Prepare the agenda, which will supply every member of the committee with a copy of the full protocol and consent form for each new project submission on the agenda. Other pertinent study-related documents such as notifications of study termination or enrollment closure, adverse event reports and any materials approved via expedited review, will also be included in the meeting agenda. The agenda will be distributed to the committee members 5 to 7 days prior to the regularly scheduled IRB meeting.
- (4) If necessary, an amended meeting agenda may be prepared by the IRB staff and distributed to committee members on or before the time the IRB meeting convenes. All members will receive pertinent information prior to the meeting in order to facilitate participation in all IRB discussions.
- (5) Draft meeting minutes and forward to Chairperson for review and comment.
- (6) Prepare all required IRB correspondence including, but not limited to, approval and deferral letters, and implement consent form revisions as needed.
- (7) File Maintenance/Organization of contents to allow a reconstruction of a complete history of all IRB actions (see [Appendix 32](#) for organization of legacy paper records).
- (8) Conduct quarterly peer reviews as described in section II.10.f.



IRB STANDARD OPERATING PROCEDURES

For Central IRB projects, a Project Manager will be assigned to the trial to coordinate the submission and review process between the Study Sponsor, Investigative Site and the BRANY IRB. Throughout the life of the project, the Project Manager will remain the point of contact for both the Study Sponsor and the Investigative Site. The Project Manager will forward IRB determination notices to the Investigative Site and copies of such correspondence to the Study Sponsor.

II.4.d. Initial Training, Continuing Education, and Professional Development of IRB Staff

All members of the IRB staff will receive a package of reference material that includes copies of the IRB Procedures Manual, *The Belmont Report*, *The Nuremburg Code*, *The Declaration of Helsinki*, 45 CFR 46, FDA Information Sheets, applicable FDA regulations (e.g., 21 CFR 11, 50, 54, 56, 312, 812), OHRP Guidelines on Genetic Testing, and NIH Guidelines on Research using Recombinant DNA. All new IRB staff will be required to complete the online National Institutes of Health (NIH) module entitled "Protecting Human Research Participants" at <http://phrp.nihtraining.com/users/login.php> or complete the Dunn and Chadwick examination contained in their book entitled *Protecting Study Volunteers in Research*. The Human Resources Department will maintain certificates of completion. IRB certification is encouraged for all Associate IRB Coordinators, but will be required to be obtained by all IRB administrators at the IRB Coordinator level or higher within 2 years of assuming such title. IRB Certification or attendance at a conference devoted to human subject protections such as those sponsored by PRIM&R/ARENA is an acceptable substitute for the online NIH training module/Dunn & Chadwick requirement.

Continuing education will also be provided to all IRB staff, in part, by regular distribution of informational material at the IRB meetings. This material may include copies of "IRB Ethics and Human Research," "Human Research Compliance Insider," "Clinical Trials Advisor," "IRB Advisor," copies of various published articles in peer reviewed journals that are relevant to IRB function and deliberations, information received from the American Association of Medical Colleges (AAMC) and any other information that the leadership believes would be beneficial to the education of the IRB staff. In-servicing of IRB policies and practices and relevant regulations will be conducted at regularly scheduled staff meetings. Additionally, IRB staff will complete any additional educational requirements for DoD supported research. Initial and continuing education regarding current DoD requirements will be provided to IRB staff by the IRB Director or designee with each DoD supported research project submitted for review. Specific requirements contained within the DoD regulations will be reviewed with the IRB staff at IRB Team meetings when a DoD supported research project is submitted for review.

II.4.e. Interactions with Affiliated IRBs

- (1) Prior to BRANY IRB meetings, the administrative heads of the affiliated IRBs are informed of new projects submitted to the BRANY IRB from their institution. A summary of IRB's decisions on such projects is also provided after the BRANY IRB meeting.



IRB STANDARD OPERATING PROCEDURES

- (2) BRANY IRB minutes are made available to institutional liaisons and/or administrative staff of the affiliated IRBs.
- (3) Audit results for BRANY IRB-approved trials are shared with the Institutional Liaison at the appropriate institutions.

II.5. Record Keeping and Required Documentation

Federal regulations (45 CFR 46.103(b) (4), and 21 CFR 56.108) require that the IRB implement written policies and procedures to govern the operations and direct the activities of the IRB.

II.5.a. Record Retention

In accordance with federal regulations (45 CFR 46.115(b), and 21 CFR 56.115) the IRB will retain research records, and all other records required to be kept by the IRB, for at least 3 years after the completion, early termination or cancellation of the research with which the research record is associated regardless of whether or not subjects were enrolled in the project.

Studies Submitted Prior to 2013

Records for studies with active BRANY IRB approval remain in the records room on site at the BRANY IRB facility. Records will be maintained on site 6 months after the study has been reported closed to BRANY IRB, and will then be sent to an external storage facility. IRB Staff will follow instructions outlined on the Document Retention Schedule (see [Appendix 33](#)). All documents will be prepared for storage as directed by the storage facility and in accordance with the Document Retention Schedule. Internal Logs will be maintained with tracking numbers for easy access to files. After the retention period ends, the records are destroyed only after consultation with the study sponsor (or sponsor's representative) or the PI for non-sponsored research.

Studies Submitted 2013 and Following

Records for studies are securely maintained in BRANY IRB's electronic protocol tracking system, *IRBManager* (see Section II.5.g.).

II.5.b. Access to IRB Records

To protect the confidentiality of subject information all IRB records will be kept secure in a locked records room. Secure electronic records shall be maintained in accordance with BRANY's policies for *IRBManager* access and 21 CFR Part 11. Access to IRB records is controlled by a designated IRB staff member. IRB records will only be released to the Chairpersons and members of the IRB, the administrative staff of the IRB, approved research site personnel, and individuals who are authorized to audit the research records on behalf of BRANY or the sponsor. Records are accessible for inspection and copying by authorized representatives of federal agencies or departments, including OHRP, FDA, and ORCA, at reasonable times and in a reasonable manner.



IRB STANDARD OPERATING PROCEDURES

Records maintained that document compliance or non-compliance with DoD regulations will be made accessible for inspection and copying by representatives of the DoD at reasonable times and in a reasonable manner as determined by the supporting DoD component.

II.5.c. IRB Records

IRB records document determinations required by laws, regulations, codes, and guidance. The IRB records will include the following:

- (1) IRB Standard Operating Procedures Manual
- (2) BRANY Assurance with OHRP (FWA #00000337)
- (3) IRB membership roster
- (4) Records of certification of education of investigators and others in protecting human subjects
- (5) Conflict of Interest (COI) Disclosure Forms
- (6) Correspondence between the IRB and the investigators.
- (7) Research Project files including protocol, investigator brochure (when applicable), protocol summary (when applicable), scientific evaluations (i.e. reviewer and/or consultant checklist(s)), other scientific evaluations when provided by an entity other than the IRB, consent documents, requests for waiver of informed or signed consent, assurances, continuing review application and documentation (progress report), individual SAE and AE reports, reports of injuries to participants, statements of significant new findings provided to participants, advertisements/recruitment materials, and protocol amendment related correspondence, data and safety monitoring reports when applicable, documentation regarding any non-compliance or unanticipated problem determinations, and correspondence acknowledging receipt of COI forms, as well as copies of all correspondence between the IRB and researchers are kept in the IRB file. When applicable, DHHS-approved sample consent documents will also be maintained in the IRB file. Files will be organized to allow reconstruction of a complete history of IRB actions related to the research project.
- (8) When a project is reviewed (either at initial or continuing review) via the mechanism of expedited review, the IRB file must include documentation (i.e. reviewer checklist) which specifies the permissible category under which the project qualified for expedited review, a description of the actions taken by the reviewer, as well as any determinations required under the regulations along with protocol-specific findings justifying those determinations.
- (9) When a project is considered for a Determination of Exempt Status, the IRB file will include documentation (e.g., completed Application for Determination



IRB STANDARD OPERATING PROCEDURES

of Exempt Status, with the Reviewer section signed by the Chairperson) which specifies the permissible category under which the project was determined to qualify for exempt status.

- (10) Electronic research protocol tracking system.
- (11) Minutes of convened meetings of the IRB, including documentation of new and continuation applications, expedited reviews, review of items requiring full board review, notifications of study termination or of closure to enrollment, and a summary of discussions.
- (12) Curriculum Vitae (CV) and membership applications of each IRB member.

II.5.d. IRB Membership Roster

The IRB Director will ensure that a current IRB membership roster is maintained and that any changes in IRB membership will be reported to OHRP (45 CFR 46.103 (b)(3)). Membership rosters will include the following information:

- (1) Names of IRB members
- (2) Gender
- (3) Names of Alternate Members
- (4) Primary member or class of primary member for whom alternate members may substitute.
- (5) Earned degrees of each member
- (6) Indication of area of specialty, where applicable
- (7) Category of membership: Scientific or Non-scientific (community)
- (8) Affiliation (if any)
- (9) Position on IRB (e.g. Chair, Co-Chair or Vice-Chair, Representative Capacity)

II.5.e. Education and Training Records

The IRB Director, with assistance from the BRANY Human Resources Department, will maintain an accurate record of all IRB staff, IRB members, investigators, coordinators and others who are considered to be “key personnel” who have fulfilled the human subject protection initial and continuing training requirements.

IRB Staff training records will be maintained in accordance with BRANY’s Human Resources employee training policy, and shall include:

- New employee training schedule, checklist and evaluation form



IRB STANDARD OPERATING PROCEDURES

- Documentation of completed human subject protection training
- Documentation of applicable continuing education activities
- Documentation of applicable certifications (e.g. CIP, CIM)

IRB member training records will be maintained in the member's file, and shall include:

- Documentation of completed human subject protection training
- Documentation of completion of OHRP assurance module
- Membership acceptance statement, which documents training on BRANY IRB's SOPs and applicable regulations and guidance (for IRB members added to the committee in 2004 or later)

Documentation of training for investigators, coordinators and "key personnel" will be maintained in each research project's file, and shall include:

- Documentation of completed human subject protection training in accordance with section II.6.a. of this policy

II.5.f. IRB Correspondence

The IRB administrative staff will be responsible for maintaining records of all correspondence to or from the IRB (45 CFR 46.115(a)(4), and 21 CFR 56.115(a)(4)). Correspondence to or from investigators that relate to a specific research project will be maintained in the file for the specific project.

IRB Correspondence will not reflect a "wet signature" of the author. BRANY IRB correspondence shall be considered valid when:

- (1) It is sent directly from a valid BRANY email address by an actively employed and designated BRANY staff member
- (2) The letter is attached to BRANY's electronic research protocol tracking system by an actively employed and designated BRANY staff member

Valid copies of BRANY IRB correspondence can be downloaded by research staff via the electronic research protocol tracking system.

II.5.g. Electronic Research Protocol Tracking System

The IRB administration will ensure that the IRB's electronic research protocol tracking system, *IRBManager*, is maintained as a reliable mechanism to track protocols. Information entered into the tracking system, at a minimum, will contain the following information:

- (1) IRB file number assigned to the research project



IRB STANDARD OPERATING PROCEDURES

- (2) Title of the Research Project
- (3) Names of the Principal Investigator(s)
- (4) Sponsor's Name and Protocol Number
- (5) Date of initial approval
- (6) Length of Approval Period(s)
- (7) Date of most recent continuing review
- (8) Date IRB approval expires
- (9) Type of review (full board or expedited)
- (10) Current Status (approved, closed, pending review, deferred, closed to enrollment, etc.)

Applications to BRANY IRB review of new studies or modifications to previously approved research submitted in 2013 and following are made via the *IRBManager* portal through electronic submission forms, called "xForms." IRB staff manages submissions via the electronic system, accessing items submitted through the relevant study record in *IRBManager*, and preparing for items for review by the convened IRB or facilitating IRB review by the expedited procedure for qualifying submissions. IRB members access assigned submissions through the *IRBManager* portal, and complete a reviewer checklist "xForm" in accordance with Section III.1.b.1. of this policy. All submissions and reviewer checklists completed through the *IRBManager* portal become part of the study record.

During convened meetings, IRB staff and IRB members access relevant agenda materials and IRB records through *IRBManager* using a secure login over the Internet.

II.5.h. IRB Minutes

The IRB minutes will document the events of the convened meeting. The minutes will include the meeting's attendees (by name) and the quorum requirements; when an alternate replaced a primary member; actions taken by the IRB on new and continuing review applications; informed consent modifications or amendments; privacy concerns; consideration of conflict of interest issues, if any; unanticipated problems involving risks to subjects or others; adverse event reports; reports from sponsors, cooperative groups, or DSMBs; reports of continuing non-compliance with regulations or IRB determinations; waiver or alteration of elements of informed consent and justification; suspensions or terminations of research; and other actions. Each action will have its own separate deliberation. The votes on each IRB action will be recorded in the minutes and categorized as "for; against; abstentions." The approval period will be documented for initial and continuing reviews. Additionally, when applicable, the names of those members who abstain from voting as well as the names of those members that exit the meeting will be recorded in the minutes for each action. In the case where a member



IRB STANDARD OPERATING PROCEDURES

exits the meeting due to conflict of interest, the reason will be explicitly stated in the minutes. Members who exit the meeting will not be included in the quorum for voting on the item under review.

The minutes will reflect the basis for requiring changes in or disapproving research, a written summary of controverted issues and their resolution, when applicable: rationale for significant risk/non-significant risk device determinations, IRB findings and determinations including those determinations required by the regulations and protocol-specific findings justifying those determinations for research involving: pregnant women, human fetuses, neonates, prisoners, participants with diminished capacity, and children, and a list of research approved utilizing expedited review procedures, which may include new submissions and continuing review of projects that meet the criteria for expedited review. When applicable, the minutes will also include justification for any deletions or substantive modification of information concerning risks or alternative procedures contained in the DHHS-approved sample consent document. The minutes will include a listing of research determined to be exempt from IRB review. The minutes will also reference notifications of study termination, notifications of closure to enrollment and expedited reviews presented at the convened meeting. The minutes will be presented to the full committee for ratification and signed by the committee Chairperson. The BRANY IRB meeting minutes will be made available upon request to the appropriate institutional official(s), IRB Chairperson or IRB liaison for institutions that include the BRANY IRB on their Federal Wide Assurance Application.

II.5.i. Creation, Review, Maintenance, Revision and Archive of BRANY IRB Standard Operating Procedures (SOPs)

Purpose:

This SOP describes the process for the development and maintenance of SOPs for BRANY IRB.

Scope:

The IRB maintains written SOPs in compliance with applicable regulatory requirements (e.g., 45 CFR 46.103(4) and (5), 21 CFR 56.108). The SOPs may be reviewed and amended periodically (at least annually) to comply with changes in regulations governing IRBs, and any other changes in internal policy. On an ongoing basis, BRANY IRB will also refer to and incorporate into its policies and practices applicable guidance and determinations issued by relevant regulatory agencies (e.g., FDA and OHRP). The IRB Director will maintain documentation related to SOP revisions (or the determination that no revisions are required) in the IRB's secure records room, along with prior published versions of BRANY IRB's SOPs.

Requirements and Procedure:

A request for a new or revised SOP may be initiated by BRANY IRB staff, IRB members, the IRB Director, the HRPP Committee, the Institutional Official (IO), or the BRANY Board of Directors. Any new or revised SOPs shall be furnished to the IRB Director, IRB Chairs, Institutional Official, and the HRPP Committee for review and approval. New or



IRB STANDARD OPERATING PROCEDURES

revised SOPs accepted by the IRB Director, IRB Chairs and the IO will undergo a quality control check, implemented by the BRANY Quality Assurance Department, using the IRB SOP Document Control Checklist ([Appendix 51](#)) to ensure consistency of references, headings and document titles. The revised SOP will then be distributed to the Board of Directors of BRANY for review. A summary of revisions will accompany the updated version of the policy. Adoption of the SOPs will be considered final when the Board of Directors of BRANY accepts the revised SOPs, and both the Institutional Official and the Board member designated to oversee the HRPP, sign and date the document. Once adopted, newly created policies, policy revisions, and other information that may affect human subject research such as new laws or regulations, changes in regulations, ethical matters or scientific issues will be disseminated to researchers and/or their staff, IRB Members and the IRB staff. Such information will be forwarded via email, and relevant forms and guidance documents are posted on the website at www.branyiiirb.com (as applicable). Upon request, all materials will be made available in hard copy. Each researcher is provided the SOP manual with each new study approval.

II.5.j. Quorum Requirements

A quorum will be based on the following standards:

- (1) A majority (more than half) of the voting membership of the BRANY IRB constitutes a quorum and is required in order to take action at a convened meeting. At least one scientific and one non-scientific member must be present at the convened meeting in order for the BRANY IRB to conduct its review of research protocols. In order for a project to be approved, it must receive the approval of a majority of the members present at the meeting.
- (2) Members may be present in person or via audio (telephone) or audiovisual teleconference.
- (3) The Chairperson shall be counted as a voting member and will count towards quorum. She/He can vote on all protocols, or choose to abstain.
- (4) Alternates may serve in place of regular members as follows:
 - Non-scientific members may replace only non-scientific members of the committee.
 - Scientific members may replace either non-scientific or scientific members of the committee, provided that at least one non-scientific member is always present at the meeting.
- (5) Consultants, local representatives and guests will not vote and will not be counted toward quorum.
- (6) At least one unaffiliated member will be present at each meeting.
- (7) At least one member who represents the general perspective of participants will be present at convened meetings.



IRB STANDARD OPERATING PROCEDURES

- (8) When the IRB reviews research that involves subject populations vulnerable to coercion or undue influence, one or more individuals who are knowledgeable about or experienced in working with such participants will be present.

Note that the unaffiliated member, the member representing the general perspective of subjects, and the non-scientific member may be the same person or they may be represented by two or three different persons.

To ensure maintenance of correct attendance records during teleconference meetings, a roll call will be taken by a designated IRB staff member or the IRB Chairperson once quorum is assumed, prior to the start of the meeting. A designated IRB staff member or the IRB Chairperson will also perform roll call during the meeting if members leave during deliberation and voting for items requiring a vote. If quorum is lost during a meeting, the IRB cannot take votes until the quorum is restored. If required members (e.g. non-scientific) leave the room and quorum is lost votes cannot be taken until the quorum is restored, even if half of the members are still present.

II.5.k. Voting

Following discussion by the BRANY IRB, a vote shall be taken. IRB minutes will include documentation of quorum and votes for each IRB action and determination shall be recorded by number for, against, and abstaining (45 CFR 46.109 and 115 and 21 CFR 56.109 and 115). If a protocol is being presented to the board for which a member of the IRB is an investigator or otherwise conflicted, he/she will be asked to leave the room for deliberation and voting on such protocol and will not count towards quorum (i.e. may not be counted among those voting or abstaining) or be counted as among the majority of members necessary to constitute a quorum during this absence. Quorum must be maintained in order to vote on the study. An individual who is not listed on the official IRB membership roster may not vote with the IRB. Ad Hoc consultants may not vote with the IRB. For research to be approved, it has to receive the approval of a majority of members present at the meeting.

For **classified research** subject to the requirements of the **Department of Defense**, any IRB member who disagrees with a majority decision approving a project may appeal to the Secretary of Defense. The appeal shall be included in the DoD Component's submission to the Secretary of Defense.

II.6. Principal Investigator (PI) Responsibilities

The investigator in a clinical trial is responsible for the conduct of the study and for leading the team of individuals coordinating the study. Investigators should design research studies so that the research will be likely to develop or contribute to generalizable knowledge. When investigators do not design a research study, they should judge the research design to be sound enough to meet its objective before agreeing to enroll subjects (refer to [Appendix 31](#) for guidelines for drafting clinical trial protocols).

The Principal Investigator (PI) bears direct responsibility for:



IRB STANDARD OPERATING PROCEDURES

- (1) Personally conducting or supervising the investigation, and protecting the rights, safety, and welfare of participants under the investigator's care. Investigators must provide evidence of qualifications through up-to-date curriculum vitae or other relevant documentation requested by the sponsor, the IRB, or the regulatory authority. Maintaining a list of appropriately qualified persons to whom the investigator has delegated significant trial-related duties;
- (2) Ensuring that an investigation is conducted according to the signed investigator statement, the investigational plan, and applicable regulations, in keeping with 21 CFR 312.60 and 21 CFR 812.100;
- (3) Assuring that an IRB that complies with the requirements set forth in 21 CFR 56 will be responsible for the initial approval and continuing review of the proposed clinical study;
- (4) Designing and/or participating in protocols that minimize risks and maximize research benefits to subjects;
- (5) Ensuring he/she is familiar with the appropriate use of the investigational product(s), as described in the protocol, in the current investigator's brochure, in the product information and in other information sources provided by the sponsor.
- (6) Drug and device studies, reading and understanding the information in the investigator's drug brochure or device brochure, including potential risks and side effects; Take adequate precautions for the storage of controlled substances in securely locked, substantially constructed enclosures, in keeping with 21 CFR 312.69; Administering the test article only to participants under the investigator's personal supervision or a sub-investigator responsible to the investigator; and the receipt, administration, use, disposition, and return of unused supplies, including documentation of quantities and dates of test article use, receipt, return, or disposal, and the names of all persons who received, used, or disposed of test article, in keeping with 21 CFR 312.59, 21 CFR 312.61, 21 CFR 312.62, 21 CFR 812.110, and 21 CFR 812.140;
- (7) Preparation of subject case histories documenting all subject experiences, including case report forms, consent forms, physician progress notes, and hospital charts;
- (8) Obtaining informed consent from each subject and report any failure to obtain informed consent to the IRB. Ensuring that the investigator and research staff do not use exculpatory language when communicating with a prospective subject or the legally authorized representative;
- (9) Ensuring the consent document that is submitted for IRB review contains the required elements as per the regulations (21 CFR 50.25 (a) and 45 CFR 46.116) and the "additional" elements recommended by ICH, and, once approved, that the consent process is appropriately carried out, regardless of which members of the research team are authorized to obtain and document consent. The investigator should maintain case histories documenting that informed consent is obtained prior to participation in the study (refer to [Appendix 34](#) for a sample enrollment note);



IRB STANDARD OPERATING PROCEDURES

- (10) Informing potential participants that test articles are being used for investigational purposes
- (11) Ensuring that all members of the research team comply with all requests, findings, determinations, and requirements of the IRB;
- (12) Ensuring that all human subject research projects conducted by the investigator have received initial prospective review and approval by the IRB (Refer to the Research Application – [Appendix 11](#) – for submission instructions);
- (13) Ensuring that applications for continuing review are submitted to the IRB a maximum of 30 days prior to expiration of IRB approval;
- (14) Ensuring that continuing review and approval of the research project has been obtained from the IRB within the time frame stipulated by the IRB (any project that does not receive continuing review approval by the IRB prior to the project's expiration date will be terminated);
- (15) Following the investigational plan (protocol); Ensuring that no changes in approved research are initiated without prior IRB approval and prior sponsor notification, except when needed to eliminate apparent immediate hazards to subjects, and to promptly report to the IRB all major protocol deviations and changes in the research activity, in keeping with 21 CFR 312.66, 21 CFR 812.35, and section III.1.k of this policy;
- (16) Providing written reports to the sponsor and the IRB on any changes significantly affecting the conduct of the clinical trial or increasing risks to subjects;
- (17) Ensuring that no research project will be continued beyond the IRB designated approval period, and report to the sponsor, within 5 working days, a withdrawal of approval by the reviewing IRB;
- (18) Contacting the IRB in the event the investigator becomes aware of unanticipated problems involving risks to human subjects or others, or any instance of non-compliance with Federal regulations or the requirements or determinations of the IRB. The investigator must report these events in keeping with sections III.1.i. and III.1.L. of this policy;
- (19) Ensuring all individuals who conduct human subject research reviewed and approved by the BRANY IRB comply with all requirements of the IRB in the conduct of human research. Those individuals must provide the IRB with copies of any reports or correspondence to or from any Federal regulatory or compliance enforcement agency (OHRP, FDA, ORCA) that exercises oversight over the protection of human subjects in research in which they are involved;
- (20) Informing subjects of all potential studies for which they may be eligible to participate;
- (21) Ensuring that he/she and the research staff use recruitment processes that are fair and equitable.



IRB STANDARD OPERATING PROCEDURES

- (22) Ensuring the continued consent of study subjects for long-term studies (defined as longer than one year);
- (23) Informing the IRB when a study has been prematurely completed, terminated or has been closed to enrollment at his or her site. (See [Appendix 23](#) for the Termination/Enrollment Closure form). If the sponsor, institution, or any other entity terminates or suspends a study, the investigator must inform BRANY IRB;
- (24) Promptly notifying the sponsor if BRANY IRB terminates or suspends its approval of the clinical trial;
- (25) Informing BRANY upon completion of the trial, and providing BRANY IRB with a summary of the trial's outcome, and the regulatory authority with any reports required;
- (26) Although a subject is not obliged to give his or her reasons for withdrawing prematurely from the clinical trial, the investigator should make a reasonable effort to ascertain the reason, while fully respecting the subject's rights.
- (27) Ensuring that research subjects are given referrals for needed health care during the research or for follow-up after the research;
- (28) Ensuring that adequate staffing and necessary resources are available for each research project conducted so that the rights and welfare of research subjects will be protected. The investigator should have access to a population that will allow recruitment of the necessary number of subjects. Staff should be sufficiently trained to administer the research protocol without impacting on subject safety or data integrity. Staff should have sufficient time available to interact with subjects as needed, and to conduct and complete the research. Trained staff should be available to provide backup coverage in emergency situations. Ensure all associates, colleagues, and employees assisting in the conduct of the study are informed about their obligations;
- (29) Being responsible to explain the role of the IRB to prospective subjects. As part of the explanation, the investigator must inform prospective subjects that they should contact IRB with any questions they may have regarding their rights as research subjects or with regard to complaints they may have about the study. The contact information for the BRANY IRB appears in the informed consent document. Subjects can also be directed to the BRANY IRB Website (www.branyearb.com) where they can make inquiries.
- (30) Being aware of any obligations to use the institution's IRB rather than the BRANY IRB.
- (31) Contacting the IRB when notified of any research finding that directly affects safety and medical care of current and/or past research subject. The investigator shall ensure that such findings are submitted to the IRB, along with a plan for communicating the findings to subjects;



IRB STANDARD OPERATING PROCEDURES

- (32) Maintaining accurate, current and complete records that FDA requires by regulation, specific requirements for a category of investigations or a particular investigation;
- (33) Furnishing all reports to the sponsor, the monitor, and the reviewing IRB on the progress of clinical investigations, including reports of adverse effects, deviations from the investigational plan, and a final report shortly after completion of the investigation, in keeping with applicable BRANY IRB policy and 21 CFR 312.64 and 21 CFR 812.150; Permit properly authorized officers of FDA to have access to establishments and to inspect and copy study records in keeping with 21 CFR 312.68 and 21 CFR 812.145;
- (34) Reporting all serious adverse events (SAEs) to the sponsor except for those SAEs that the protocol or other document (e.g., Investigator's Brochure) identifies as not needing immediate reporting. The investigator follows regulatory requirements related to the reporting of unexpected serious adverse drug reactions to the regulatory authority and the IRB;
- (35) For reports of deaths, the investigator supplies the sponsor and the IRB with any additional requested information (e.g., autopsy reports and terminal medical reports);
- (36) Disclosing relevant financial information in keeping with 21 CFR 54, 21 CFR 312, and 21 CFR 812 (refer to Section VI.1.b of this manual for reporting procedures);
- (37) Supervising record keeping and record retention, including all correspondence with another investigator, an IRB, the sponsor, a monitor, or FDA;
- (38) Retaining records for a period of 2 years following the date a marketing application is approved, or if no application is to be filed or the application is not approved, until 2 years after the investigation is discontinued and FDA is notified in keeping with 21 CFR 312.57.

Principal investigators should promote open and honest communication with regard to all issues and concerns raised about the conduct of all clinical research activities (refer to section II.12. Reporting of Research Concerns).

For Central IRB projects, the Study Sponsor will be required to submit protocol-specific information to BRANY IRB [[Appendix 42](#)- Sponsor/CRO Research Application (CIRB)]. Additionally, the Principal Investigator will be required to submit site-specific information to the BRANY IRB as part of the Initial Review process [[Appendix 41](#) – Site Research Application (CIRB)]. Study Sponsor, upon selection of the Principal Investigator, will forward to the Investigator the study specific BRANY IRB Submission requirements. After initial review, the Principal Investigator will continue to submit all site specific requests, such as consent revisions, advertising material etc, as well as, any Serious Adverse Event Reports to the BRANY IRB Project Manager with a fully completed Request for IRB Review Form ([Appendix 15](#)).

For research projects where the Investigator is also serving as the Sponsor (see Policy VIII.3), the Investigator must assume the responsibilities of the Sponsor, including reporting requirements to the FDA, in addition to the responsibilities of the Investigator.



IRB STANDARD OPERATING PROCEDURES

II.6.a. Investigator (and Key Personnel) Human Subject Protection Education Requirement

The IRB Director and IRB staff, in conjunction with the IRB Chairperson, are responsible for ensuring that all who are involved in human subject research have been educated in the protection of human subjects. The NIH has mandated and OHRP strongly recommends that all investigators and those identified as “key personnel” in human subject research must provide evidence of education in the protection of human subjects. “Key personnel” are defined as individuals who are responsible for the design and conduct of a study. Therefore, all investigators and key personnel, including all co-investigators, and others participating in the conduct of the research must satisfy this requirement. The IRB will deny the privilege of participation to investigators or key personnel until proof of certification is submitted. The IRB will maintain a record of all those who have been certified. Every new and continuation application that is submitted to the IRB will be assessed to ensure that all individuals who will participate in the conduct of the research have been certified.

The BRANY IRB will accept certification programs from individual institutions. Investigators must be in compliance with their institution’s re-certification policies. In the absence of an Institutional certification program or participation in a BRANY program, the IRB will accept evidence of completion of the National Institutes of Health (NIH) Office of Extramural Research’s online module entitled “Protecting Human Research Participants” at <http://phrp.nihtraining.com/users/login.php> or a certificate evidencing completion of the Dunn and Chadwick examination contained in their book entitled *Protecting Study Volunteers in Research*, which may be obtained through CenterWatch Publications at <http://www.centerwatch.com/>.

BRANY IRB will also consider other forms of human subject protection education on a case-by-case basis. For example, an independent investigator may have completed comprehensive human subject protection education while previously affiliated with an Institution or other organization; in such cases, prior research education completed at an Institution may be accepted by BRANY IRB. The IRB Director (or designated IRB staff), with consultation from the IRB Chairperson(s) and/or the Institutional Official as needed, will evaluate and make determinations of acceptable forms human subject protections education beyond those defined above based on program content. Examples of acceptable evidence of training include, but are not limited to:

- Certified Principal Investigator (“CPI” designation offered currently by ACRP)
- Certified Clinical Research Coordinator (“CCRC” designation offered currently by ACRP)
- CITI Course Completion: Basic Biomedical Research Module (or equivalent)
- Other equivalents that include training in the US federal research regulations, informed consent requirements, process, and documentation, The Belmont Report, The Declaration of Helsinki, and The Nuremberg Code.



IRB STANDARD OPERATING PROCEDURES

Additionally the BRANY IRB encourages Investigators and research staff to complete Good Clinical Practice Training and HIPAA (Health Insurance Portability and Accountability Act) training. Certificates evidencing completion of such training programs should be submitted to the BRANY IRB.

For DoD supported research, Researchers and Research Staff are required to complete any additional educational requirements imposed by the DoD component supporting the research. Evidence of training in the specific requirements of the applicable DoD component must be provided with each DoD supported research project application that is submitted to BRANY IRB for review (e.g., CITI Training Module for DON-Supported Extramural Performers, as per the Department of the Navy Training and Education Guidance issued April 15, 2011).

II.6.b. Remedial or Additional Training

At its discretion, the IRB may require an investigator to obtain additional instruction in human subjects protection and good clinical practice.

II.6.c. Change of Principal Investigator

A request for change of Principal Investigator is considered a modification to the previously approved research, and must be submitted to BRANY IRB for review and approval. **An investigator may not act as the Principal Investigator (PI) of a study without IRB approval.** Change of Principal Investigator requests should be submitted in a timely fashion to assure that the study has the proper oversight at all times.

II.6.c.1. Planned Changes of PI

A planned change of PI must be submitted for BRANY IRB review and approval before the new PI may take on responsibility for the research. The previously approved PI must maintain oversight of the research until the change of Principal Investigator is approved.

If a PI plans to take a temporary or permanent leave of absence during his or her role as PI (e.g., maternity/paternity leave, planned medical leave, retirement, etc.), it is the PI's responsibility (with assistance from the study sponsor, if appropriate) to ensure that an appropriate individual will be designated as the new PI and maintain personal and direct supervision of the research.

A change of PI must be submitted to BRANY IRB for review and approval so that subjects may continue to participate in the research under appropriate supervision. In such instances, the PI may be changed back to the original PI upon return from the anticipated leave via the change of Principal Investigator submission process outlined below.

II.6.c.2. Unplanned Changes of PI

PIs bear direct responsibility for the research they conduct, and should ensure that an appropriate individual is available to serve as PI in their absence. However,



IRB STANDARD OPERATING PROCEDURES

BRANY IRB recognizes that certain circumstances may lead to the unexpected departure of a PI from an institution/organization (e.g., unplanned medical leave, sudden change in employment). In the event BRANY IRB is notified of the unexpected departure of a PI prior to submission of a change of PI, BRANY IRB will request that study key personnel (with assistance from the study sponsor and institution, if appropriate) identify an appropriate individual to take on personal and direct supervision of the research and submit a request for change of PI within 10 business days via the change of Principal Investigator submission process outlined below or the approval for the study may be terminated, at the discretion of the IRB.

II.6.c.3. Change of PI Submission Process

If the newly proposed Principal Investigator is already approved by BRANY IRB to participate in the research as a sub-investigator or other key study personnel, then the request for change of Principal Investigator can be submitted as follows:

- (1) Submit the "Change of Principal Investigator" form ([Appendix 47](#))
- (2) Current CV and license
- (3) If appropriate, submit:
 - a. A revised informed consent document reflecting the change of PI and contact information.
 - b. A revised FDA Form 1572
 - c. Any relevant subject materials reflecting the change of PI and contact information

Information/documentation (e.g. CV, license) already on file with BRANY IRB need not be re-submitted if it has not been revised since the last submission to BRANY IRB.

If the new PI is not currently approved as part of the research, the request for change of PI should include:

- (1) "Change of Principal Investigator" form ([Appendix 47](#))
- (2) Current CV and license
- (3) Evidence of training in human subject protections (see Section II.6.a of this policy for acceptable forms of training) for new PI
- (4) "Financial Conflict of Interest in Research Disclosure Form" completed by new PI
- (5) If appropriate, submit:



IRB STANDARD OPERATING PROCEDURES

- a. A revised informed consent document reflecting the change of PI and contact information.
- b. A revised FDA Form 1572
- c. Any relevant subject materials reflecting the change of PI and contact information

II.7. Responsibilities of the Research Staff

All individuals of the research staff, including co-investigators, study coordinators, nurses, research assistants, and research staff have a responsibility to protect research subjects. Members of the research staff also have a strict obligation to comply with all IRB determinations and procedures, to rigorously adhere to all requirements of a protocol, to inform investigators of all adverse reactions or unanticipated problems, to ensure the adequacy of the informed consent process and to take measures, as necessary, to ensure adequate protection of the subjects. All members the research staff are responsible for promptly notifying the IRB of any non-compliance with applicable regulatory requirements or IRB determinations when they become aware of the issue(s).

All members of the research staff and personnel of the Institution where the research is taking place, be it a pharmacist, a nurse, an assistant, or a sub-investigator, have a responsibility to bring any concerns they might have regarding the recruitment of research subjects or the conduct of the research to the immediate attention of the principal investigator (PI) without concern of recrimination (refer to section II.12.Reporting of Research Concerns).

Research staff is responsible for disclosing relevant financial information in keeping with 21 CFR 54 (refer to Section VI.1.b. of this manual for reporting procedures).

II.8. Sponsor Responsibilities

The Sponsor takes responsibility for initiating the clinical investigation and holding the IND or IDE, but does not typically conduct the investigation. Although the sponsor is generally a pharmaceutical, biotech, or medical device company, an individual or group of individuals or medical center can also be considered a sponsor of an investigation. An investigator is referred to as the sponsor/investigator when the individual investigator is also the initiator of the clinical investigation. Research studies should be designed so that the research will be likely to develop or contribute to generalizable knowledge. The design of a research study should be sound enough to meet its objective before allowing an investigator to enroll subjects (refer to [Appendix 31](#) for guidelines for drafting clinical trial protocols).

Some of the responsibilities of sponsors are:

- (1) Selecting qualified investigators and monitors in keeping with 21 CFR 312.53 and 21 CFR 812.43;



IRB STANDARD OPERATING PROCEDURES

- (2) Providing investigators with the information they need to conduct the investigation properly including but not limited to all relevant safety information, data safety monitoring board reports, site specific monitoring reports, and interim study analysis;
- (3) Ensuring proper monitoring of the investigation. Generally, the sponsor should establish an independent data monitoring committee (DMC) or a Data and Safety Monitoring Board (DSMB) when the research is blinded, involves multiple sites, targets vulnerable subjects, and/or utilizes high-risk interventions. The DMC or DSMB should include members who would not otherwise be associated with the research sponsor. The IRB has the authority to require a DMC or DSMB as a condition of approval of research when the IRB determines that such monitoring is required;
- (4) Ensuring that the FDA (for drugs, devices and biologics), and any reviewing IRB or all participating investigators are promptly informed of significant new information about an investigation.
- (5) Ensuring that clinical investigations of a drug product intended to be reported to FDA as a well-controlled study in support of a marketing application, or if lawfully marketed, to support a new indication, significant change in labeling or advertising, route of administration, dosage, or patient population that significantly increases the risk, are conducted under a valid IND in keeping with 21 CFR 312.2 and 21 CFR 312.23. The sponsor is to provide the IND # to the IRB.
- (6) Ensuring that clinical investigations of devices are conducted in keeping with 21 CFR 812 and section VIII.5 of this policy. The sponsor is to provide the IRB with the FDA Letter granting the investigational device exemption (IDE) for a significant risk device, or a rationale when a device is considered to be a non-significant risk device.
- (7) Before permitting an investigator to begin participating in an investigation, the sponsor shall obtain a commitment from the investigator that he/she will:
 - (a) Personally conduct or supervise the investigation,
 - (b) Obtain IRB approval,
 - (c) Inform potential participants that test articles are being used for investigational purposes,
 - (d) Read and understand the information in the investigator's drug brochure or device brochure, including potential risks and side effects,
 - (e) Ensure all associates, colleagues, and employees assisting in the conduct of the study are informed about their obligations,
 - (f) Obtain informed consent from each subject,
 - (g) Follow the investigational plan (protocol),
 - (h) Comply fully with the regulations,



IRB STANDARD OPERATING PROCEDURES

- (i) Supervise all device testing and investigational drug administration to human subjects.

The FDA regulatory requirements for sponsors can be found in the Code of Federal Regulations. The following is a list that a sponsor-investigator may need to comply with:

Drugs or devices:

- 21 CFR 11 (Electronic records and electronic signature)
- 21 CFR 54 (Financial Disclosure by Clinical Investigators)

Drugs and Biologics:

- 21 CFR 210 (Current Good Manufacturing Practice In Manufacturing, Processing, Packing, Or Holding of Drugs; General)
- 21 CFR 211 (Current Good Manufacturing Practice for Finished Pharmaceuticals)
- 21 CFR 312 (Investigational New Drug Application)
- 21 CFR 314 (Drugs for Human Use)
- 21 CFR 320 (Bioavailability and Bioequivalence Requirements)
- 21 CFR 330 (Over-The-Counter (OTC) Human Drugs Which are Generally Recognized as Safe and Effective and Not Misbranded)
- 21 CFR 601 (Biologics Licensing)

Devices:

- 21 CFR 807 (Establishment Registration and Device Listing for Manufacturers and Initial Importers Of Devices)
- 21 CFR 812 (Investigational Device Exemptions)
- 21 CFR 814 (Premarket Approval of Medical Devices)
- 21 CFR 820 (Quality System Regulation)
- 21 CFR 860 (Medical Device Classification Procedures)

BRANY requires a written contract be in place between the Sponsor (or their agent) and the research site prior to enrolling any subjects in a research project. Terms that must be addressed in such contracts include:



IRB STANDARD OPERATING PROCEDURES

- Intellectual Property (IP)
- HIPAA
- Indemnification
- Research Related Injury
- Publications
- Protocol Registration (if applicable)
- Budget
- Sponsor's obligations to monitor and report findings, including those that may affect the subject's willingness to continue participation in the research, influence the conduct of the study, or alter the IRB's approval to continue the study.

The BRANY IRB may review and approve research for which a written contract with the sponsor has not yet been finalized. However, no subjects may be enrolled in a research project until a signed contract is in place with a valid indemnification. The BRANY IRB reminds investigators of this requirement in each letter of approval.

For Central IRB projects the Sponsor will ensure that the Investigators selected to conduct the clinical trial are able to use the services provided by a Central IRB, and receive all the appropriate BRANY IRB submission documents. For the Initial Review Process, Sponsor will submit information specific to the clinical trial directly to the BRANY IRB including, but not limited to:

- Protocol and any amendments
- Investigator Brochure and any amendments
- Recruitment materials
- IND reports
- Diaries
- Questionnaires

Additionally, throughout the course of the Clinical Trial, the Study Sponsor will continue to submit all project specific information, such as protocol amendments, data safety monitoring reports, etc., to the BRANY IRB Project Manager using a CIRB submission form ([Appendix 12](#) - CIRB Sponsor Request for IRB Review Form). All amendments should be accompanied by a document delineating the revisions to the document (i.e., summary of changes). The BRANY IRB Project Manager will process such project specific information



IRB STANDARD OPERATING PROCEDURES

including the implementation of informed consent revisions for all Investigative Sites conducting the study through the BRANY IRB. Once processing is complete, IRB determination notices will be forwarded by BRANY IRB to each Investigative Site and copies of all correspondence will be provided to the Study Sponsor. The BRANY IRB will not require the Investigator to complete a Request for IRB Review form in these instances. If the Sponsor elects to send amendments to each participating site, the Investigator will be required to submit the Request for IRB Review of Modifications form ([Appendix 15](#)) in accordance with the policy stated in section III.1.f.1(b). Prior to review of any Central IRB projects, a written agreement between BRANY IRB and the Sponsor delineating the responsibilities of each party will be executed.

II.9. On Site Quality Assurance Auditing and Compliance Reporting

All studies facilitated by BRANY are subject to audit by BRANY auditors to ensure compliance with federal regulations, FDA's GCP guidelines, and the policies of the IRB. The responsibility to perform routine and for-cause audits is assigned to BRANY's QA division. Audits may be directed by the QA division or the IRB (as applicable).

II.9.a. Organization and Responsibilities

II.9.a.1. The QA Group

The QA group consists of one or more qualified individuals whose responsibilities will include, but may not be limited to the following:

- (1) Conduct of on-site audits of clinical investigators and Institutional Review Boards (IRBs).
- (2) Issuance of reports of the QA audits.
- (3) Issuance of periodic reports to the President and CEO and the HRPP Committee summarizing the activities of the QA group and the results of audits conducted.
- (4) Issuance of an annual report summarizing the previous year's activities, changes in the QA program, suggestions for improvement in QA and a projection of activities for the coming year.

II.9.b. Audits

II.9.b.1. Auditing Process

The QA group conducts an audit of any or all aspects of a particular clinical trial, including compliance with the determinations of the IRB. The QA specialist will review the IRB file prior to meeting with the Investigator. The QA review will include the essential documents compliant with Federal regulations including *Curriculum vitae* for all study personnel, FDA Form 1571 or 1572, delegation of authority, financial disclosure, laboratory essential documents including reference ranges, financial disclosures, signed protocol page, amendments, all IRB approvals including



IRB STANDARD OPERATING PROCEDURES

the informed consent, IRB membership roster, all correspondence, sponsor monitor reports, SAE reports, Data Safety Monitoring Board reports and documentation of study drug or device receipt and dispensation. For trials requiring subject participation longer than 1 year there must be documentation showing the subject's desire to continue participation (e.g., consent form updated to reflect continued consent or source document added to medical record by the Investigator noting subject indicates continued consent).

II.9.b.2. Selection of Trials to be Audited

Routine Audits

Selection of studies for routine audits by the BRANY QA Department is based upon evaluation the following criteria:

- High probability and magnitude of anticipated risks to the subjects.
- Inclusion of vulnerable subject populations or those with complex or serious medical conditions.
- A greater than expected frequency of changes than may ordinarily be expected in the type of research proposed.
- Identification of an inexperienced principal investigator or inexperience among other key members of the research team.
- History of the investigator's past non-compliance with IRB requirements or HHS regulations, or significant negative findings from prior audits.
- Other factors which the IRB considers relevant to the protection of the subjects.

Copies of BRANY audit reports are provided to the Director of the IRB, Institutional Official and the IRB Chairperson. While the purpose of the audit is generally considered to be corrective and not punitive, any serious protocol violations (whether discovered by BRANY audit, sponsor monitoring visit, or other means) will as soon as discovered, be brought to the attention of the Chairperson, and the Institutional Official. The entire IRB will also be informed at its next convened meeting.

In the event that an audit reveals serious protocol violations or other serious non-compliance involving immediate issues of subject safety, or if there is question as to the ability of the investigator to continue the trial in accordance with applicable regulations, FDA's GCP guidelines, and BRANY policies, the Chairperson may suspend the research or enrollment or take such other measures as the Chairperson may deem appropriate until such time as the matter can be reviewed by the board at its next convened meeting.



IRB STANDARD OPERATING PROCEDURES

IRB-Directed Audits

In addition to the routine audit procedures identified above, the IRB may request a QA review based on, but not limited to, one or more of the following factors:

- rapid enrollment of a large number of subjects,
- excessive number of protocol amendments,
- a seemingly disproportionate number of serious adverse events reported
- identification of an inexperienced Principal Investigator,
- an investigator's history of previous audit with significant negative findings,
or
- identification of consent forms signed by someone other than the subject,
the IRB may request an audit to investigate if surrogate consent was
properly obtained in accordance with the involved Institution's policy.
- any other reason identified by the IRB.

For-Cause Audits

Receipt of any of the following may trigger a "for cause" audit by the BRANY QA Department:

- A complaint from a subject, research staff or other individual,
- Allegations or findings of serious or continuing non-compliance,
- Allegations or findings of fraud or misconduct,
- Reports of unanticipated problems involving risks to participants or others,
- Suspected conflicts of interest not previously disclosed and managed, or
failure to comply with the management plan,
- Failure to comply with the IRB's approval for the research, or
- A request of senior officials responsible for oversight of research at a given
institution/study site.

This list is not intended to be all-inclusive, as there may be other reasons to conduct a for-cause audit that are not included above.



IRB STANDARD OPERATING PROCEDURES

For **Department of Defense (DoD)** supported research, BRANY IRB will promptly (no longer than within 30 days) report to the DoD human research protection officer when the organization is notified by any Federal department, agency or national organization that any part of an HRPP is under investigation for cause involving a DoD-supported research protocol.

Follow-up Audits

Follow-up audits for a given study may be required when the investigator fails to adequately respond to a QA audit report. A history of past non-compliance or significant negative findings from prior audits may lead to subsequent audits of other studies conducted by such investigator.

II.9.b.3. Reports

Each of the audits described above will result in the issuance of a detailed report to the Principal Investigator, IRB Chairperson, the Institutional Official, and the IRB Committee. The Principal Investigator will be given opportunity to respond to any findings. Such reports are confidential BRANY documents and are not to be included in the site's Study Files.

II.9.c. Post Auditing Activities

If the Chairperson(s) determines, from the audit report and after review of the report with the investigator, that the conduct of the research is not in compliance and consequently poses a potential threat to research subjects, the Chairperson(s) have the authority to immediately suspend enrollment in the project or temporarily terminate the rights of the individual to be an investigator. If the latter, all BRANY reviewed research for which the suspended investigator is the principal investigator will be discontinued. The investigator will be informed verbally and in writing by the Chairperson(s) or the administrative staff of the IRB, as designated by the Chairperson(s). The contents of such audit reports will be shared with the IRB at a convened IRB meeting. If the IRB concurs with the action of the Chairperson(s), the IRB may suspend or terminate IRB approval, or request more information. Suspension or termination of approval shall be reported to the appropriate Institutional Official, the relevant Federal agencies (OHRP and FDA) and the study sponsor. Reinstatement of the investigator can only occur if there is concurrence from the investigator's Institution, and will require that the investigator and their research team complete a corrective action plan that will be developed with assistance from the BRANY IRB, and monitored by the BRANY IRB and the Institution.

II.10. Quality Improvement Activities to Monitor Institutional Review Board Functions and HRPP Effectiveness

BRANY maintains a Quality Assurance (QA) Department, reporting to Senior Administration. This department is responsible for assuring compliance by the various departments with the applicable regulations, rules and guidelines issued by the US Food and Drug Administration and International Conference on Harmonization.



IRB STANDARD OPERATING PROCEDURES

The QA division will perform an internal audit of the BRANY IRB at least annually. Results of such internal auditing will be reported to the IRB Director and the IRB Chair. Further actions will be taken as deemed appropriate by the Director and the Chair.

A Final Report of all findings, including descriptions of non-compliance (if any) and recommendations will be issued to the Institutional Official, IRB Director, and IRB Chairpersons for each project audited.

When deficiencies are discovered during such auditing, plans for improvement will be developed in conjunction with the following individuals as applicable: department manager, Institutional Official, IRB Director, and/or IRB Chairpersons. Improvement plans may include staff development and education, development of new policies and procedures or revision of current policies. The final plan for improvement will be promptly implemented and will include a timeline for implementation as well as a monitoring plan and measures to determine the effectiveness of the improvements (i.e. a follow up audit may be scheduled).

At its regularly scheduled meetings, the HRPP Committee will review any observed deficiencies and attendant improvement plans to consider whether the observations represent IRB non-compliance, and if so, whether such non-compliance was serious or continuing.

In the event that the potential IRB non-compliance involves potential risks to a subject's rights or welfare, an ad-hoc meeting of the HRPP committee will be scheduled within one week to review to the observation for IRB non-compliance, and if so, whether such non-compliance was serious or continuing.

If the HRPP Committee determines that IRB non-compliance is serious or continuing, it will report such determination in accordance with section III.1.o. of this policy.

Audits may include:

II.10.a. Review of Standard Operating Procedures (SOPs)

The IRB Director and/or QA division will review the BRANY IRB SOPs annually to ensure that policies and procedures incorporate current regulations and guidance. Any recommended revisions will be processed in accordance with policy II.5.i.

II.10.b. Review of IRB Meeting Minutes

The QA division will review IRB meeting minutes on a quarterly basis (refer to SOP QAIRB01).

II.10.c. Review of IRB Member Files

The QA division will review the IRB member files to ensure all members have supplied a membership acceptance statement, completed Conflict of Interest disclosure forms, documentation of Human Subjects Protection Training, and a CV.

II.10.d. Review of IRB Member Composition



IRB STANDARD OPERATING PROCEDURES

The QA division will review the IRB member composition to confirm that it is in keeping with section II.3. of this manual.

II.10.e. Review of Protocol-Specific IRB Records

The QA division will review protocol specific IRB records, which may include:

- (1) Correspondence to/from Investigator, research subjects, and IRB
- (2) Documentation for substantive and meaningful continuing review of IRB approval
- (3) Documentation and/or acknowledgements of serious adverse event reports
- (4) Proposed changes or amendments to previously approved research
- (5) Relevant IRB meeting minutes
- (6) Documentation of review of informed consent documents, advertisements used for recruiting subjects, or other amendments to the research project
- (7) Use of expedited review procedures
- (8) Personnel interviews of research staff involved in protection of human subjects. This may include interviews with IRB staff, IRB members, Institutional Officials.
- (9) Review of all communications between the BRANY IRB and the FDA and OHRP

II.10.f. Institutional Review Board – Peer Review

At least quarterly, the IRB staff will conduct a peer review. The IRB coordinators will exchange files for a detailed review of at least one study each, to be chosen at random by the IRB administration or the IRB Chairpersons.

II.10.g. Accreditation

The BRANY HRPP demonstrated its commitment to safeguarding the interests of human research participants by achieving accreditation from the Partnership of Human Research Protections (PHRP) in April 2004. PHRP was a collaboration between the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) and National Committee for Quality Assurance (NCQA). BRANY subsequently pursued and achieved a full accreditation from the Association for the Accreditation of Human Research Protection Programs, Inc. (AAHRPP). To earn accreditation, BRANY completed a thorough evaluation of its compliance with published standards and an on-site review of its practices and procedures, and continues to self-evaluate in order to maintain the standards set by the accreditation process. BRANY's reporting requirements for AAHRPP are outlined in section III.1.p.



IRB STANDARD OPERATING PROCEDURES

II.10.h. Community Outreach

Community Outreach initiatives are reviewed on a quarterly basis at the HRPP Committee meeting and will be periodically reviewed by the QA department. If any deficiencies in the programs are observed, or if enhancements are decided upon, adjustments to the program will be promptly implemented.

II.11. Responsibilities of the Institutional Official (IO)

The BRANY IRB is an integral part of the organization's Human Research Protection Program (HRPP). Overall responsibility for the HRPP has been delegated to the Institutional Official (IO). The IO will serve as the chairperson of the HRPP meetings. The IO reports directly to the Board of Directors of BRANY.

The IO must ensure that adequate mechanisms are in place so that:

- human subjects are protected;
- the HRPP program receives adequate support; and
- the IRB functions independently, and free from coercion and undue influence.

The responsibilities of the Institutional Official will include:

- (1) Review of credentials of potential IRB members prior to appointment;
- (2) Periodic Review of Chairperson(s) and designation of replacements when necessary;
- (3) Receipt and review reports of any attempt to influence the decisions of the BRANY IRB;
- (4) Receipt, review and address any questions, concerns, complaints, or suggestions posed directly from Investigators;
- (5) Guidance on resources necessary to sustain the activities of the IRB (i.e., staffing, number of IRB committees, space);
- (6) Facilitate access to legal counsel for the IRB when warranted. Legal counsel shall not be conflicted by other organizational responsibilities;
- (7) Provide access to the BRANY Board of Directors when such access is warranted;
- (8) Receipt and review of QA reports
- (9) Notification of any suspicion of scientific misconduct or fraud

II.12. Reporting of Research Concerns

It is the policy of the BRANY IRB to consider concerns and/or suggestions regarding the Human Research Protections Program and/or Institutional Review Board, and to investigate all complaints received regarding human subjects research conducted under its jurisdiction.



IRB STANDARD OPERATING PROCEDURES

Concerns, suggestions, and/or complaints may come from IRB Committee members, Investigators, participants and their families, Research Staff, anonymous sources, or the public. In some cases complaints concerning research or the conduct of research may or may not involve non-compliance with BRANY IRB policies or federal, state, or local law or regulations and will be processed in accordance with Policy III.1.I. re: non-compliance.

Reports can be made via mail, telephone, facsimile, or via the BRANY website as follows:

Mail: BRANY IRB – Research Complaints/Concerns
1981 Marcus Avenue, Suite 210
Lake Success, NY 11042

Telephone: (516) 470-6909

Facsimile: (516) 470-6903

Website: www.branyirb.com

II.12.a. Complaints/Concerns from Research Subjects and/or Family Members of Subjects

During the course of a research study questions, concerns or complaints from research participants or their family members may arise. Investigators should encourage subjects and their family members to voice any concerns at any time during the course of their participation in the research project. Research subjects can also be directed to contact the Director of the BRANY IRB to discuss concerns and/or complaints. As part of the Research Application ([Appendix 11](#)), the investigator is required to describe the procedure that is in place for participants to voice questions, concerns or complaints about the research. The informed consent form must alert research participants to contact the Principal Investigator or the BRANY IRB if they have any concerns, complaints or questions about their participation in the research. BRANY IRB requires the Informed Consent Document to include contact information for both the Principal Investigator and the BRANY IRB (see the Sample Informed Consent Form – [Appendix 19](#) – for language requirements).

If an Investigator or any member of the research staff receives a complaint from a research subject or a family member, such complaint must be promptly forwarded to the Director of the BRANY IRB. Initial notification of the complaint may occur via telephone to the Director of the BRANY IRB, but must be followed by a written report within 5 business days describing the complaint and any actions taken by the research personnel as a result.

II.12.b. Research Staff Complaints/Concerns

Principal investigators should promote open and honest communication with regard to all issues and concerns raised about the conduct of all clinical research activities. All members of the research staff and personnel of the Institution where the research is taking place, be it a pharmacist, a nurse, an assistant, or a sub-investigator, should feel free to bring any concerns they might have regarding the recruitment of research



IRB STANDARD OPERATING PROCEDURES

subjects or the conduct of the research to the immediate attention of the principal investigator without fear. Commitment to such policy and practice helps to further promote human subject protections for both research subjects and their families.

To reinforce this commitment Investigators should:

- meet frequently with their staff to review the progress of the research, and to encourage the discussion of any concerns about the research in general or a specific research subject.
- inform the staff of their duty to bring to the attention of the Investigator or the BRANY IRB any concerns regarding the conduct of the research without fear of repercussions.
- investigate any such reports and report back to the individual who raised the concern. All reports should be investigated; no report should be dismissed without investigation.
- report to the IRB any such reports that have or may affect subject safety, compliance with the research protocol, informed consent violations, or integrity of the research data collected.
- If for any reason research staff or other personnel cannot discuss such concerns or complaints with the Principal Investigator directly, individuals are encouraged to contact the Director of the BRANY IRB directly at (516) 470-6909.

II.12.c. Complaints/Concerns From IRB Members

Any IRB member may report any attempt to influence the decision of the BRANY IRB to the Institutional Official or the Director of the BRANY IRB. The Institutional Official, the Director, and/or the BRANY Quality Assurance department will investigate such allegations, and the results of the investigation will be documented. A response to the allegations will be prepared along with a corrective action plan, if needed, to ensure that there is no undue influence on the IRB members or on the committee's actions and determinations.

II.12.d. Complaints/Concerns From Investigators

Investigators may report any complaints, questions, concerns and/or suggestions regarding the Human Research Protections Program and/or Institutional Review Board, directly to the Director of the BRANY IRB as indicated above in Section II.12.a. Complaints or concerns of a sensitive nature, as well as any questions, concerns of a general nature, and suggestions may be brought directly to the attention of the Institutional Official, Cynthia L. Hahn, at (516)562-2018 or via e-mail at chahn@nshs.edu.

II.12.e. Processing Complaints

Complaints and allegations of non-compliance shall be processed in accordance with BRANY IRB SOP III.1.1.i.: "Reports of Non-Compliance" or III.1.i.: "Review of Reports of Unanticipated Problems Involving Risks to Subjects or Others" as appropriate.



IRB STANDARD OPERATING PROCEDURES

The IRB Director shall promptly inform the Quality Assurance Manager and Institutional Official of the receipt of any such complaint or allegation. In the event the site has not been audited during the period involved in the complaint or allegation, and the allegation warrants further on site investigation, the Quality Assurance department shall schedule a visit to the site as soon as reasonably possible to investigate. The Institutional Official, together with the IRB Director and Quality Assurance Manager shall evaluate the findings and determine appropriate action. All negative findings shall be immediately reported to the appropriate IRB Chairperson, who may take action necessary to protect human subjects including suspension of research or enrollment. The Institutional Official may also take action as appropriate to prevent subject harm and improve performance going forward. Allegations shall be investigated and the IRB may make all reasonable inquiries in connection with same. Findings of serious and continuing non-compliance shall be reported in accordance with federal regulations to the appropriate institutional official(s), the FDA and OHRP. A summary of the concern/complaint and the investigation will be provided to the IRB.

In the event an Investigator is found to be out of compliance with the Human Research Protection Program and/or IRB policies, the IRB and/or the Institutional Official may take whatever remedial action deemed necessary. Such action may include, but is not limited to, requirement for further training or additional research staff, provision of additional information to subjects, or suspension from participation in BRANY IRB-approved trials.



IRB STANDARD OPERATING PROCEDURES

III. The Substance of IRB Review

The BRANY IRB's policy is to comply with all applicable local, state, and federal regulations in the conduct of research.

III.1. Actions Taken by the IRB

The actions taken by the IRB will be provided in writing to the investigator, institutional liaisons designated by the institution in collaboration with BRANY IRB (e.g., the PI's local institution's HRPP liaisons, when applicable), and BRANY staff as soon as possible after the convened IRB meeting at which the specific research application was discussed. As stated in Section II.5.h., the IRB minutes will reflect all actions taken by the convened IRB and the votes that underlie those actions (45 CFR 46.109(d) and 115 and 21 CFR 56.109(e) and 115). IRB actions for initial review, continuing review and review of modifications to previously approved research requiring full board review may include the following:

- A) **Approved:** The research may proceed as submitted.

The date of IRB approval will be the date of the convened meeting at which the research was approved, or the date on which the designated IRB reviewer approved research qualifying for expedited review. The IRB approval period may not extend beyond 365 days after approval of the project was granted, or such shorter time period determined by the board at the time of approval.

- B) **Approved with Modification (also referred to as conditional or contingent approval):** The IRB makes directed changes. If approved with modifications, the BRANY IRB staff shall incorporate into each relevant document (i.e. informed consent form, assent form, advertising materials, etc.) any revisions required by the committee. The IRB staff will prepare a "red-lined" document, which will highlight all changes made to the text of the document. The researcher may also provide written responses to address the IRB's requested modifications. The IRB staff will submit the researcher's response and any "red-lined" documents to the IRB Chair or another IRB member designated by the Chair for approval on behalf of the IRB under an expedited review procedure as described in Section III.1.d.2., and will be reported to the committee in a subsequent meeting agenda. When the convened IRB requests substantive clarifications or modifications that are directly relevant to the determinations required by the IRB, the protocol will return to the convened IRB for reconsideration, and will not be approved by the expedited procedure.

The date of IRB approval will be the date the IRB determines the conditions of approval have been satisfied. The IRB approval period may not extend beyond 365 days after this approval date, or such shorter time period determined by the board at the time of approval. If the research expires before the conditions are reviewed and approved by the IRB, all research activities must stop until IRB approval is obtained.

- C) **Deferred:** Deferred projects may be approvable but require substantive changes or additional substantive information that must be reviewed at a convened meeting of the IRB. For research that the IRB approves contingent upon substantive modifications or clarifications to the protocol or the informed consent, IRB approval



IRB STANDARD OPERATING PROCEDURES

will not occur until subsequent review by the committee. The research may proceed only after the convened IRB has reviewed and approved the required changes to the research or the information provided (see Approved with Modifications above).

- D) **Disapproved:** The IRB has determined that the research cannot be conducted. The BRANY IRB shall provide the investigator with a document outlining reasons for the decision to disapprove the research protocol and an opportunity for the investigator to respond in person or in writing. The minutes of the IRB meeting will include the rationale for disapproving the research (45 CFR 46.109(d) and 21 CFR 56.109(e)). Any response provided by the investigator will be considered by the IRB at a subsequent convened meeting.

Once approved (see A and B above), final versions of consent documents will be generated. An initial approval notice (for an example, see [Appendix 10](#) - Sample IRB Approval Letter), including copies of both the “red-lined” and the final versions of each document, will be sent to the Principal Investigator, while copies are forwarded to the Research Coordinator and the Grants Manager (if applicable). The Chairperson(s) of the committee or the administrative staff of the IRB, as designated by the Chairperson(s), may compose and send IRB approval notices.

To ensure the Principal Investigator is aware of the approval period granted by the IRB, the footer of the approved informed consent document will contain the following phrase “IRB approved _____ through _____.”

The IRB approval and expiration dates will be inserted into the final approved version of the informed consent by the IRB administrative staff; copies of this consent must be used by the research staff to obtain informed consent from subjects. The PI may then begin recruiting subjects for the study. A sample IRB approval letter and sample informed consent form are attached in [Appendix 10](#) and [Appendix 19](#), respectively. Notification that such approvals have been issued will be communicated to the committee at a subsequent IRB meeting.

Once approved (see A and B above), the Investigator is charged with the responsibility of keeping the BRANY IRB and appropriate agencies informed of (i) any unanticipated problems involving risk to subjects, (ii) changes in research activities, (iii) any non-compliance with regulations or IRB requirements, and (iv) termination or suspension of IRB approval. Whenever the IRB becomes aware of any such instances, under (i), (iii), and (iv) herein, the IRB Director will report them in accordance with the reporting procedure outlined in Section III.1.o.

III.1.a. Appeal of IRB Decision

If a protocol was deferred or disapproved by the Institutional Review Board, the PI will receive written notification as to the reasons for such action.

Decisions of the IRB may be appealed by investigators, in writing to the IRB through the IRB Chairperson. Investigators will be given the opportunity to present, in-person or in writing, the basis of the appeal at the next convened meeting of the IRB. The IRB will



IRB STANDARD OPERATING PROCEDURES

hear the appeal and after discussion, without the investigator present, vote on whether to reverse, modify or uphold its decision.

(1) **Deferral:** A deferral may warrant:

- (a) A resubmission of the protocol after making the necessary adjustments suggested by the IRB or otherwise addressing the IRB's questions/concerns. **The amended consent form, amended protocol, summary and/or any other information needed for re-review must be included in the resubmission.**

OR

- (b) Withdrawal of the protocol from re-review.

(2) **Disapproval:** In response to disapproval, the investigator may:

- (a) Redesign the protocol as per suggestions made by the IRB and resubmit for approval to the committee for re-review.

AND/OR

- (b) Submit or present a rebuttal at a subsequent meeting of the IRB.

A disapproved or deferred protocol may not be submitted to any other IRB.

III.1.b. Types of IRB Review

No human subject research, as defined in Section II.2. of this policy, unless categorized as exempt, may be initiated or continued without prospective approval from an Institutional Review Board. Regardless of the type of review (review at a convened meeting or expedited), the investigator will be notified in writing of the IRB's determination. A list of documents required for Initial IRB review is contained in the Research Application ([Appendix 11](#)).

Federal regulations (45 CFR 46.108(b), and 21 CFR 56.108(c)) require that the IRB conduct initial and continuing reviews of all non-exempt research at convened meetings at which a majority of the members are present, unless the research falls into one or more of the categories appropriate for expedited review (see Section III.1.d.1.). See Section II.5.j. for quorum requirements at convened meetings.

III.1.b.1. Initial Review by the Convened IRB

Approximately 5-7 days prior to the convened meeting of the IRB, all members of the IRB will be provided with detailed initial review materials including the Research Application, full protocols, informed consent and assent documents (or waiver requests), HIPAA authorization forms, protocol summaries and various ancillary materials describing the research (e.g., Transfer of IRB Oversight application, subject diaries, instructions, questionnaires, recruitment/advertisement materials)



IRB STANDARD OPERATING PROCEDURES

that will enable them to discuss all projects adequately and determine the appropriate action to be taken at the convened meeting (45 CFR 46.103(b)(4) and 21 CFR 56.108-109). NOTE: Financial Conflict of Interest in Research Disclosure forms submitted as part of the Research Application are processed in accordance with Section VI of this policy. Evidence of human subject protection training is confirmed by IRB administrative staff prior to distributing the Research Application to the IRB for review.

Prior to distribution of the materials, a primary and secondary reviewer will be assigned to review each project. Reviewers will receive copies of:

- the completed Research Application, including (if applicable): form FDA 1572, or IDE form, or other IND/IDE correspondence
- the full protocol,
- the investigator's brochure and safety reports, DSMB; DMC reports, drug/device inserts or other documents relating to the investigator brochure (when applicable),
- the Curriculum Vitae of the Principal Investigator (or other documentation evidencing qualifications),
- the protocol summary, when applicable (e.g., when not already contained within the protocol, or when protocol is brief and summary is not required),
- the informed consent form and assent form (if applicable), and HIPAA authorization forms(or any waivers requested)
- ancillary materials describing the research (e.g., Transfer of IRB Oversight application, subject diaries, instructions, questionnaires, recruitment/advertisement materials)
- additionally, when applicable, reviewers will also receive relevant grant applications, DHHS-approved sample informed consent document (when one exists) and the complete DHHS-approved protocol (when one exists), and
- the IRB reviewer's checklists (see [Appendix 6](#) - Reviewer Checklist, and as needed, [Appendix 7](#) - Addendum Checklist – Consultant Review, which may be amended from time to time in response to assessments of the IRB).

Reviewers are expected to conduct a thorough review of all documents, complete the IRB reviewer checklist and, if indicated, provide recommendations for changes that will maximize protection of the potential subjects and ensure that the consent document is fully informative.



IRB STANDARD OPERATING PROCEDURES

III.1.b.2. Primary and Secondary Reviewer System

For non-exempt research, the IRB considers the scientific merit of the research. The primary reviewer will review all aspects of the submission and will present the protocol to the committee. Assigned reviewers discuss the scientific merit and scholarly validity, the selection and protection of human subjects, the expertise and experience of the investigator, local research context, staffing for the project and appropriate intervals for continuing review. The IRB may rely on outside experts to provide an evaluation of the scientific merit.

Review for scientific merit should include:

- Does the research uses procedures consistent with sound study design? Is the clinical trial scientifically sound and described in a clear, detailed protocol?
- Can the research reasonably be expected to answer its proposed question?
- What is the importance of the knowledge to be gained as a result of the research?
- Is the available nonclinical and clinical information on an investigational product adequate to support the proposed clinical trial?

The expiration date will be the last date for which the protocol is approved. For example, if the IRB approved a protocol from January 28, 2006 to January 27, 2007, the project will expire at 11:59 PM on January 27, 2007.

The secondary reviewer will review all aspects of the submission and will present more detailed analysis of the construct of the informed consent form for the study, including the clarity of procedure description and the terminology used in the consent form. In addition, the secondary reviewer may offer the committee a general review of the protocol. In cases where the primary reviewer is unable to present their assigned protocol and the secondary reviewer is a scientific member, the secondary reviewer may present both the primary and secondary review. Similarly, the primary reviewer (always a scientific member) may present both primary and secondary reviews. The Chairperson may also present a primary and/or secondary review.

IRB reviewers will utilize an IRB reviewer checklist that will also serve as a guide for review during the convened meeting, and that will document findings and determinations. These checklists will be filed in the IRB files. Other findings and determinations may be recorded in the minutes. (See [Appendix 6](#) and [Appendix 7](#) for reviewer checklists, which may be amended from time to time in response to assessments of the IRB).

The BRANY IRB shall review the information given to the subjects as part of the informed consent to ascertain that the subject is informed as per to the general requirements for informed consent as specified in 45 CFR 46, and 21 CFR 50. Review of Research involving drugs, devices, biologics, etc., and research involving



IRB STANDARD OPERATING PROCEDURES

special populations may be subject to additional requirements; these issues shall be addressed in the review. It is the responsibility of the Principal Investigator to inform the BRANY IRB of such issues.

Individual institutions may have scientific review committees in place. If the institution requires prior approval by a scientific review committee or division or department head, it is the investigator's responsibility to obtain such approval prior to submission to the BRANY IRB, and prior to commencing the research.

III.1.c. Continuing Review

Federal regulations require that the IRB conduct substantive and meaningful continuing review of research at intervals appropriate to the degree of risk of the project. Continuing reviews are granted at intervals no less frequently than annually (45 CFR 46.103 and 109(e) and 21 CFR 56.109(f)). The initial IRB approval period may not extend beyond 365 days after approval the initial approval date for the project, or such shorter time period determined by the board at the time of approval. Expedited review and approval of modifications in the protocol or consent document that are reviewed during an approved project period will not modify the approval period granted the project. No grace period is permitted beyond the approval period.

Review periods are decided on a per protocol basis at the discretion of the committee and should be recommended at the time of initial review. The minutes should reflect that the review period is considered for each protocol.

IRB approval must remain in full effect for the project's entirety including completion of all research interventions and data aggregation – this includes research that is closed for subject entry but open only for follow-up or collection of private identifiable health information.

It is the responsibility of the Principal Investigator to ensure that the IRB approval does not lapse. IRB approval for any project that does not receive continuing review approval (or re-approval) by the IRB prior to the project's expiration date will expire. Enrollment of new subjects and/or performance of research beyond the IRB approved project period are prohibited by Federal regulations. No research may be conducted without an active IRB approval. Accordingly, activity on any project that has not received the IRB's final approval for continuation prior to the project's stipulated expiration date must cease. This includes recruitment, enrollment, interventions, and interactions, and collection of private identifiable health information.

Investigators are required to submit a complete Application for Continuing Review to the IRB a maximum of 30 days prior to study expiration (See [Appendix 8](#) - Application for Continuing Approval). Continuing review and re-approval of research must occur on or before the date when IRB approval expires. A study's IRB approval will expire at 11:59 PM on the last date for which the research is approved. Research activity may be performed until 11:59 PM on the expiration date for the study.



IRB STANDARD OPERATING PROCEDURES

BRANY IRB recognizes the logistical advantages of keeping the IRB approval period constant from year to year throughout the life of each project (i.e., retaining the project's anniversary date). In accordance with OHRP's Guidance on Continuing Review (updated November 10, 2010), when continuing review occurs annually and BRANY IRB performs continuing review within 30 days before the IRB approval period expires, BRANY IRB will retain the anniversary date as the date by which the continuing review must occur. The new approval period will not extend beyond 365 days from the anniversary date.

If BRANY IRB performs continuing review more than 30 days before the IRB approval period expires, the anniversary date will not be retained. The date by which the next continuing review must occur will be changed to reflect a time period (no greater than 365 days) based upon the date of the IRB meeting at which continuing review occurred (or the date that continuing review qualifying for expedited review was completed by the IRB Chair or designee). The date of IRB approval will be the date the IRB determines the conditions of approval have been satisfied.

Correspondence informing the Principal Investigator of continuing approval will reflect the date of the IRB meeting at which continuing review occurred (or the date that continuing review qualifying for expedited review was completed by the IRB Chair or designee), and the effective dates for the continuing approval period granted by the IRB. The footer of each page of informed consent documents issued with continuing approval notices will also reflect the effective dates for the continuing approval period granted by the IRB.

For **Department of Defense (DoD)** supported research, BRANY IRB will promptly (no longer than within 30 days) report the results of the IRB continuing review to the DoD human research protection officer.

As part of the continuing review submission, Investigators are to obtain and forward the DSMB reports (if available) to the IRB. The review of these reports will be conducted in accordance with the guidelines provided in Section III.1.n.6 and III.1.n.7.

The same considerations for IRB review of new applications will apply to continuation applications (45 CFR 46.111 and 21 CFR 56.111), whether reviewed by the convened IRB or by expedited review. Prior to the convened meeting, one Continuing Reviewer will be provided with detailed continuing review materials that are sufficient to allow substantive and meaningful review. All continuing reviews will be reviewed by an assigned reviewer, and must be voted on by the full board, unless eligible for expedited review as described in Section III.1.d. Assigned reviewers will utilize an IRB reviewer checklist that will also serve as a guide for presenting the review during the convened meeting, and that will document findings and determinations. These checklists will be filed in the IRB files. Other findings and determinations may be recorded in the minutes. (See [Appendix 6](#) and [Appendix 7](#) for reviewer checklists, which may be amended from time to time in response to assessments of the IRB).

III.1.c.1. Continuing Reviewer's Responsibilities



IRB STANDARD OPERATING PROCEDURES

The Continuing Reviewer will be given the following material:

- (a) Completed Application for Continuing Approval ([Appendix 8](#)), including a summary of subject experiences, complaints, and any unanticipated problems at the investigative site
- (b) Reviewer Checklist ([Appendix 6](#))
- (c) Full Protocol (most recent version approved by the IRB)
- (d) Information regarding any Serious Adverse Events that have occurred at the investigational site
- (e) Most recent version of the informed consent form approved by the IRB
- (f) Data Safety Monitoring Board Reports, when available
- (g) A copy of the BRANY Quality Assurance IRB audit report, when available
- (h) Protocol Deviation reports, if any (i.e., major protocol deviations not previously reported to the IRB, and minor protocol deviation log – see SOP III.1.k.)
- (i) Investigator’s Brochure (most recent version approved by the IRB), if applicable
- (j) Copies of any Sponsor Monitoring Reports
- (k) Copies of the last 2 consents signed by subjects in the research project
- (l) A summary of adverse events since the last IRB review. Recognizing that local investigators participating in multi-center clinical trials usually are unable to prepare a meaningful summary of adverse events for their IRBs because study-wide information regarding adverse events is not readily available to them, the IRB will accept a current report from a monitoring entity like the Sponsor, a coordinating or statistical center, or a DSMB/DMC.
- (m) Copies of any relevant recent literature
- (n) Copies of any interim findings
- (o) Copies of any relevant multi-center trial reports
- (p) A current risk-potential benefit assessment based on study results
- (q) For multi-center research, a summary of study-wide information provided by the sponsor. (Sponsor may use [Appendix 26](#) “Continuing Review Multi-Center Sponsor Supplement” or provide the same information requested on the supplement in another format.)



IRB STANDARD OPERATING PROCEDURES

Additional information, which may include the complete IRB file and relevant minutes will be made available upon request.

The Continuing Reviewer is expected to thoroughly review all documents, complete the Reviewer Checklist and provide recommendations for changes, if indicated, that will maximize protection to the potential and/or currently active subjects and ensure that the consent document is fully informative.

Prior to the scheduled IRB meeting, all IRB members will be provided with a, and c-q above in their meeting agenda. Members are required to review these materials, and will vote to approve or disapprove the continuation of the research after the Continuing Reviewer's presentation and recommendation.

The IRB must determine that the frequency and extent of continuing review for each study is adequate to ensure the continued protection of the rights and welfare of research subjects. The factors considered in setting the frequency of review may include: the nature of the study; the degree of risk involved; the vulnerability of the subject population, and, staffing and resources available at the site. For example, Phase I studies, Phase II studies enrolling pediatric subjects and gene therapy trials may be considered for assignment of a 6 month approval period. The IRB may also consider any available information about projected slow recruitment rates, target recruitment start dates, and any available information about lengthy study start-up timing that may impact the approval period determination. When such trials are subsequently submitted for continuing review, the IRB, at its discretion, will determine the approval period based on the adverse events reported or other pertinent information available. The rationale for determining the approval period will be documented in the meeting minutes.

If during the process of continuing review, any significant new findings arise that might affect a participants' willingness to continue participation in the research, the IRB will require that such findings be reported to subjects.

Some ongoing previously approved research projects may qualify for expedited review of the continuing review application, as described in "Categories of new and continuing research that may be reviewed by the IRB through an Expedited Review Procedure" (see Section III.1.d.1.). The review of such projects will be carried out in accordance with the expedited review procedure outlined in Section III.1.d. of this manual. The Expedited Reviewer assigned is expected to receive and review all the same information that would have been required if the project was being reviewed by the convened IRB.

If the IRB becomes aware of concerns about a research project or has concerns about the information provided with the continuing review application, the IRB may require verification from sources other than the investigator that no material changes have occurred since the previous IRB review. The IRB may require such verification when there is doubt that the information provided is valid or accurate, information received is inconsistent, or when there is non-compliance by the investigator. Verification may include a review of the investigator's records by a Quality Assurance



IRB STANDARD OPERATING PROCEDURES

Auditor, discussions with subjects enrolled in the research or interviews with the research staff.

Note: When the IRB becomes aware of non-compliance, the matter will be processed in accordance with BRANY IRB policy III.1.I Reports of Non-compliance. At continuing review, the IRB may also make a determination that a reported event represents an unanticipated problem involving risks to participants or others, which will be processed in accordance with BRANY IRB SOP III.1.i.

III.1.c.2. Study Termination

The BRANY IRB requires that a Notification of Study Termination Form be submitted at the completion of every IRB approved study (exempt research is not applicable). Termination forms should be filed promptly and prior to expiration of IRB approval. If no termination form is received by the expiration date, the IRB will issue an Expiration Letter, informing the investigator that no research activity may continue, and that the investigator has failed to meet continuing review obligations. Investigators who fail to file final reports may be subject to sanctions including, but not limited to, required additional education and training or suspension of investigator privileges. Failure to submit a Notification of Study Termination or a request for reinstatement of IRB approval post-expiration will be reported to the convened IRB for consideration of whether such failure represents minor, serious, or continuing non-compliance.

It is the responsibility of the Investigator to ensure that the report is accurate and submitted in a timely fashion.

Research projects should be closed when the following criteria are met:

- A) Data collection is complete;
- B) Study procedures are complete for subjects enrolled in the research project (i.e. phone calls, long term follow up, data collection visits, surveys are completed); and
- C) Research activity is no longer being conducted at the site.

If an Investigator relinquishes his position as Principal Investigator for a project, he must notify the BRANY IRB. If the Principal Investigator leaves his post at the investigational site without notifying the BRANY IRB, the BRANY IRB will seek a notification of study termination from a responsible party at the site to provide a final study report and to allow the IRB to safely close out the research project.

III.1.c.3. Short Term Continuation and Reinstatement

For the safety of subjects who are enrolled in research projects in which investigational therapy is being administered, short-term continuation of the therapy beyond the IRB approval date may occur, but only if abrupt cessation of that therapy would be detrimental to the patient's health. It is the investigator's responsibility to



IRB STANDARD OPERATING PROCEDURES

ensure that IRB approval is continuous. If IRB approval has expired, and a research subject requires the investigational therapy, the investigator must contact a member of the IRB staff as soon as s/he becomes aware of such expiration. The IRB administrative staff will consult with the IRB Chairperson to determine if the short-term continuation criteria apply. If the criteria apply, the matter will be referred to the convened IRB. If the convened IRB agrees to allow a subject to continue to take the investigational therapy, the investigator must rapidly seek to reinstate the research project's IRB approval.

III.1.c.4. Reinstatement of a Terminated or Lapsed Research Project

A project that has been terminated, for any reason, or for which IRB approval has lapsed, cannot be reinstated unless it is re-reviewed and approved at a convened meeting of the IRB. Within 30 days of expiration, the investigator must re-submit the project for review at a convened meeting of the BRANY IRB. A PI's failure to submit a Notification of Study Termination or submit a request for reinstatement of IRB approval within 30 days will be reported to the convened IRB for consideration of whether such failure represents minor, serious, or continuing non-compliance.

Reinstatement and approval of a research project requires that the IRB review and approve the following at a convened meeting of the IRB:

- (1) A completed Application for Continuing Approval ([Appendix 8](#)).
- (2) A memo to the IRB that incorporates the following information:
 - (a) An explanation of the circumstances that led to failure to submit the application at the appropriate time, and a corrective action plan detailing measures to prevent future occurrences;
 - (b) A statement indicating whether patients were enrolled during the period that the project was not IRB approved; and
 - (c) A statement indicating if there were any subjects maintained on a therapeutic intervention after the expiration date of IRB approval, the number maintained on therapy and why abrupt cessation of that therapy would have been detrimental to each patient's health.

The convened IRB will review the final report and provide acknowledgement to the investigator. The IRB will also determine whether the lapse in IRB approval represents serious or continuing non-compliance in accordance with the definitions in section III.1.i. of this policy, and if so, report such determination in accordance with section III.1.o. of this policy.

III.1.d. Expedited Review of Research

Expedited reviews may be conducted by the Chairperson or other designated IRB member(s). Designated IRB members for the purposes of expedited review may include only scientific members. Expedited reviewers of the IRB must be experienced, and will



IRB STANDARD OPERATING PROCEDURES

be selected by the committee Chairperson (see Section II.3.g.). In determining sufficient experience to conduct expedited review, the Chairperson will consider the IRB member's length of service on BRANY IRB, service on another IRB (if any), and training and experience in human subject protections. Expedited reviewers cannot disapprove research; they can approve, require modification to, or refer research to the convened IRB for review.

The designated IRB staff member(s), with concurrence of the expedited reviewer will make the determination that a submission qualifies for expedited review. In the event of any ambiguity or uncertainty on the part of the designated IRB staff member(s) or designated expedited reviewer as to eligibility, the submission shall be referred to the IRB Chairperson for further determination.

For expedited initial review, the submission procedures are the same as those required for initial review (see Research Application - [Appendix 11](#)). The IRB administrative staff will forward to the designated reviewer, all the same documents that would have been reviewed by the convened IRB (see Section III.1.b.1) with the appropriate reviewer checklist(s). The reviewer is expected to conduct a thorough assessment of all documents that will maximize protection to the potential subjects and ensure the consent is fully informative. The reviewer is provided and reviews the investigator's current curriculum vitae or other documentation evidencing qualifications.

The same considerations for IRB review of new applications will apply to IRB expedited review of new research applications (45 CFR 46.111 and 21 CFR 56.111).

Included with the materials will be a Reviewer Checklist ([Appendix 6](#)).

If at any time, the reviewer cannot complete expedited reviewer assignments, the reviewer must so advise the IRB staff as soon as possible and another expedited reviewer will be assigned to complete the reviews, or the items may be forwarded to the full board for review at a convened meeting of the IRB.

If the assigned reviewer cannot complete any of the expedited reviews for reasons of conflict of interest as outlined in Section VI.1.e, those specific reviews will be sent to the Chairperson or another expedited reviewer of the committee.

All of the performed expedited reviews will be presented to the full committee in the meeting agenda at a subsequent meeting, and any discussion of the expedited reviews presented to the committee will be recorded in the meeting minutes.

For new research projects approved via expedited review, the approval period shall begin on the date the project was reviewed and approved or approved with modifications by the designated expedited reviewer.

III.1.d.1. Categories of new and continuing research that may be reviewed by the IRB through an Expedited Review Procedure [per 45 CFR 46.110 and published in the Federal Register]



IRB STANDARD OPERATING PROCEDURES

NOTE: Non-exempt classified research must be conducted following the requirements of Instruction 3216.02 13, and is not eligible for expedited review.

- (1) Clinical studies of drugs and medical devices only when condition (i) or (ii) is met.
 - (i) Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required. (NOTE: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.)
 - (ii) Research on medical devices for which
 - (a) An investigational device exemption application (21 CFR part 812) is not required; **or**
 - (b) The medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling
- (2) Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:
 - (i) From healthy, non-pregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week; or
 - (ii) From other adults and children, considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week
- (3) Prospective collection of biological specimens for research purposes by noninvasive means.
 - (i) Hair and nail clippings in a non-disfiguring manner;
 - (ii) Deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction;
 - (iii) Permanent teeth if routine patient care indicates a need for extraction;
 - (iv) Excreta and external secretions (including sweat);
 - (v) Uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gum base of wax or by applying a dilute citric solution to the tongue;
 - (vi) Placenta removed at delivery;



IRB STANDARD OPERATING PROCEDURES

- (vii) Amniotic fluid obtained at the time of rupture of the membrane prior to or during labor;
 - (viii) Supra and sub gingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques;
 - (ix) Mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings;
 - (x) Sputum collected after saline mist nebulization
- (4) Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. **(NOTE: Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.)**

Examples:

- (i) Physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subjects privacy;
 - (ii) Weighing or testing sensory acuity;
 - (iii) Magnetic resonance imaging;
 - (iv) Electrocardiography, electroencephalography, thermolgraphy, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography;
 - (v) Moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual
- (5) Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for non-research purposes (such as medical treatment or diagnosis). **(NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects – refer to 45 CFR 46.101 (b)(4). This listing refers only to research that is not exempt.)**
- (6) Collection of data from voice, video, digital, or image recordings made for research purposes.



IRB STANDARD OPERATING PROCEDURES

- (7) Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies. **(NOTE 1: Some research in this category may be exempt from the HHS regulations for the protection of human subjects – refer to 45 CFR 46.101 (b)(2) and (b)(3). This listing refers only to research that is not exempt.) It is important to note that research that is exempt under 45 CFR 46.101(b)(2) may not apply to children.) (NOTE 2: For Department of Defense (DoD) supported research that involves surveys being performed on Department of Defense personnel, the investigator must submit to, and ensure review and approval by the Department of Defense after the research protocol is reviewed and approved by the IRB.)**
- (8) Continuing review of research previously approved by the convened IRB as follows:
- Where:
 1. The research is permanently closed to the enrollment of new subjects,
 2. All subjects have completed all research related interventions, **AND**
 3. The research remains active only for long-term follow up of subjects, **OR**
 - Where no subjects have been enrolled and no additional risks have been identified, **OR**
 - Where the remaining research activities are limited to data analysis.
- (9) Continuing review of research, not conducted under an investigational new drug (IND) application or investigational device exemption (IDE) where categories two through eight do not apply but the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified.

III.1.d.2. Documentation for Expedited Review

Approval will consist of the reviewer's written concurrence in the IRB record that the research described in the application satisfies the conditions and one or more of the categories, cited above, for expedited review and approval. If the expedited reviewer requests modifications to any of the materials submitted for review, the submission will not be completed or finally approved unless and until such modifications have been returned to an expedited reviewer or the full committee, if necessary, for final review and approval. All projects that are granted approval by expedited review will be included in the agenda and minutes of a subsequent convened meeting of the IRB. The IRB members will be given the opportunity to review or comment on any



IRB STANDARD OPERATING PROCEDURES

project approved by expedited review. Following the committee's review at the convened meeting it may be decided that a project should not be approved by expedited review. The project will then be reviewed at the next convened meeting using standard practices for new and continuation applications.

III.1.d.3. Expedited Review of Minor Changes in Previously Approved Research

Investigators must report any proposed changes in IRB approved research to the IRB, including proposed changes in the informed consent documents. (See Section III.1.e for submission guidance). No changes may be initiated without prior approval of the IRB, except where necessary to eliminate apparent immediate hazards to subjects (Note: if an investigator implements a change without IRB approval to eliminate immediate hazards to subjects, it must be reported to the IRB and reviewed by the IRB in accordance with BRANY IRB SOP III.1.i **Review of Reports of Unanticipated Problems Involving Risks to Subjects or Others** in order to determine that the change was consistent with ensuring the participants' continued welfare. The IRB may utilize expedited procedures to review a proposed change to a previously approved research project if it represents a minor change that will be implemented during an approved project period (45 CFR 46. 110).

Minor changes are those which make no substantial changes in the level of risks, the research design or methodology, the number of subjects enrolled in the research, the qualifications of the research team, the facilities available to support the safe conduct of the research, or any other factor that would require review at a convened meeting of the IRB, and include procedures that fall into categories (1)-(7) listed in Section III.1.d.1. above. The IRB Chairperson or his/her designee reserves the right to refer any project that may be eligible for expedited review for consideration at a convened meeting of the IRB.

For expedited review of modifications to previously approved research, the IRB administrative staff will forward to the designated reviewer the same documents that would have been reviewed by the convened IRB (see Section III.1.b.1 of this policy), including the completed Request for IRB Review Form ([Appendix 15](#)), copies of the items requiring review, the complete protocol, the investigator's brochure (when applicable), the informed consent form(s) (and assent forms if applicable), any other materials pertinent to the review, and the Reviewer Checklist ([Appendix 6](#)). The reviewer is expected to conduct a thorough assessment of all documents that will maximize protection to the potential subjects and ensure the consent is fully informative.

The same considerations for IRB review of new applications will apply to IRB expedited review of modifications to previously approved research (45 CFR 46.111 and 21 CFR 56.111), when the modification affects a criterion for approval.

III.1.d.4. Expedited Review of Additional Investigators for Previously Approved Studies



IRB STANDARD OPERATING PROCEDURES

Via the mechanism of expedited review as provided in 21 CFR 56.110, a physician can be approved to be an additional Principal Investigator at another site for research protocols and consent documents that have been previously approved by the BRANY Institutional Review Board. The submission procedures are the same as those required for initial review (see Research Application - [Appendix 11](#), or Site Research Application (CIRB) – [Appendix 41](#)).

In keeping with 21 CFR 312.53, the physician must be determined by Sponsors with BRANY IRB concurrence to be qualified by training and experience to investigate the drug/device in the study.

The BRANY IRB is obligated to inform the appropriate institutional official, IRB Chairperson or IRB liaison of such submission for approval. Furthermore, the BRANY IRB will inform the Principal Investigator and the affiliated institution's IRB whether such a submission has been approved or rejected.

Advertisements and additional material (surveys, diaries, etc.) may also be approved via expedited review provided they are in accordance with previously approved research.

Factors that may cause the additional investigator's application to warrant review by the convened IRB include, but are not limited to:

- (1) Inadequate qualifications of the research team
- (2) Inadequate facilities, staff, and/or resources available to support the safe conduct of the research
- (3) A request of senior officials responsible for oversight of research at a given institution/study site.
- (4) History of complaints from subjects, research staff or other individuals
- (5) History of allegations or findings of serious or continuing non-compliance
- (6) History of allegations or findings of fraud or misconduct
- (7) Evidence of inadequate corrective action or remediation in response to audit findings (e.g., FDA audits, IRB audits, sponsor monitoring)
- (8) Suspected conflicts of interest not previously disclosed and managed, or failure to comply with the management plan
- (9) Any other reason identified by the Chair or designee

III.1.e. Modifications to Previously Approved Research

Modifications to previously approved research that also fall into categories 1.)- 9.) above (section III.1.d.1.), except for interviews and surveys with children, may also be approved via the mechanism of expedited review. Such submissions will be processed in accordance with BRANY IRB SOP III.1.d. Expedited Review, as appropriate. Modifications that do not qualify for expedited review will be processed in accordance with BRANY IRB SOP III.1.g. Full Board Review (More Than Minor Modifications to Previously Approved Research). The same considerations for IRB review of new



IRB STANDARD OPERATING PROCEDURES

applications will apply to Modifications to Previously Approved Research (45 CFR 46.111 and 21 CFR 56.111), when the modification affects a criterion for approval (see BRANY IRB SOP III.1.b and III.1.n). The designated reviewer will utilize the Reviewer Checklist ([Appendix 6](#)) as a guide for the review and to document findings and determinations.

Investigators are required to submit all modifications to previously approved research using the Request for IRB Review Form (see [Appendix 15](#)). This request form provides detailed information with regard to what materials the Investigator must submit to the IRB to ensure that the IRB can conduct a substantive review the materials. The Request for IRB Review form must be complete and signed by the Investigator in order for the materials submitted to be reviewed. Investigators sign the Request for IRB Review form and are provided with automatic notification of receipt emails, which state that the IRB review is not complete and that the outcome of the review will not be complete until BRANY IRB staff contacts them with correspondence documenting the IRB's determination for the submission,

III.1.f. Amendments

An amendment is any change to previously approved research projects submitted from either a Principal Investigator or the sponsor of a research protocol. All amendments must be submitted to the BRANY Institutional Review Board for review. The IRB then will determine if the amendment is acceptable and either approve, require modification to, or disapprove it. The BRANY IRB requires that subjects be informed of any changes to previously approved research that might affect their willingness to continue to take part in the research.

III.1.f.1. Amendment Review

(a) Amendments to any of the following should be submitted:

- i. Clinical Research Protocol
- ii. Informed consent form
- iii. 1572 form
- iv. Investigational Drug Brochure
- v. Advertisement for the research protocol
- vi. Any other pertinent documents relevant to the research protocol

(b) In order for an amendment to be processed by the IRB, the amendment plus a completed Request for IRB Review Form (see [Appendix 15](#)) signed by the Principal Investigator must be submitted to the IRB. Requested revisions initiated by the IRB will not require submission of a Request for IRB Review Form ([Appendix 15](#)).



IRB STANDARD OPERATING PROCEDURES

- (c) If these amendments fall under the category of expedited review, then they are sent out to an appointed IRB reviewer, along with a Reviewer Checklist (see [Appendix 6](#)).
- (d) Should the reviewer feel that expedited approval is inappropriate, the amendment will be presented to the full board for discussion and vote. The reviewer/committee receives a copy of all relevant documents related to the amendment as described in section III.1.g , **Full Board Review (More Than Minor Modifications to Previously Approved Research)**.

III.1.f.2. Amendment Approval/Rejection

- (a) In the case of approval, a copy of the approval notice, the amendment and the new version of the consent form, if applicable, are prepared for the IRB files. An original copy of the new version of the consent form, if applicable, the amendment and the original signed IRB notice are then forwarded to the principal investigator by the IRB staff. The study expiration date will not be affected; the date of expiration of IRB approval will continue to be based on the date of initial IRB approval, or that last continuing review approval.
- (b) If the amendment is rejected by the full board, a notice of disapproval is sent to the principal investigator. This notice will itemize why the amendment was not approved and allow the PI an opportunity to appeal.
- (c) Amendments approved on an expedited basis will be reported to the full IRB committee in a subsequent meeting agenda and they will appear in the minutes of the meeting at which they were presented to the IRB.
- (d) For projects with Multiple sites: Once an amendment has been reviewed by the BRANY IRB for a multi-center project, the corresponding IRB approval/disapproval can only be issued to those sites that have submitted the amendment and the fully completed Request for IRB Review Form. If an amendment is submitted by one site of a multi-center project and not the others, the IRB staff will forward such amendment to all additional sites with the corresponding Request for IRB Review Form and a memo expressing the site's responsibility to submit the required paperwork to the IRB for review.

For Central IRB projects the Sponsor will submit directly to the BRANY IRB amendments to any of the following using CIRB submission forms ([Appendix 12](#) - CIRB Sponsor Request for IRB Review Form):

- Protocol
- Investigator Brochure
- Recruitment materials
- Informed Consent



IRB STANDARD OPERATING PROCEDURES

- FDA Form 1572
- Any other pertinent documents relevant to the research study

Additionally, throughout the course of the Clinical Trial, the Study Sponsor will continue to submit all project specific information, such as protocol amendments, data safety monitoring reports, etc., to the BRANY IRB Project Manager. All amendments should be accompanied by a document delineating the revisions to the document (i.e. Summary of Changes). The BRANY Project Manager will process such project specific information including the implementation of informed consent revisions, for all Investigative Sites conducting the study under the oversight of the BRANY IRB. Once processing is complete, the BRANY IRB will forward IRB determination notices to each Investigative Site and copies of all correspondence will also be provided to the Study Sponsor. The BRANY IRB will not require the Investigator to complete a Request for IRB Review form in these instances. If the Sponsor elects to send amendments to each participating site, the Investigator will be required to submit the Request for IRB Review of Modifications form ([Appendix 15](#)) in accordance with the policy stated in section III.1.f.1(b).

III.1.g. Full Board Review (More than Minor Modifications to Previously Approved Research)

Modifications that may NOT be reviewed via the mechanism of expedited review and will require full board review include:

- (1) Addition of a new drug
- (2) Addition of a new device
- (3) Addition of an invasive procedure
- (4) Increase in medication dose or a decrease in dose that may increase the risk
- (5) Addition of vulnerable subjects as a study population
- (6) Prolongation of the patient's participation in the study other than for observational purpose
- (7) Change in the inclusion/exclusion criteria which may involve incorporation of populations at greater risk
- (8) Identification of new, potentially significant risks
- (9) Collection of additional blood samples that exceed the limits set in expedited category 2.) (Section III.1.d.1.)
- (10) Unanticipated problems which caused harm (or placed person at increased risk of harm), were related to the research and was unforeseen



IRB STANDARD OPERATING PROCEDURES

- (11) Substantial changes in the level of risks, the research design or methodology, the number of subjects enrolled in the research, the qualifications of the research team, the facilities available to support the safe conduct of the research
- (12) Any item deemed to warrant full board review by the Chair or designee

Items that do not meet criteria for expedited review will be presented to the full board for review. A primary reviewer will be assigned. The primary reviewer will receive the completed Request for IRB Review Form ([Appendix 15](#)), copies of the items requiring Full Board Review, the complete protocol, the investigator's brochure (when applicable), the informed consent form(s) (and assent forms if applicable), any other materials pertinent to the review, and the Reviewer Checklist(s) ([Appendix 6](#)). The reviewer is expected to conduct a thorough assessment of all documents that will maximize protection to the potential subjects and ensure the consent is fully informative. The reviewer will present the changes at the convened meeting. All members of the IRB will be provided with the previously approved protocol, informed consent, assent and various ancillary materials. They will also receive the amended items. All Members are required to review these materials, and will vote to approve, approve with modification, defer or disapprove the modification after the Primary Reviewer's presentation and recommendation. When the review relates to significant new findings that may affect the participant's willingness to continue participation, the IRB will make determinations to ensure current participants are provided with information about such findings. The same considerations for IRB review of new applications will apply to IRB review of modifications to previously approved research (45 CFR 46.111 and 21 CFR 56.111) when the modification affects a criterion for approval.

The BRANY IRB must review and approve the proposed change at a convened meeting of the IRB before the change can be implemented. Assigned reviewers will utilize an IRB reviewer checklist that will also serve as a guide for presenting the review during the convened meeting, and that will document findings and determinations. These checklists will be filed in the IRB files. Other findings and determinations may be recorded in the minutes. (See [Appendix 6](#) and [Appendix 7](#) for reviewer checklists, which may be amended from time to time in response to assessments of the IRB).

For **Department of Defense (DoD)** supported research, BRANY IRB will report promptly (no longer than within 30 days) to the DoD human research protection officer when significant changes to the research protocol are approved by the IRB, or when there is a change of the reviewing IRB.

III.1.h. Administrative Reviews

To be conducted by the Director of the IRB or the designated IRB staff member ONLY for the following:

- (1) Typographical and grammatical error correction
- (2) Administrative and formatting changes such as contact names/numbers and study/sponsor identifier information



IRB STANDARD OPERATING PROCEDURES

- (3) Addition/substitution of investigators, sub investigators, and study personnel (provided that there is no increase in risk). This will include acknowledgement of receipt of any applicable required forms (e.g., evidence of training in human subject protections, financial conflict of interest disclosure forms).
- (4) When applicable, the addition/removal of witness signature lines to satisfy individual Institutional policy requirements
- (5) Addition of Lay language from the section of these standard operating procedures entitled "Glossary of Lay Terms for Use in Preparing Informed Consent Documents" (see [Appendix 5](#))
- (6) Changes in advertisement format when content (including text and images) has been previously approved (e.g., using approved internet ad text as a flyer), or verification of final format of advertisement after conditional approval
- (7) Foreign language translations of materials already approved by the IRB in English. Translated materials must be accompanied by a certificate of translation/affidavit of accuracy. Translations should be performed by a certified translator, or an individual reasonably believed by the IRB to be competent to provide them. Translated, already published, standard clinical or other validated questionnaires/materials will be accepted by the IRB without a certificate of translation (e.g., EQ-5D, brochures describing disease conditions published by recognized medical societies, regulatory agencies, or advocacy groups).

A Request or IRB Review Form ([Appendix 15](#)) will be required for all administrative reviews. Requested revisions initiated by the IRB will not require submission of a Request for IRB Review Form ([Appendix 15](#)).

III.1.i. Review of Reports of Unanticipated Problems Involving Risks to Subjects or Others

Investigators are required to notify the IRB promptly, but no later than 5 days after the Investigator's first knowledge, of any unanticipated problems involving risks to subjects or others that occur in research (45 CFR 46.103(b)(5), 21 CFR 56.108(b) and 21 CFR 312.66). The review process will be the same for all unanticipated problems involving risk to subjects or others, regardless of risk level.

Definitions:

"Related or possibly related to the research"

An event is "related or possibly related to the research" if in the opinion of the investigator it is more likely than not related to a subject's participation in research.

"Unexpected"

An event is "unexpected" when its specificity and severity are not accurately reflected in the informed consent document or other protocol-related documents, and the characteristics of the population being studied.

"Unanticipated"



IRB STANDARD OPERATING PROCEDURES

An event is “unanticipated” when it was unforeseeable at the time of its occurrence. The word unanticipated, is not a synonym for unexpected. A research protocol can monitor for an unexpected event, but cannot monitor for an unforeseen event. All unanticipated events are unexpected, but not vice versa.

“Unanticipated Problem Involving Risks to Subjects or Others”

Any event that (1) is unforeseen, (2) suggests that research places subjects or others at greater risk than was previously known or recognized, and (3) is related or possibly related to a subject’s participation in research.

Principal investigators must report:

- (1) Event (including on-site and off-site adverse event reports, injuries, side effects, breaches of confidentiality, deaths, or other problems) that occurs any time during or after the research study, which in the opinion of the principal investigator:
 - (a) Involve harm to one or more subjects or others, or placed one or more subjects or others at increased risk of harm
 - (b) Unexpected (An event is “unexpected” when its specificity and severity are not accurately reflected in the informed consent document or other protocol-related documents, and the characteristics of the population being studied.)
 - (c) Related to the research procedures (An event is “related to the research procedures” if in the opinion of the principal investigator, it was more likely than not to be caused by the research procedures or if it is more likely that not that the event affects the rights and welfare of current participants)
- (2) Information that indicates a change to the risks or potential benefits of the research, in terms of severity or frequency. For example:
 - (a) An interim analysis indicates that participants have a lower rate of response to treatment than initially expected
 - (b) Safety monitoring indicates that a particular side effect is more severe, or more frequent than initially expected
 - (c) A paper is published from another study that shows that an arm of the research study is of no therapeutic value
- (3) Change in FDA labeling or withdrawal from marketing of a drug, device, or biologic used in a research protocol.
- (4) Change to the protocol taken without prior IRB review to an eliminate apparent immediate hazard to a research participant



IRB STANDARD OPERATING PROCEDURES

- (5) Incarceration of a participant
- (6) Event that requires prompt reporting to the sponsor
- (7) Complaint of a participant when the complaint indicates unexpected risks or cannot be resolved by the research team
- (8) Protocol deviation that placed one or more participants at increased risk, or has the potential to occur again (see SOP III.1.k.).
- (9) Unanticipated adverse device effect (Any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.)

Investigators should also report:

- Findings from other studies (such as epidemiological studies, pooled analysis of multiple studies, or clinical studies) that suggest a significant risk in humans exposed to the study intervention.
- Findings from animal or *in vitro* testing that a significant risk in humans exposed to the drug (e.g., reports of mutagenicity, teratogenicity, or carcinogenicity, or reports of significant organ toxicity at or near the expected human exposure).
- Clinically important increase in the rate of occurrence of a serious suspected adverse reaction over that listed in the protocol or investigator brochure.

The IRB will accept other reports when the investigator is unsure whether the event should be reported.

Principal investigators should report the above events using the Reportable Event Form (Appendix 13). Reports may be submitted by mail, fax, e-mail, or phone (with the completed report form to follow). The report should include Principal Investigator's name, protocol title, a full description of the activities leading to the problem, date of the event, the type and nature of the problem, actions taken in response to the problem, relationship to the study, and the current status of the subject. Any additional documents that may be of relevance should also be included with the report.

III.1.i.1. Processing reports of unanticipated problems involving risks to subjects or others

- (1) Reports of unanticipated problems involving risks to subjects or others, will initially be received by IRB staff. The IRB staff will review submissions for completeness. If the submission is incomplete, the IRB staff will request missing information. If the report requires immediate action before receipt of the missing



IRB STANDARD OPERATING PROCEDURES

information, the IRB staff person will refer the information immediately to the IRB Chair.

- (2) If the investigator indicates the event (1) was foreseen, (2) did not cause harm or did not place a person at increased risk of harm, OR (3) was not related to the research procedures:
 - (a) If the IRB Chair or designated IRB reviewer considers the submitted information to be consistent with the investigator's assessment, the event is not considered to be an unanticipated event involving risks to subjects or others, and the IRB Chair or designated IRB reviewer indicates this on the Reportable Event Form.
 - (b) If the investigator indicated that the consent document, or protocol should be revised, or that currently enrolled participants should be notified, then IRB Chair or designated IRB reviewer processes these requests according to BRANY IRB SOP III.1.e. "Modifications to Previous Approved Research." The IRB Chair or designated IRB reviewer indicates on the Reportable Event Form that the event will be referred to IRB for review of proposed modifications to previously approved research, signs and dates the form, and the form is added to the research file.
 - (c) Otherwise, the IRB Chair or designated IRB reviewer indicates on the Reportable Event Form that no changes are needed, signs and dates the form, and the form is added to the research file.
- (3) If after consultation with the IRB staff, the IRB Chair or designated IRB reviewer considers the submitted information to be inconsistent with the investigator's assessment or have reason to doubt the determinations of the investigator, the IRB Chair or designated IRB reviewer indicates on the Reportable Event Form that the event will be referred to convened IRB for review as a possible unanticipated problem involving risks to subjects or others, and signs and dates the form. If assigned to a Chairperson for review, the Chair will also determine whether immediate suspension or other action needs to be taken to eliminate apparent immediate harm to subjects until the convened committee can consider the matter. If assigned to a designated reviewer for consideration, and the designated reviewer feels that immediate suspension or other action needs to be taken to eliminate apparent immediate harm to subjects, the report will be referred to the IRB Chair immediately for such determination. The IRB staff adds the event on the agenda of the next available IRB meeting for review.
- (4) If the investigator indicates the event (1) was unforeseen, (2) suggests that research places subjects at greater risk than was previously known or recognized, AND (3) was related or possibly related to a subject's participation in research, the IRB Chair or designated IRB reviewer indicates on Reportable Event Form that the event will be referred to IRB for review of as a possible unanticipated problem involving risks to subjects or others, and signs and dates the form. The Chairperson will determine whether immediate suspension or other action needs to be taken to eliminate apparent immediate harm to subjects until



IRB STANDARD OPERATING PROCEDURES

the convened committee can consider the matter. The event is added to the agenda of the next available IRB meeting for review.

- (5) All IRB members scheduled to attend the IRB meeting will receive the Unanticipated Problems Report Form and any other relevant materials.
- (6) The IRB Chair or designated IRB reviewer will be assigned the primary review of item and will present the review to the convened IRB. In addition to the items listed above the Chair/designated reviewer will also receive the currently approved protocol and consent document, all previous reports of unanticipated problems involving risks to subjects or others, and the Investigator brochure (if applicable).
- (7) The IRB will consider the following actions:
 - (a) Modification of the protocol
 - (b) Modification of the information disclosed during the consent process
 - (c) Providing additional information to current participants (This must be done whenever the information may relate to the participant's willingness to continue participation)
 - (d) Providing additional information to past participants
 - (e) Requiring current participants to re-consent to participation
 - (f) Alteration of the frequency of continuing review
 - (g) Observation of the research or the consent process
 - (h) Requiring additional training of the investigator
 - (i) Notification of investigators at other sites
 - (j) Termination or suspension of the research according BRANY IRB SOP III.1.m, Suspension/Termination of IRB Approval.
 - (k) Referral to other organizational entities
 - (l) Obtaining additional information
 - (m) Taking no action

Note: If any required actions are considered more than minor modifications to the research, such changes must be submitted for full board review by the IRB. The IRB may allow changes that do not involve more than minor modifications to be reviewed by Expedited Review.



IRB STANDARD OPERATING PROCEDURES

- (8) The IRB will also consider whether the event represents an unanticipated problem involving risks to subjects or others by considering whether the event (1) was unforeseen, (2) suggests that research places subjects at greater risk than was previously known or recognized, AND (3) was related or possibly related to a subject's participation in research. If the IRB considers the event to represent an unanticipated problem involving risks to subjects or others, the matter is referred to the IRB staff to handle according to BRANY IRB SOP III.1.o, Reporting Procedures. Otherwise no further action is taken.
- (9) Vote counts and determinations made by the IRB will be documented in the IRB meeting minutes. All documentation will be maintained in the IRB Record.

III.1.j. Serious Adverse Events (SAEs) (ON-SITE adverse events)

The BRANY Institutional Review Board is charged with the responsibility of reviewing and maintaining records of all Serious Adverse Events occurring in patients who are participating in BRANY IRB approved research trials at BRANY sites.

III.1.j.1. Definitions of AE and SAE

(a) ***For studies subject to 21CFR312 (Investigational New Drugs)***

An "**adverse event**" (AE) is defined as any untoward medical occurrence associated with the use of a drug in humans, **whether or not considered drug related**.

Adverse events may be categorized as follows:

- (i) "**Adverse reaction**" - any adverse event **caused by a drug**.
- (ii) "**Suspected adverse reaction**" - any adverse event for which there is a **reasonable possibility that the drug caused the adverse event**. For the purposes of IND safety reporting, "reasonable possibility" means there is **evidence to suggest a causal relationship between the drug and the adverse event**. Suspected adverse reaction implies a lesser degree of certainty about causality than adverse reaction.
- (iii) "**Unexpected Suspected Adverse Reaction**"- A suspected adverse reaction is considered "unexpected" if it is not listed in the investigator brochure or is not listed at the specificity or severity that has been observed; or, if an investigator brochure is not required or available, is not consistent with the risk information described in the general investigational plan or elsewhere in the current application, as amended. For example, under this definition, hepatic necrosis would be unexpected (by virtue of greater severity) if the investigator brochure referred only to elevated hepatic enzymes or hepatitis. Similarly, cerebral thromboembolism and cerebral vasculitis would be unexpected (by virtue of greater specificity) if the investigator brochure listed only cerebral vascular accidents.



IRB STANDARD OPERATING PROCEDURES

"Unexpected," as used in this definition, also refers to adverse events that are mentioned in the investigator brochure as occurring with a class of drugs or as anticipated from the pharmacological properties of the drug, but are not specifically mentioned as occurring with the particular drug under investigation.

As sub-categories of "adverse events," adverse reactions and suspected adverse reactions may also be unexpected.

(iv) **"Serious Adverse Events (SAEs)"** - An *adverse event* is considered "serious" if, in the view of either the investigator or sponsor, it results in any of the following outcomes:

- (i) Death,
- (ii) A life-threatening adverse event,
- (iii) Inpatient hospitalization or prolongation of existing hospitalization,
- (iv) A persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions, or
- (v) A congenital anomaly/birth defect.

Additionally, *important medical events* that may not result in death, be life-threatening, or require hospitalization may be considered serious when, based upon appropriate medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition. Examples of such medical events include allergic bronchospasm requiring intensive treatment in an emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse.

(b) ***For studies subject to 21CFR812 (Investigational Devices)***

"Unanticipated Adverse Device Effect" - any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects

III.1.j.2. Reporting Procedures for SAEs

This paragraph applies to serious adverse events occurring at BRANY IRB-approved investigational sites. For reporting adverse events occurring external to BRANY IRB-approved investigational sites, see the section III.1.j.3. below, titled "**External Adverse Events.**"



IRB STANDARD OPERATING PROCEDURES

Investigators are required to notify the IRB promptly of any unanticipated problems involving risks to subjects or others that occur in research (45 CFR 46.103(b)(5), 21 CFR 56.108(b) and 21 CFR 312.66). Investigators are also required to report promptly to the IRB any serious adverse event that is reported to the FDA or the Study sponsor in accordance with FDA requirements. Investigators must report all SAEs to the sponsor except for those SAEs that the protocol or other document (e.g., Investigator's Brochure) identifies as not needing immediate reporting. Investigators must follow regulatory requirements related to the reporting of unexpected serious adverse drug reactions to the regulatory authority and the IRB. For reports of deaths, investigators must supply the sponsor and the IRB with any additional requested information (e.g., autopsy reports and terminal medical reports).

Reporting Study Endpoints

Study endpoints (e.g., mortality or major morbidity) as described in the protocol ordinarily would not be reported as a serious adverse event or unexpected suspected adverse reactions to the IRB. However, if a serious and unexpected adverse event occurs for which there ***is evidence suggesting a causal relationship between the drug/device/study intervention and the event*** (e.g., death from anaphylaxis), the event must be reported to the IRB as serious and unexpected suspected adverse reaction even if it is a component of the study endpoint (e.g., all-cause mortality).

All serious adverse events and unexpected suspected adverse reactions that occur during a study, or in a post-study period of reasonable duration (30 days, or longer if in the judgment of the PI reporting is appropriate after 30 days), must be reported via the Reportable Event Form ([Appendix 13](#)), with supporting documentation as soon as possible, but in no event later than 5 business days of the researcher becoming aware of the event.

In keeping with 21CFR812.150(a)(1), an investigator shall submit to the sponsor and to the reviewing IRB a report of any unanticipated adverse device effect occurring during an investigation as soon as possible, but in no event later than 10 working days after the investigator first learns of the effect.

Reports to the IRB must contain a sufficient amount of information to permit the reviewer to judge whether the event raises new questions about risks to participants. All reports will be preliminarily reviewed by a member of the IRB administrative staff and will be subsequently reviewed by the IRB Chairperson, or designee.

If the event does not raise new concerns about risks to subjects then the report may be accepted with no further action required. The reviewer will note that the report was reviewed. The report and documentation of the review will be maintained in the IRB research application file for the project. If an event is determined by the reviewer to raise new concerns about risks to subjects, the report with the reviewer's recommendations will be forwarded to all IRB members for review at the next convened meeting. Prior to review by the convened IRB, the Chairperson may immediately take any of the actions listed in the section below titled, "**Possible**



IRB STANDARD OPERATING PROCEDURES

Actions of IRB after Review of SAEs.” The actions taken by the Chairperson will be recorded in the IRB research application file for the project.

The reviewer or the convened IRB may require the PI to: provide further information and/or clarification including a review of the occurrence of this AE in other protocols using the same drug/device; inform already enrolled subjects of the risk of the AE; and/or revise the consent document (and protocol, if applicable). The convened IRB may also change the duration of the approval period, require an increase in monitoring, suspend the project pending further information, or terminate the project. The investigator will be promptly informed of the determination of the IRB. The IRB Chairperson or Director will provide prompt written notification to relevant Federal agencies (OHRP and FDA, for FDA regulated research) of any serious unanticipated problems involving risks to subjects or others.

Upon receipt of a completed SAE report (via the [Reportable Event Form – Appendix 13](#)), it is sent to an expedited reviewer. The reviewer will consider the investigator’s summary and compare it to the risks section of the consent to determine whether any modification to the consent or the research is required.

All events should be followed up to resolution. Any new findings pertaining to a previously reported event must be submitted as a follow-up report. Such submission should indicate whether it is an Initial or Follow-up report.

III.1.j.3. External Adverse Events

Reports involving external events (those occurring outside the local investigator’s site) should only be reported to the IRB when a determination has been made that the events meet the criteria for an unanticipated problem involving risks to subjects or others as defined in section III.1.i above.

When an investigator receives a report of an external adverse event, the investigator should review the report and assess whether it identifies the adverse event as being:

- (1) unexpected;
- (2) related or possibly related to participation in the research; and
- (3) serious or otherwise one that suggests that the research places subjects or others at a greater risk of physical or psychological harm than was previously known or recognized.

Only external adverse events that are identified in the report as meeting all three criteria must be reported promptly by the investigator to the IRB as unanticipated problems under HHS regulations at 45 CFR 46.103(b)(5). Unrelated events do not require reporting to the IRB.

See section III.1.i. of this policy for procedures for reporting unanticipated problems involving risks to subject or others



IRB STANDARD OPERATING PROCEDURES

Investigators are required to notify the IRB promptly, but no later than 5 days after the Investigator's first knowledge, of any unanticipated problems involving risks to subjects or others that occur in research (45 CFR 46.103(b)(5), 21 CFR 56.108(b) and 21 CFR 312.66). A Reportable Event Form ([Appendix 13](#)) must be completed for each such report.

For Central IRB projects, the Study Sponsor may submit external adverse events determined to meet the criteria for an unanticipated problem involving risks to subjects or others directly to the BRANY IRB using the CIRB Sponsor Request for IRB Review Form ([Appendix 12](#)). The BRANY IRB will process the qualifying external adverse event reports as submitted by the Study Sponsor and forward correspondence regarding the IRB's determination to participating sites after review. The BRANY IRB will not require the Investigator to complete an Reportable Event Form in these instances. If the Sponsor elects to send qualifying external adverse event report to each participating site, the Investigator will be required to submit the qualifying external adverse event report in accordance with the policy stated above.

III.1.j.4. Possible Actions of IRB after Review of SAEs:

Actions that may be taken by the IRB include, but are not limited to one or more of the following:

- (1) The report may be accepted with no further action required.
- (2) The PI may be required to provide further information and/or clarification to the IRB.
- (3) The PI may be required to inform already enrolled subjects of the risk of the SAE.
- (4) The PI may be required to revise the consent document (and protocol, if applicable) to include the SAE.
- (5) The project may be added to the agenda of the next full board IRB meeting for review of a revision in the consent document and/or protocol.
- (6) The project may be added to the agenda of the next full board IRB meeting for consideration of: change in approval period; determination of whether event represents an unanticipated problem involving risks to participants or others; increase in monitoring; suspension of project; or termination of project.
- (7) The Chairperson of the IRB may immediately suspend enrollment in the project.
- (8) The Chairperson may immediately terminate the project.
- (9) The IRB may review the occurrence of this SAE in other protocols using the same drug/device.

The Reportable Event Form ([Appendix 13](#)) must be completely filled out with all information requested and signed by the Principal Investigator. The form should be attached to a narrative or supporting documentation describing the adverse event.



IRB STANDARD OPERATING PROCEDURES

III.1.k. Deviations

Definitions:

“Protocol Deviation”

Any temporary alteration/modification to the IRB-approved protocol. The protocol may include the detailed protocol, protocol summary, consent form, recruitment materials, questionnaires, and any other information relating to the research study. Deviations can be major or minor.

“Major Protocol Deviation”

A deviation that affects subject safety, rights, welfare, or data integrity.

Examples of major protocol deviations include (but are not limited to):

- Failure to obtain informed consent (i.e., no documentation of informed consent, consent obtained after study procedures were initiated)
- Enrolling subject who does not meet inclusion/exclusion criteria
- Use of study procedures not approved by the IRB
- Failure to report serious adverse events to the IRB and/or sponsor (per applicable requirements)
- Failure of subject to show up for a study appointment that results in missing treatment
- Failure to perform a required study procedure or lab test that could affect subject safety or integrity of study data (e.g., procedure or lab test results needed to determine eligibility for the research)
- Error in dispensing or dosing of drug/study medication, whether committed by subject or study team
- Error involving use of device
- Study visit conducted outside of required timeframe, only if it affects subject safety
- Failure to follow safety monitoring plan
- Enrollment of subjects after IRB-approval of study expired



IRB STANDARD OPERATING PROCEDURES

“Minor Protocol Deviation”

A deviation that does not affect subject safety, rights, welfare, or data integrity.

Examples of minor protocol deviations include (but are not limited to):

- Missing original signed and dated consent form (only photocopy available)
- Inappropriate documentation of informed consent, including:
 - Copy not given to the person signing the consent form
 - Someone other than the subjects dated the consent form
 - Expired consent used, but the version letter is identical to the currently approved consent form.
- Deviations from the approved study procedure that do not affect subject safety or data integrity
- Study procedure conducted out of sequence
- Omitting an approved portion of the protocol
- Failure to perform a required lab test
- Missing lab results
- Study visit conducted outside of required timeframe
- Failure of subject to return study medication

“Protocol Exception”

A deviation that has been submitted to the IRB for review, and has been approved by the IRB prior to initiation.

III.1.k.1. Procedure for Reporting Protocol Deviations to BRANY IRB

It is the responsibility of the PI to determine if a deviation is major or minor. Reports of protocol deviations should also be submitted to the sponsor according to the sponsor’s protocol.

Major Protocol Deviations

Major protocol deviations must be reported to the IRB within ten (10) working days of discovery using the Reportable Event Form ([Appendix 13](#)).



IRB STANDARD OPERATING PROCEDURES

The IRB Chairperson or designee will review the major protocol deviation, and the following actions may result:

- (a) If the IRB chairperson or designee, after consideration of the major protocol deviation, does not have concerns about human subject safety or determines it represents minor non-compliance (see BRANY IRB SOP III.1.1.), the investigator will receive written notification indicating that a major protocol deviation has been reviewed by the IRB and no additional action is required at this time. Such deviations will be reported promptly to the IRB committee in the agenda of a subsequent IRB meeting.
- (b) If the IRB Chairperson or designee determines that the major protocol deviation does not qualify for expedited review, represents serious and/or continuing non-compliance (see BRANY IRB SOP III.1.1.), or raises new concerns about risks to subjects, the reviewer will forward the item for review by the convened IRB. The Chairperson or designee may initiate further inquiry or review, depending on the major protocol deviation. The IRB may then acknowledge the major protocol deviation, require additional information, request remedial action, or suspend or terminate IRB approval.

Major protocol deviation may also be considered unanticipated problems involving risks to participants or others, and will be processed in accordance with BRANY IRB SOP III.1.i. Numerous major protocol deviations may reflect non-compliance by the investigator and will be processed in accordance with BRANY IRB SOP III.1.i Reports of Non-Compliance.

Minor Protocol Deviations

Minor protocol deviations should be reported in aggregate to the IRB at continuing review or with notification of study closure, using a protocol deviation log (see [Appendix 54](#)).

The designated IRB reviewer will review the minor protocol deviation log in conjunction with the materials provided in the application for continuing approval or the notification of study closure. The designated IRB reviewer will consider whether the reported minor deviations represent serious and/or continuing non-compliance, and if so, will forward to the convened IRB for review in accordance with BRANY IRB SOP III.1.1. Logs processed with applications for continuing approval will be processed in accordance with BRANY IRB SOP III.1.c Continuing Review; acknowledgement of IRB review will appear on the IRB decision notice. Logs provided with notification of study closure will be processed in accordance with the BRANY IRB SOP III.1.d.3. Expedited Review of Minor Changes in Previously Approved Research; acknowledgement of IRB review will appear on the IRB notification acknowledging receipt of the notification of study closure.

Deviation Report Contents

All reports of protocol deviations submitted to the IRB should include:



IRB STANDARD OPERATING PROCEDURES

- A detailed description of the incident
- Indication as to whether the deviation placed any subject at risk
- Indication as to whether the deviation affected the integrity of the study data
- A description of any changes to the protocol or other corrective actions that have been taken or are proposed in response to the deviation
- Information regarding changes implemented by the study team to ensure that such deviations will not occur in the future.

III.1.k.2. Procedure for Requesting Approval of Protocol Exceptions from BRANY IRB

If the investigator wishes to deviate from the IRB-approved protocol, he or she must submit such a request using the Reportable Event Form (Appendix 13) to the IRB for review and approval prior to initiation of such deviation. The IRB Chairperson or designee will review the deviation. The following actions may result:

- (a) If the IRB approves the temporary change to the IRB-approved protocol, the investigator will receive written notification indicating that a **protocol exception** has been approved by the IRB.
- (b) If the IRB Chairperson or designee determines that the temporary change in the IRB-approved protocol does not qualify for expedited review or raises new concerns about risks to subjects, the reviewer will forward the item to the full board for review at an IRB meeting. The IRB may then approve, require modification to, or disapprove the requested protocol exception.

III.1.l. Reports of Non-Compliance

All reports of non-compliance must be reported to the BRANY IRB staff and to the IRB committee for investigation and corrective action as appropriate. In accordance with Federal Regulations (45 CFR 46.103(b)(5)) the IRB must promptly report any serious or continuing non-compliance with regulations that govern research in human subjects to the Institutional Official, relevant Federal regulatory and compliance enforcement agencies or offices (i.e. OHRP, FDA, ORCA).

Investigators and research staff may report non-compliance directly to the Director of the BRANY IRB. Initial notification of the non-compliance may occur via telephone to the Director of the BRANY IRB, but must be followed by a written report within 5 business days describing the non-compliance, the reason for the non-compliance (if known), the means by which the non-compliance was identified, to whom the non-compliance has been reported thus far (if anyone), and any actions taken by the research personnel as a result. Non-compliance may also be brought directly to the attention of BRANY's Institutional Official, Cynthia L. Hahn, at (516) 562-2018 or via e-mail at chahn@nshs.edu.



IRB STANDARD OPERATING PROCEDURES

Definitions:

“Non-Compliance” is defined as a failure of the Investigator or any member of the research staff to adhere to applicable federal, state, or local laws or regulations, IRB policies and procedures, and any requirements or determinations made by the IRB as part of the review of a research project. Failure to submit a research project for review and approval prior to commencing a research project is also considered non-compliance. Non-compliance can vary in nature, severity and frequency. In some cases complaints concerning research or the conduct of research may or may not involve non-compliance with BRANY IRB policies or federal regulations. Such complaints will be processed as potential unanticipated problems involving risks to subjects or others. Complaints that do not have elements of non-compliance will be processed in accordance with Policy II.12 Reporting of Research Concerns.

“Serious non-compliance” is defined as a failure of the investigator or any member of the research staff to adhere to applicable laws or regulations, IRB policies and procedures, and any requirements or determinations made by the IRB as part of the review of a research project, and such failure increases risk to subjects, or adversely affects the rights and welfare of research subjects. A single instance of non-compliance may be serious. Any failure to comply may be serious or continuing if it either actually, or potentially, increases risks or adversely affects the rights and welfare of the participants.

Examples of serious non-compliance include, but are not limited to:

- (1) Failure to obtain IRB approval prior to initiation of research project;
- (2) Continuation of research activities when the IRB approval for the research protocol has expired (i.e., failed to file for continuing review);
- (3) Failure to notify the IRB of changes in ongoing research (e.g., major protocol deviations, amendments, SAEs);
- (4) Failure to obtain informed consent;
- (5) Failure to document informed consent; or
- (6) Failure to properly document the research and research procedures.

“Continuing non-compliance” is defined as a pattern of reports of non-compliance that, if unaddressed, may compromise the integrity of the human research protection program. The pattern may reflect a lack of knowledge on the part of the investigator or a lack of commitment by the investigator or the research staff to human subject protection.

“Minor non-compliance” is neither serious nor continuing.

Reports of non-compliance may be reported anonymously or by any of the following:



IRB STANDARD OPERATING PROCEDURES

- (1) Investigators
- (2) Research Staff
- (3) Administrators
- (4) IRB Chair(s)
- (5) IRB committee members
- (6) IRB Staff
- (7) BRANY or Institutional Q/A auditors
- (8) Via a complaint

Note: The BRANY IRB will investigate all reports of non-compliance regardless of their origination.

III.1.I.1. Investigation and Processing of Allegations of Non-compliance

- (1) The IRB Director and Quality Assurance Manager will initially review all allegations of non-compliance to determine if the allegation is truly non-compliance. When necessary additional information may be sought from the Investigator, research staff or other appropriate parties. If the IRB Director and Quality Assurance Manager deem that there is merit to the allegation it will be forwarded to the IRB Chair or designated IRB reviewer for further evaluation.
- (2) Allegations of non-compliance will be forwarded to the IRB Chairperson or designated IRB reviewer to determine if the non-compliance is serious or continuing. If it is determined that the allegation is neither serious nor continuing, the IRB will provide documentation to the investigator indicating this determination. The IRB Chairperson or designated IRB reviewer will determine an appropriate corrective action plan, if applicable, to prevent future non-compliance. The IRB Director and/or Quality Assurance Manager will be responsible for ensuring such corrective action plan has been enacted. The QA Department may conduct a subsequent audit to confirm the corrective action plan.
- (3) If the IRB Chairperson or designated IRB reviewer determines that the allegation of non-compliance might be serious or continuing, the QA Department will conduct an audit to investigate the allegation, unless the allegation resulted from an observation during a BRANY QA audit. If the IRB Chairperson determines the allegation appears to place subjects at risk, the Chairperson may call for immediate suspension or termination of the research project. If the designated IRB reviewer determines the allegation appears to place subjects at risk, he/she will immediately notify the IRB Chairperson, and the IRB Chairperson may call for immediate suspension or termination of the research project.



IRB STANDARD OPERATING PROCEDURES

- (4) Audit findings will be presented to the Institutional Official, IRB Chair(s) and the item will be reviewed by the IRB at a convened meeting.
- (5) All IRB members scheduled to attend the IRB meeting will be sent the relevant materials for review, including a synopsis of the event, audit report results and any other information deemed pertinent.
- (6) The IRB Chair or designated IRB reviewer will be assigned the primary review of the item and will present the review to the convened IRB. In addition to the materials referenced above, the Chair will receive the currently IRB approved protocol and consent document, any other reports of unanticipated problems involving risks to subjects or others and the Investigator Drug/Device Brochure, if applicable. If possible, the QA auditor who conducted the initial investigation will also be in attendance at the meeting to assist in the presentation of the issues and address any additional questions or concerns pertaining to the matter.
- (7) The IRB will consider whether the allegation of non-compliance is based on fact and decide, by vote, whether or not the allegations represent non-compliance. If so, the IRB will further determine if the non-compliance is serious or continuing.
- (8) When the IRB determines that serious or continuing non-compliance has occurred, the committee must further determine one or more of the following:
 - (a) Is suspension or termination of the research warranted (if so policy III.1.m Suspension/Termination of IRB Approval, will be followed)?
 - (b) Is additional investigation of the Investigator warranted?
 - (c) Is a corrective action plan required and if so will the IRB require:
 - (i) Modification to the research protocol
 - (ii) Modification to the informed consent document
 - (iii) Subjects to be re-consented
 - (iv) Earlier continuing review of the project
 - (v) Monitoring of the consent process
 - (vi) Increased monitoring of the research
- (9) The Investigator will be informed of the IRB's findings in writing from the IRB Director. The letter will be drafted by the IRB director, or designee, and will be reviewed by the QA Manager and the IRB Chair. The letter will include:
 - (a) a summary of the IRB's findings,
 - (b) actions required by the IRB;
 - (c) a request for the Investigator to provide a corrective action plan
 - (d) a deadline by which the Investigator must respond
 - (e) a date when the information will be considered by the full board



IRB STANDARD OPERATING PROCEDURES

Prior to distribution the letter will be approved by the IRB Chair(s) and the Institutional Official.

- (10) The Investigator must address the IRB's findings in writing within the specified timeline assigned by the IRB. The Investigator may, upon request, make a presentation directly to the IRB at a convened meeting. If any part of the corrective action plan requires more than minor modifications to the research, such changes must be submitted for full board review by the IRB. The IRB may allow changes that do not involve more than minor modifications to be reviewed by Expedited Review.
- (11) The Investigator's response will be reviewed by the IRB at a convened meeting. All members scheduled to attend the meeting will be provided with the response and any other relevant materials. The IRB Chair will be assigned as the primary reviewer.
- (12) The IRB may:
 - (a) Accept the Investigator's response and report that the issue was satisfactorily resolved and no further action is needed.
 - (b) Request additional information from the Investigator (which will also be submitted to the IRB in accordance with the procedures described above)
 - (c) Suspend and/or terminate the research
- (13) Vote counts and determinations made by the IRB will be documented in the IRB meeting minutes. All documentation will be maintained in the IRB Record.

In addition, BRANY IRB SOP III.1.o. Reporting Procedures will be followed as appropriate.

III.1.m. Suspension/Termination of IRB Approval

The BRANY IRB retains the authority to suspend or terminate its approval of a project that is not being conducted in accordance with the IRB's requirements or that has been associated with unexpected serious harm to subjects. Upon utilizing this authority, the BRANY IRB will always take the rights and welfare of subjects into consideration. Reasons for suspension or termination may include, but are not limited to, serious or continuing non-compliance, serious protocol violations/major protocol deviations, concerns regarding subject safety, or failure to conduct the research in accordance with applicable regulations, FDA's GCP guidelines, BRANY policies, or Institutional Review Board requirements. Any suspension or termination of IRB approval shall be reported in accordance with BRANY IRB SOP III.1.o. Reporting Procedures.

Definitions:

"Suspension"



IRB STANDARD OPERATING PROCEDURES

A directive of the convened IRB or IRB designee, or of a person/entity other than the convened IRB, either to stop temporarily some or all previously approved research activities, or to stop permanently some previously approved research activities. Suspended protocols remain open and require continuing review.

“Termination”

A directive of the convened IRB or IRB designee, or of a person/entity other than the convened IRB, to stop permanently all activities in a previously approved research protocol. Terminated protocols are considered closed and no longer require continuing review.

III.1.m.1. Suspension of IRB Approval

The IRB can suspend enrollment in the project or temporarily terminate the rights of the individual to be an investigator, thus halting all BRANY-IRB reviewed research for which the suspended investigator is the principal investigator. Suspensions may also be initiated by entities other than the IRB (e.g., investigator’s institution, regulatory agency). When the IRB makes a decision to suspend IRB approval of a project, the IRB will consider actions that may be necessary to protect the rights and welfare of currently enrolled participants (e.g., whether or not current participants should be notified of the suspension, procedures for safe withdrawal of enrolled participants and any needed follow-up procedures, and whether any adverse events or outcomes have been reported to the IRB). The investigator will be informed in writing by the Chairperson(s) or the administrative staff of the IRB, as designated by the Chairperson(s) of the decision to suspend the research.

Suspensions initiated by a person/entity other than the convened IRB must be reported to and reviewed by the convened IRB. When notified of a suspension initiated by a person/entity other than the convened IRB, BRANY IRB will request a prompt report (as soon as possible but in no case later than within 10 working days of discovery) from the suspending person/entity that describes:

1. actions taken to protect the rights and welfare of currently enrolled participants, if any,
2. whether procedures for withdrawal of enrolled participants take into account their rights and welfare (e.g., making arrangements for medical care outside of a research study, transfer to another researchers, and continuation in the research under independent monitoring),
3. a proposal for informing current participants of the termination or suspensions, or rationale for not informing current participants, and
4. whether any adverse events or outcomes need to be reported to the IRB.

Reinstatement of the investigator can only occur if there is concurrence from the investigator’s institution and will require that the investigator and their research team complete a corrective action plan that will be developed with assistance from the BRANY IRB or the institution, as appropriate, and monitored by the BRANY IRB and



IRB STANDARD OPERATING PROCEDURES

the institution. When the IRB has made the decision to suspend approval of a project, no new study activity is permitted. Only follow-up of already enrolled subjects should occur. The Principal Investigator has the opportunity to respond to the IRB's findings. BRANY IRB's suspension may be lifted or result in termination of IRB approval.

III.1.m.2. Termination of IRB Approval

The IRB can terminate IRB approval for a project, thus halting all research activity. Terminations may also be initiated by persons/entities other than the IRB (e.g., investigators' institution, regulatory agency). When the IRB has made the decision to terminate approval of a project, the IRB will ensure that: current participants are notified that the study has been terminated; procedures for withdrawal of enrolled participants will consider their rights and welfare with regards to health and safety; the participants will be informed if follow-up is permitted/required for safety reasons; adverse events should be reported to the IRB/sponsor.

Terminations initiated by a person/entity other than the convened IRB must be reported to and reviewed by the convened IRB. When notified of a termination initiated by a person/entity other than the convened IRB, BRANY IRB will request a prompt report (as soon as possible but in no case later than within 10 working days of discovery) from the terminating person/entity that describes:

1. actions taken to protect the rights and welfare of currently enrolled participants, if any,
2. whether procedures for withdrawal of enrolled participants take into account their rights and welfare (e.g., making arrangements for medical care outside of a research study, transfer to another researchers, and continuation in the research under independent monitoring),
3. a proposal for informing current participants of the termination or suspensions, or rationale for not informing current participants, and
4. whether any adverse events or outcomes need to be reported to the IRB.

III.1.n. Institutional Review Board Review and Approval Considerations

Federal regulations (45 CFR 46.111 and 21 CFR 56.111) detail specific criteria for the approval of research in human subjects. The BRANY IRB will determine that all of the following requirements are fulfilled before granting approval to the proposed research. When necessary, the IRB may seek assistance from a consultant to provide additional expertise to the IRB. The conclusions of the consultant's review will be communicated to the IRB as part of the IRB review and approval process. These criteria will be considered by the IRB upon initial review, as well as at the time of continuing review or when reviewing modifications to previously approved research.

III.1.n.1. Levels of Risk



IRB STANDARD OPERATING PROCEDURES

The IRB must consider the overall level of risk to subjects when evaluating proposed research. This evaluation must include consideration of physical, psychological, social, economic and legal risks that might be associated with the research. The IRB will distinguish between research that is greater than minimal risk from that which is no greater than minimal risk.

“Minimal risk means that the probability and magnitude of harm or discomfort in the research are not greater in and of themselves than those encountered in daily life or during the performance of routine physical or psychological examinations or test” (45 CFR 46.102 (i)).

For research subject to the requirements of the **Department of Defense**, the definition of the minimal risk based on the phrase “ordinarily encountered in daily life or during the performance of routine physical or physiological examinations or tests” must not be interpreted to include the inherent risks certain categories of human subjects face in their everyday life. For example, the risks imposed in research involving human subjects focused on a special population should not be evaluated against the inherent risks encountered in their work environment (e.g., emergency responder, pilot, soldier in a combat zone) or having a medical condition (e.g., frequent medical tests or constant pain).

This distinction is required in consideration of projects that might be eligible for expedited review, for a waiver or alteration of informed consent requirements (waiver of informed consent, 45 CFR 46.116 (d) and), or for a waiver of the requirement to obtain written documentation of consent (waiver of signed consent, 45 CFR 46,117 (c)), since only projects that are no greater than minimal risk are eligible for expedited review or a waiver of informed or signed consent. The IRB must also be particularly careful in its assessment of the level of risks for research that involves vulnerable subjects. However, the IRB has to assess the risk/benefit in all research proposals. For those categories of research requiring assessment of risk level, such consideration will be recorded in the IRB meeting minutes.

For research subject to the requirements of the **Department of Defense** that is greater than minimal risk, the IRB will require the appointment of a **research monitor independent of the team conducting the research**. Department of Defense requirements also permit the IRB to require this for research or studies involving no more than minimal risk, if appropriate. The IRB will ensure:

- The research monitor is appointed by name and must be independent of the team conducting the research. There may be more than one research monitor (e.g. if different skills or experience are needed). The monitor may be an ombudsman or a member of the data safety monitoring board.
- The IRB must approve a written summary of the monitors’ duties, authorities, and responsibilities. The IRB will communicate with research monitors to confirm their duties, authorities, and responsibilities.
 - The duties of the research monitor are determined on the basis of specific risks or concerns about the research. The monitor may:

IRB STANDARD OPERATING PROCEDURES

- perform oversight functions (e.g. observe recruitment, enrollment procedures, and the consent process, oversee study interventions and interactions, review monitoring plans and unanticipated problems involving risks to participants or others, oversee data matching, data collection and analysis).
 - discuss the research protocol with researchers, interview human subjects, and consult with others outside of the study.
 - report observations and findings to the IRB or a designated official.
- The research monitor will have the authority to:
 - Stop a research study in progress.
 - Remove individuals from study.
 - Take any steps to protect the safety and well-being of participants until the IRB or EC can assess.

III.1.n.2. Risks minimized

To approve a research proposal the IRB must determine that the risks are minimized by using procedures that are consistent with sound research design, do not expose subjects to unnecessary risks, and whenever appropriate, the research utilizes procedures that are already being performed on the subjects for diagnostic or treatment purposes (45 CFR 46.111(a)(1)). The IRB reviewer will assess the impact of study design on risk and assess the research plan, including research design and methodology, to determine that there are no obvious flaws that would place subjects at unnecessary risk. The design should be sound enough to reasonably expect the research to answer the proposed question, and the information gained is expected to be of scholarly or scientific importance. This assessment may include an evaluation that the research is so poorly designed or is so lacking in statistical power that meaningful results cannot be obtained. The IRB will also consider the professional qualifications and resources of the research team on a case-by-case basis.

III.1.n.3. Risks Reasonable Relative to Anticipated Benefits and to the Importance of the Knowledge to be Gained

To approve research, the IRB must determine that the risks of the research are reasonable in relation to the anticipated benefits (if any) to subjects, **and** the importance of the knowledge that may reasonably be expected to result (45 CFR 46.111 (a)(2)). The IRB will develop its risk/benefit analysis by evaluating the most current information about the risks and benefits of the interventions involved in the research, in addition to assessing the reliability of such information. Investigators must provide relevant information to the IRB as part of their research application. Additional information may be requested of the investigator or be sought by the IRB. The IRB will only consider those risks that result from the research, and will not



IRB STANDARD OPERATING PROCEDURES

consider long-range effects (e.g. public policy implications) of applying the knowledge gained in the research (45 CFR 46.111(a)(2) and 38 CFR 16.111 (a)(2)).

III.1.n.4. Equitable Selection of Subjects

To approve research, the IRB must determine that the selection of subjects is equitable and, in making this decision should take into account the purposes of the research, the setting in which the research will be conducted, and be particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, mentally disabled persons or economically or educationally disadvantaged persons (45 CFR 46.111). In general, a population that has no chance of benefiting from the research should not be selected to assume the risk associated with participation in the research. However, when the research holds out the prospect for benefit to individual subjects or groups, their participation should be sought. Limited English proficient participants should not be excluded because of inconvenience in translating informed consent documents. The IRB should also ensure that individuals are not enrolled in a research project only because it is convenient. The IRB must be aware of the importance of including women, men and children as research subjects and should not allow the arbitrary exclusion of persons of reproductive age. If specific groups of persons are excluded, the investigator must justify the exclusion on the basis of a sound scientific rationale.

For research that is subject to the requirements of the Department of Defense, when the research involves military personnel, the research must include additional protections for military research participants to minimize undue influence, including:

- Officers are not permitted to influence the decision of their subordinates.
- Officers and senior non-commissioned officers may not be present at the time of recruitment.
- Officers and senior non-commissioned officers have a separate opportunity to participate.
- When recruitment involves a percentage of a unit, an independent ombudsman is present.

III.1.n.5. Evaluation of Staff Available to Conduct Research

The IRB must consider whether or not the investigative site maintains the necessary staffing required to adequately conduct the research. To make this determination the reviewer will consider the number of research protocols the investigator is performing that are actively enrolling participants, the total number of subjects enrolled across all research projects, the expected rate of accrual for the project under review, the number, complexity and length of study visits required by the protocol, the condition



IRB STANDARD OPERATING PROCEDURES

under study, and the frequency and complexity of side effects that may result from the research.

The experience of the research staff must also be evaluated. Based on the Investigator's CV and information provided in the Research Application submitted, the reviewer will determine if the principal investigator and research staff has appropriate experience in conducting research and maintaining accurate and complete study records.

III.1.n.6. Review of Plans for Data and Safety Monitoring

To approve research, the IRB must determine that, where appropriate, the research plan makes adequate provision for monitoring the data to ensure the safety of subjects. A general description of the data and safety monitoring plan should be submitted to the IRB as part of the proposal for research projects in which the risks are substantial. For sponsored studies, the study sponsor may establish an independent data monitoring committee (DMC) or a Data and Safety Monitoring Board (DSMB) when the research is blinded, involves multiple sites, targets vulnerable subjects, and/or utilizes high-risk interventions. The DMC or DSMB should include members who would not otherwise be associated with the research sponsor. The IRB has the authority to require a DMC or DSMB as a condition of approval of research when the IRB determines that such monitoring is indicated.

III.1.n.7. Review of Interim Analysis Reports, Data Monitoring Committee (DMC), Data and Safety Monitoring Board (DSMB) Reports

Investigators are required to forward any interim analysis and/or DMC and DSMB reports to the IRB upon receipt. The review of these reports will be handled in the same manner as detailed above (Section III.1.i.) for internal reports of unanticipated problems involving risks to subjects or others or adverse events.

Interim Analysis and/or DMC and DSMB reports should be submitted (if available) on continuing review.

III.1.n.8. Local Research Context

Federal guidance requires the IRB to consider the local research context in reviewing research proposals. Federal regulations at 45 CFR 46.107(a) further require that IRBs be (i) sufficiently qualified through the diversity of the members, including consideration of race, gender, and cultural backgrounds and sensitivity to such issues as community attitudes, to promote respect for its counsel; and (ii) able to ascertain the acceptability of proposed research in terms of the institutional commitments and regulations, applicable law, and standards of professional conduct and practice.

In accordance with this obligation, and when appropriate, an IRB member shall serve as the local representative. In the absence of an appropriate IRB member to serve as local representative, the IRB shall obtain a written review of the Investigator's report of the local research context from one or more appropriate local



IRB STANDARD OPERATING PROCEDURES

representatives, in conjunction with participation of the local representative as a guest in convened meetings of the IRB, when such participation is deemed warranted by either the local representative or by any member of the IRB (for example, if the project involves gene transfer or a vulnerable subject population).

The IRB application for review of a research project includes questions designed to obtain information from the researchers about the community and local research environment. This section includes an area for the designated local representative to indicate concurrence with, disagreement with and/or to comment about the information provided by the investigator. The IRB's assigned primary reviewer will receive a copy of the Local Research Context Addendum ([Appendix 11](#) – part of the Research Application) for consideration with the materials he or she is assigned to review, and document his or her consideration in the appropriate area on the Reviewer Checklist ([Appendix 6](#)). The IRB will discuss any local research environment issues it feels may be relevant to the consideration of the item under review and may recommend approval, disapproval, or may defer action for the project until further information is made available for review. The minutes of the IRB meeting will also reflect any discussion by the IRB of the local research environment.

IRB staff responsibilities related to Local Research Context:

- A member of the IRB Staff will pre-review the submitted research application to assure that local research context has been addressed, when applicable.
- The IRB Staff will identify a local representative(s) and will assure distribution of the appropriate review materials, when applicable.
- The IRB Staff will maintain all documentation of local research context review in the IRB file and database as needed.

Quality Assurance Auditors may monitor the sufficiency of the information submitted from the Investigator during its auditing and monitoring activities.

III.1.n.9. Privacy of Subjects and Confidentiality of Data

To approve research, the IRB must determine that, where appropriate, there are adequate provisions to protect the privacy of subjects and the confidentiality of data. The IRB will assess the methods used to identify potential research subjects or to gather information about subjects and ensure that the privacy of the individuals is not invaded. In general, the IRB will not permit identifiable information to be obtained from private (non-public) records without the approval of the IRB and the informed consent of the subject. This will be the case even for activities intended to identify potential subjects who will later be approached to participate in research. However, there are circumstances that are exempt from the regulations, and circumstances in which the IRB may approve a waiver of the usual informed consent requirements (see Section IV.1.h. and IV.2.) for Categories of research that may be exempt from IRB review [as written in 45 CFR 46.101(b)(1-6), and 21 CFR 56.104]. Each request for waiver will be considered on a case-by-case basis.



IRB STANDARD OPERATING PROCEDURES

The IRB will also ensure that adequate measures are taken to protect individually identifiable private information once it has been collected to prevent a breach of confidentiality that could lead to a loss of privacy and potentially harm subjects.

The informed consent procedure shall include and document the extent to which a research subject can expect his confidentiality to be maintained.

The privacy of potential research subjects must also be protected. A potential subject should have the opportunity to refuse to participate before his identity is disclosed. This would be relevant when subjects are being located through files of a practitioner, clinic or institution.

Information contained in medical records (patient charts) is privileged and cannot be accessed for research purposes except with IRB approval. The IRB minutes will indicate if the IRB has granted approval to access medical records in a specified research project. The IRB may require that an investigator obtain a Department of Health and Human Services (DHHS) Certificate of Confidentiality (see Section III.4.). The Certificate of Confidentiality protects against the involuntary release of sensitive information about individual subjects for use in Federal, State, or local civil, criminal, administrative, legislative, or other legal proceedings.

While Federal and State laws allow access to medical records for approved research purposes, approval of such protocols does not convey permission to contact or recruit identified patients. Guidelines for recruiting subjects into research studies are detailed in Section III.n.11-18. of this manual. Procedures that will be used to recruit subjects (which must comply with these guidelines) must be specified in the submitted research protocol.

Research protocols that include review of medical records must also specify which procedures will be followed to ensure confidentiality of the information abstracted from the chart. For studies involving prospective chart review, informed consent for such review should be obtained from the subjects. If this is not feasible, investigators must request a waiver of informed consent following the procedures detailed in Section IV.1.h. and IV.2. See [Appendix 29](#) for form to submit a request for waiver or alteration of informed consent.

In reviewing confidentiality protections, the IRB will consider the nature, probability and magnitude of harms that would be likely to result from a disclosure of collected information outside the research. The IRB will evaluate the effectiveness of techniques for anonymizing information, coding systems, encryption methods, storage facilities, limitations on access to the data and other relevant factors in determining the adequacy of protecting subject's confidentiality. Investigators should not access medical records without IRB approval for review of those records.

NOTE:

There are risks of disclosure that remain beyond the control of the investigator and/or the hospital. Government agencies may inspect subject records for research within their jurisdiction, if they have reason to believe that the consent of subjects was not



IRB STANDARD OPERATING PROCEDURES

obtained or that the study records do not represent actual data or results. The courts may subpoena hospital treatment records on a patient, including records of a patient while on study. Additional considerations are applicable when conducting Genetic Research (see Section V.5.).

III.1.n.10. Research Using Data or Tissue Banks (also called Repositories)

All investigators who wish to develop tissue banks, repositories, and databases that utilize stored data or materials (cells, tissues, fluids, and body parts), whether the material is identifiable or not identifiable must submit their plans as projects for consideration by the IRB. Protocols must detail the policies and procedures for: a) obtaining, storing, and sharing the material in the tissue bank, repository or database for future use in research, b) assuring that the investigators who request the material have IRB approval (or exemption from IRB review) for the project that will utilize the material and c) verifying the informed consent provisions in those projects (when applicable), and for protecting the subject's privacy and maintaining the confidentiality of the data.

Projects in which the tissue banks, repositories and databases store only **non-identifiable or anonymous** material may be reviewed by expedited review. Exemptions from IRB review for such projects will be considered on a case-by-case basis, as described in Section II.2.c. (see [Appendix 27](#) for submission form for determination of exempt status).

The development of tissue banks, repositories, and databases that utilize stored data or materials (cells, tissues, fluids, and body parts) from individually **identifiable** living persons represents human subject research and requires full-board IRB review. When a principal investigator requests release of identifiable data or material from an IRB approved tissue bank, repository, or database, the BRANY IRB requires that the Director of the bank, repository, or database obtain evidence (prior to release of such data or materials) that the requesting principal investigator has an IRB approved project for the conduct of such research and that IRB approval is current. The Director should maintain the evidence for IRB approval of the specific project along with his/her records of distribution of the identifiable material.

Tissue Bank activities involve three components:

- (1) the collectors of data or tissue samples;
- (2) the bank/repository storage and data management center; and
- (3) the recipient investigators.

Since the repository must submit its protocol for review and approval to the BRANY IRB, the IRB will formally oversee all elements of repository activity, including the collection, secure storage, maintenance, and appropriate sharing of the data and/or tissues with external investigators. The IRB will review and approve the parameters for sharing data and/or tissues (which are identifiable within the repository) in a manner such that additional informed consent of subjects is, or is not, required.



IRB STANDARD OPERATING PROCEDURES

The repository may develop written agreements with investigators stipulating conditions as follows:

- (1) Whether the repository will release any identifiers to the investigator.
- (2) If material is released without identifiers, then the investigator agrees to not attempt to recreate identifiers, identify subjects, or contact subjects.
- (3) The investigator agrees to use the data only for the purposes and research specified in their protocol.
- (4) The investigator agrees to comply with any conditions determined by the BRANY IRB to be appropriate for the protection of subjects.

III.1.n.11. Recruitment of Subjects

Protocols submitted to the IRB for review and approval must specify how subjects will be identified and recruited. Recruitment plans must be submitted to the IRB for review prior to implementation. Access to all types of databases is an evolving issue, particularly with the federal laws relative to confidentiality (HIPAA). The IRB prohibits payment of a referral fee (“finder’s fees”) to individuals who refer subjects for enrollment in research projects. The IRB also prohibits providing financial incentives for recruiting subjects (“bonus payments”), which may include payments for rapid enrollment, or other gifts. Such incentives can lead to the appearance of inappropriate conduct, which may compromise the integrity of the research.

Subjects recruited for a research study must be free of any outside influences while deciding whether to participate. Even in the absence of overt coercive or inducing statements, the relationship between the potential subject and the investigator can introduce latent influence. Patients may feel obliged to agree because their physicians have asked them. Co-workers in an investigator’s laboratory, office or clinic may agree in order to preserve the good will of the investigator. Prospective research subjects must be re-assured, verbally, that refusal to participate will in no way affect their care. In addition, the IRB strongly discourages the recruitment of workers who are directly supervised by an investigator. Co-investigators and colleagues (in the specific sense of having a comparable position to the investigator) may be considered appropriate potential control subjects if such a population is needed.

If investigators are involved in more than one research project that may involve the same study population, the investigator should not influence which project the potential subject participates in, and should provide a plan describing how potential subjects will be presented with information about the various research projects available.

III.1.n.12. Guidelines for Pre-Screening Subjects for Recruitment



IRB STANDARD OPERATING PROCEDURES

The potential subject's permission to be contacted must be obtained prior to direct contact by study staff. Those subjects who respond to advertisements or recruitment letters have implicitly given their permission to be contacted.

Questions during pre-screening should address the research project's inclusion/exclusion criteria and other issues related to the potential subjects' participation in the research, such as, the ability to come to the research site multiple times. Pre-screening should not include gathering specific information about an individual's medical history or any other specific details of the individual's condition. Such information should only be solicited once informed consent is obtained and the subject is enrolled in the research project.

III.1.n.13. Telephone Screening

At the beginning of a phone pre-screening conversation, potential subjects should be informed of the nature and sensitivity of the questions, asked whether this is an appropriate time for them to answer these questions, and told how long the phone call is expected to take. The questionnaires or screening tools that will be used must be submitted to the BRANY IRB for review prior to use. A script of what will be said by study staff must also be submitted for review and approval.

In the interests of confidentiality, the researcher should record only the subject's first name or initials at the beginning of the screening conversation; explain to the subject that s/he will be asked a set of questions to determine eligibility and that at the end, only if s/he appears to be eligible and is interested in pursuing the study, will s/he be asked to provide contact/identifying information (e.g. last name, address, birth date, Social Security number or hospital medical record number). By following this procedure, **identifiable** healthcare information is only created for those persons who likely meet eligibility criteria. And for those persons who do not meet entry criteria, only **non-identifiable** health information is created. This distinction is of particular import in light of Health Insurance Portability and Accountability Act (HIPAA) privacy regulations (see section VII). The collection of non-identifiable health information is not subject to privacy regulations. But the collection of identifiable, historical medical information (even by telephone) creates new "Protected Health Information" and obligates the researcher to provide all of the HIPAA Privacy protections.

For the Collection of Identifiable Health Information: The following guidelines for handling identifiable new healthcare information became effective on April 14, 2003: Under the "preparatory to research" provision of the HIPAA Privacy Rule, an investigator may maintain identifying information at the end of the screening conversation until the subject meets with study staff to discuss the study further and sign the consent form. (If identifiable health information is collected on persons who are not enrolled, there are two options: (1) destroy the information or (2) if a failure log must be maintained, the PI must obtain authorization from each individual - see IV.4. below). During this meeting, the subject must be asked to sign the written authorization to use and disclose his/her identifiable healthcare information and be given a copy of the authorization form.

III.1.n.14. Pre-Screening Through Centralized Phone Banks



IRB STANDARD OPERATING PROCEDURES

National advertisements are sometimes used to recruit subjects for large multi-center studies. Typically, centralized phone banks or operators receive calls from individuals who see such advertisements, and then screen subjects and refer those eligible and interested to local investigators. Phone screeners interacting with potential subjects in this setting are generally not employees or healthcare providers, and typically work from a script or data collection tool that must be reviewed and approved by the BRANY IRB before use. Such a recruitment plan should be noted in the protocol, and forwarded to the IRB for review and approval prior to implementation. Research sponsors must comply with HIPAA privacy regulations regarding the use of such a centralized phone bank. Potential subjects should be told they are speaking to a non-medical screener at a centralized phone bank, and not be led to believe they're speaking with a physician or member of the actual clinical research team. This is especially relevant to protocols involving depression or other psychiatric illnesses. Study Sponsors or their screeners should have policies on what will happen if subjects calling are found to be at serious risk of harm to self and others (e.g. suicidal) and provide such plans to the BRANY IRB for review.

The guidelines listed above may not be applicable to every situation that arises in the research process. Alternative approaches may be considered on a case-by-case basis.

III.1.n.15. Retaining Information Obtained From Pre-Screening

It is acceptable to retain non-identifying information about individuals who are pre-screened for a study, but do not actually pursue the study or enroll. In fact, this is often desirable or even requested by industrial or academic sponsors to obtain information about the entire pool of individuals interested or potentially eligible for the study. Pre-screening sheets from individuals who did not provide identifying information can be retained with no further action. Pre-screening logs with identifying information may also be retained in research files, but must have segments containing identifiable information redacted. If identifiable health information is to be retained, a HIPAA Authorization must be secured from each of the individuals screened.

III.1.n.16. HIPAA Waivers for Recruitment Purposes

The nature of some studies may make the use of traditional recruitment methods unrealistic. An alternative to asking each research subject for an authorization is to ask the IRB or Privacy Board for a waiver of authorization or an alteration of the standard elements of an authorization. The Privacy Rule includes specific guidelines for the IRB or Privacy Board to follow in granting the request for a waiver of authorization. Investigators may apply for a waiver from the requirements of HIPAA (see [Appendix 11](#) – part of the Research Application) for recruitment purposes. The investigator must provide justification to the Privacy Board and the IRB, and must receive approval for this recruitment method prior to implementation.

III.1.n.17. Family Members



IRB STANDARD OPERATING PROCEDURES

If recruitment of family members is planned, for confidentiality reasons, the primary patient should not be asked to provide the name of the family member(s) directly to the investigator. Rather, the subject should be asked to contact family members. If the family member is willing to speak with the investigator, then the family member should be asked to contact the investigator. When research includes family members, the protocol and consent form must indicate how family members will be contacted.

III.1.n.18. Physician-to-Physician Referrals

Investigators may contact other physicians as appropriate to assist in identifying potentially eligible subjects. The other physician can then inform the potential subjects of the study opportunity and provide the investigator's study contact information. To protect patient privacy and maintain confidentiality, the information exchanged about potential subjects between physicians and investigators must comply with HIPAA (see section VII).

III.1.o. Reporting Procedures for Unanticipated Problems Involving Risks to Subjects or Others, Non-Compliance, or Suspension or Termination of IRB Approval

Reports of: a) unanticipated problems involving risk to subjects or others, b) serious or continuing non-compliance, and/or c) suspension or termination of approved research, must be promptly reported to the IRB, the Institutional Official, sponsor, the appropriate institutional liaison, and the appropriate regulatory agencies.

The BRANY IRB will comply with all applicable local, state, and federal regulations concerning the conduct of research.

Once the BRANY IRB has taken any of the following actions:

- Determined that an event represents an unanticipated problem involving risks to subjects or others
- Determined that non-compliance was serious or continuing
- Suspended or terminated approval of research.

Or, once the HRPP Committee has determined that IRB non-compliance was serious or continuing, then the IRB Director or designated staff will prepare a letter including the following information, as applicable:

- the nature of the event (unanticipated problem involving risks to subjects or others, serious or continuing non-compliance, suspension or termination of approval of research),
- the name of the institution conducting the research,
- title of the research project in which the problem occurred,
- name of the principal investigator on the protocol,
- the BRANY IRB file number,



IRB STANDARD OPERATING PROCEDURES

- a detailed description of the problem including the findings and the reasons for the determination,
- actions the organization/institution is taking or plans to take to address the problem the (e.g., revise the protocol, suspend subject enrollment, terminate the research, revise the informed consent document, inform enrolled subjects, increase monitoring of subjects, corrective and preventative actions, etc.), and
- any plans to send a follow-up or final report by the earlier of a) a specific date or b) when an investigation is completed or a corrective action plan has been implemented

The IRB Chair(s) and the Institutional Official will review such correspondence and recommend modifications as necessary.

The IRB Director will compose the letter and copies will be sent to:

- Principal Investigator
- The Institutional Official
- Institutional Liaison
- Sponsor and/or CRO (Contract Research Organization), if applicable
- OHRP, if the study is subject to DHHS regulations or subject to a DHHS Federalwide Assurance
- FDA, if the study is subject to FDA regulations.
- Other sites involved in the research, when appropriate.
- If the study is conducted or funded by any Federal Agency other than DHHS that is subject to "The Common Rule" such as:
 - (i) Agency for International Development (22 CFR 225)
 - (ii) Central Intelligence Agency (Executive order)
 - (iii) Consumer Products Safety Commission (16 CFR 1028)
 - (iv) Department of Agriculture (7 CFR 1c)
 - (v) Department of Commerce (15 CFR 27)
 - (vi) Department of Defense (32 CFR 219)
 - (vii) Department of Education (34 CFR 97)
 - (viii) Department of Energy (10 CFR 745)
 - (ix) Department of Homeland Security (Public law 108-458 Sec. 8306)
 - (x) Department of Justice (28 CFR 46)
 - (xi) Department of Transportation (49 CFR 11)
 - (xii) Department of Veterans' Affairs (38 CFR 16)
 - (xiii) Environmental Protection Agency (40 CFR 26)



IRB STANDARD OPERATING PROCEDURES

- (xiv) Housing and Urban Development (24 CFR 60)
- (xv) National Aeronautics and Space Administration (14 CFR 1230)
- (xvi) National Science Foundation (45 CFR 690)
- (xvii) Office of Science and Technology Policy (Adoption of policy)
- (xviii) Social Security Administration (Public law 7.5.26)

The report is sent to OHRP or the head of the agency as required by the agency.

- If the event involves unauthorized use, loss, or disclosure of PHI, the Privacy Officer should be sent a copy of the letter.
- If the event involves serious or continuing non-compliance by the IRB, OHRP and/or FDA, will be notified as applicable.

For multi-center research projects, only the institution at which the subject(s) experienced an adverse event determined to be an unanticipated problem (or the institution at which any other type of unanticipated problem occurred) must report the event to the supporting agency head (or designee) and OHRP (45 CFR 46.103(b)(5)). Reporting to FDA is not required if the event occurred at a site that was not subject to the direct oversight of the institution/organization, and the agency has been notified of the event by the investigator, sponsor, another organization, or other mechanisms.

The IRB Director will ensure that such reporting is completed within 30 days after the IRB's or HRPP Committee's determination has been made. Whenever possible and in the event of more serious actions, the IRB Director will expedite this process.

For research supported by the **Department of Defense** (DoD), prompt reporting (no longer than within 30 days) to the DoD human research protection officer.

III.1.p. Reporting and Procedures for AAHRPP Accreditation

In accordance with the requirements of its accreditation and timelines specified by AAHRPP, BRANY HRPP will submit annual reports to AAHRPP. BRANY HRPP will also re-apply for accreditation at intervals determined by the accrediting organization, and will fulfill other interim reporting requirements, including:

- Notification to AAHRPP as soon as possible, preferably within 72 hours, of any:
 - Inquiries from a government oversight office, such as the OHRP or the FDA, when the inquiry could result in a for-cause investigation.
 - Any findings or changes concerning its Human Research Protection Program that might affect its ability to continue to meet AAHRPP standards.



IRB STANDARD OPERATING PROCEDURES

- Notification to AAHRPP within 24 hours of any sanctions taken by a government oversight office.

III.2. Advertising

Advertising for recruitment of subjects should be seen as an extension of the informed consent and subject selection process. All advertisements should be submitted to the IRB for approval. IRB review is necessary to ensure that the information is not misleading to subjects, especially when a study will involve persons with acute or severe physical or mental illness or persons who are educationally or economically disadvantaged. Advertising may be approved via expedited review when the advertisements can be easily compared to the information in the approved consent form. When the advertisements submitted are more complicated, the advertising should be reviewed at a convened meeting of the IRB. The expedited reviewer and/or the IRB will review the information contained in the advertisement, its mode of communication and visual effects.

III.2.a. Information Required on an Advertisement for Recruitment

Advertisement for recruitment of subjects or patients to participate in clinical research studies should consider the target audience. Basic consideration should be given to the following points:

- (1) The advertisement must state that an activity is research.
- (2) The purpose of the research and, in summary form, the eligibility criteria that will be used to admit subjects into the study.
- (3) Information regarding the contact point, such as the address, e-mail information and/or telephone number must be included.
- (4) If benefits are discussed, a straightforward and truthful description of the benefits to the subject from participation in the study.
- (5) Any advertisement that may be read or heard by the target population must be submitted to for review to the BRANY Institutional Review Board. This includes "Dear Patient" letters, fliers and posters.
- (6) "Advertisements" to the medical community need not be reviewed by the Institutional Review Board. This includes "Dear Colleague" letters and posters for nursing stations, unless it is likely that prospective subjects will see the advertisement. Such letters should be HIPAA compliant and not include a plan for collecting PHI. Rather, the letter should direct the colleague to have the potential subject contact the research investigator.

Advertisements for subject recruitment should include eligibility criteria that are written in lay terminology.



IRB STANDARD OPERATING PROCEDURES

To avoid misleading subjects and violating the FDA's regulations concerning the promotion of investigational drugs (21 CFR 312.7 (a)) and of investigational devices (21 CFR 812.7 (d)), the advertisement should NOT:

- (a) State or imply a favorable outcome beyond what is described in the consent document
- (b) Make claims that the drug or device is safe and effective.
- (c) Make claims that the test article is equivalent or superior to any other drug or device.
- (d) Use terms such as "new treatment", "new medication" or "new drug" without explaining it is investigational
- (e) Promise "free medical treatment" when the intent is to say the subject will not be charged.
- (f) Emphasize the payment or the amount to be paid, by such means as larger or bold type, or by use of formatting, graphics or backgrounds that would emphasize payment. Study completion bonuses are not permitted by BRANY IRB and should not be included in any advertisement for the research.
- (g) Include exculpatory language

III.2.b. Submission of Advertisements to the IRB

Advertisements may be submitted to the BRANY Institutional Review Board by the Principal Investigator or their authorized designee at the time of initial protocol submission or following receipt of IRB approval with the appropriate Request for IRB Review Form ([Appendix 15](#)).

NOTE: The final copy of a printed advertisement must be submitted; BRANY IRB will not approve incomplete or template forms of advertisements. BRANY IRB will review a script of an audio/video tape advertisement; however, the advertisement may not be broadcast until the final audio/video advertisement is submitted for BRANY IRB review and approval.

III.2.c. Listing of Clinical Trials on the Internet and/or Public Registries

IRB review is not required when the information is limited to basic trial information, such as title, purpose of the study, protocol summary, basic eligibility criteria and study site location and contact information.

III.3. Payment to Research Subjects:



IRB STANDARD OPERATING PROCEDURES

III.3.a. Justifying External Factors

While the IRB recognizes that an offer of payment might encourage a greater willingness of volunteers to participate, the importance of recruiting voluntary subjects in non-therapeutic research justifies such payments. Since almost any amount of such payment could be considered an undue inducement in certain circumstances, the IRB recognizes that such payments must be reasonable and not excessive.

III.3.b. Review of Compensation for Reasonableness

Generally, payments to cover travel or childcare expenses per visit are acceptable for routine study visits, with higher amounts allowable for extended stays or increased inconvenience. However, excessive compensation should not be offered as it might unduly influence a subject to participate. The IRB will review the compensation offered and ascertain the reasonableness in light of the study specific details and the subject population. The informed consent document should describe when and in what form subjects can expect to receive compensation, including a payment schedule. Compensation should not be contingent upon completion of the study. Compensation should not include coupons to purchase the study product. BRANY IRB does not permit bonus payments to complete the study, as they may induce participants to stay in the study when they would otherwise have withdrawn.

For research that is subject to the requirements of the **Department of Defense**, when the research involves military personnel, the research must include additional protections for military research participants to minimize undue influence, with limitations on dual compensation. The research must address the following:

- Prohibit an individual from receiving pay of compensation for research during duty hours.
- An individual may be compensated for research if the participant is involved in the research when not on duty.
- Federal employees while on duty and non-Federal persons may be compensated for blood draws for research up to \$50 for each blood draw.

Non-Federal persons may be compensated for research participating other than blood draws in a reasonable amount as approved by the IRB according to local prevailing rates and the nature of the research.

III.3.c. Compensation in Pediatric Research

In reviewing pediatric research, the IRB must consider the appropriateness of the payment to the parents/guardian, as well as to the child, if any. Reimbursements must not unduly influence either the parents or the children, and must be reasonable in relation to the visits and discomfort involved in the research.

III.4. Certificates of Confidentiality



IRB STANDARD OPERATING PROCEDURES

The IRB may determine that special protections are needed to protect subjects from the risks of investigative or judicial processes in research projects that include the collection of highly sensitive information about individually identifiable subjects and such information is necessary to achieve the research objectives. Research will be considered sensitive if it involves the collection of information in any of the following categories (see OHRP guidance at <http://www.hhs.gov/ohrp/policy/certconf.html>):

- (1) Information relating to sexual attitudes, preferences, or practices;
- (2) Information relating to the use of alcohol, drugs or other addictive products;
- (3) Information pertaining to illegal conduct;
- (4) Information that if released could reasonably be damaging to an individual's financial standing, employability, or reputation within the community;
- (5) Information that would normally be recorded in a patient's medical record, and the disclosure of which could reasonably lead to social stigmatization or discrimination;
- (6) Information pertaining to an individual's psychological well being or mental health;
- (7) Genetic Information.

For such sensitive research, the IRB may at its discretion require that the investigator obtain a Certificate of Confidentiality from the DHHS (federal funding is not a prerequisite). For studies not funded by DHHS the sponsor/investigator can request a Certificate of Confidentiality from FDA if there is an Investigational New Drug Application (IND) or an Investigational Drug Exemption (IDE). The purpose of the Certificate of Confidentiality is to protect against involuntary release of sensitive information about individual subjects for use in Federal, state, or local civil, criminal, administrative, legislative, or other legal proceedings. The Certificate of Confidentiality does not prohibit voluntary disclosure of information by an investigator, such as voluntary reporting to local authorities of child abuse or a communicable disease. In addition, the Certificate of Confidentiality does not protect against the release of information to DHHS, FDA or the VA for audit purposes. The investigator must detail in the consent document the information that will be protected and that which will not be protected by the Certificate of Confidentiality. Additional information on Certificates of Confidentiality can be obtained at the NIH Web site: <http://grants.nih.gov/grants/policy/coc/>.

III.5. Compliance with All Applicable State and Local Law

In addition to Federal law regarding the protection of human research subjects, all human subject research that is conducted must comply with all relevant State and local laws and regulations. Each site is responsible for compliance with all applicable laws or regulations which provide protections for human subjects, including but not limited to laws regulating privacy, age of majority, dispensing of drugs, registration and/or approval of study by state or local officials, mental capacity, guardianship, agency, consent, civil rights, emergency care, malpractice, caregiver qualifications, records retention, patient referral, conflicts of interest, HIV/AIDS, billing, insurance, and all public health laws



IRB STANDARD OPERATING PROCEDURES

When federal regulations and other applicable laws conflict, BRANY IRB will adhere to the stricter regulation. When necessary, a legal consult will be sought for an opinion on a sites particular state law.

Note: The New York State law that is relevant is part of the Public Health Law, Article 18 and 24-A. (Article 24-A regarding protection of Human Subjects defers to applicable federal regulations.) Additional relevant New York State Law is included in the Civil Rights Law, Article 79-1, Confidentiality of Records of Genetic Tests, as well as HIV laws contained in the Public Health Law and NYCCRR section 63 and laws protecting psychiatric patients contained in the Mental Hygiene Law.

III.6. Emergency Use of a Test Article Without IRB Review

FDA regulations may allow the use of a test article (e.g., investigational drug, biologic, or investigational device) without IRB review in an emergency situation when the following circumstances are met:

- (1) A human subject is in a life-threatening situation or the subject's disease or condition is severely debilitating (e.g. blindness, loss of limb, paralysis or stroke).
- (2) The situation necessitates the use of the test article.
- (3) No standard acceptable treatment is available.
- (4) There is insufficient time to obtain IRB approval.
- (5) The emergency use of an unapproved investigational drug or biologic has an IND.
- (6) The emergency use must be reported to the IRB within five working days.
- (7) Any subsequent use of the test article is subject to prior IRB review.

The emergency use of an unapproved investigational drug or biologic requires an IND. If the intended subject does not meet the criteria of an existing study protocol, or if an approved study protocol does not exist, the usual procedure is to contact the manufacturer and determine if the drug or biologic can be made available for the emergency use under the company's IND.

The need for an investigational drug or biologic may arise in an emergency situation that does not allow time for submission of an IND. In such a case, FDA may authorize shipment of the test article in advance of the IND submission. Requests for such authorization may be made by telephone or other rapid communication means [21 CFR 312.310(d)].

In addition, in order to meet requirements for allowing emergency use of a test article without IRB review, the research must not be subject to DHHS regulations (meet the DHHS



IRB STANDARD OPERATING PROCEDURES

definition of “research” and involve “subjects” as defined by DHHS regulations) since DHHS regulations have no corresponding exemption (see 45 CFR 46.101(b)).

Although the FDA regulations allow for an exemption from prior review and approval by the IRB for emergency use, the BRANY IRB requires prior notification, if possible, of emergency use of test article so that the investigator’s intent for such use can be reviewed by the IRB Chairperson to determine if the circumstances of the emergency are in accord with FDA regulations.

If additional patients may need the test article, the investigator must submit a protocol and consent document to the IRB for review and approval. Any subsequent use of the test article is subject to IRB review whenever there has been sufficient time to convene a meeting to review the issue. IRB notification prior to the emergency use of the test article should not be construed as IRB approval.

The emergency use must be reported to the IRB within five working days using the Emergency Use Notification Form ([Appendix 39](#)). IRB staff will forward such report to the IRB Chair to determine if the emergency use met the regulatory requirements. The IRB Chairman will complete the IRB Checklist – Emergency Use ([Appendix 38](#)). Information pertaining to such emergency use will be communicated to the full committee on the agenda for the next convened IRB meeting. This reporting must not be construed as an approval for the emergency use by the IRB. The IRB will notify the appropriate institutional liaison of the emergency use.

When an investigator conducts human research that involves the emergency use of a test article in a life-threatening situation without prior IRB review, the activity is research under FDA regulations and the patient is a subject under FDA regulations. However, to comply with DHHS regulations the activity must not be considered research as defined by DHHS regulations (a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge) so that the patient will not become a subject as defined in DHHS regulations. To maintain this distinction, data from an emergency use of a test article in a life-threatening situation may not be reported in a prospectively conceived systematic investigation designed to develop or contribute to generalizable knowledge. The IRB will consider allowing an investigator to publish a retrospective report of the emergency use of a test article in a life-threatening situation. However, this process must not be used to circumvent IRB review of a prospectively conceived systematic investigation designed to develop or contribute to generalizable knowledge. Investigators may not use the emergency exception to get around the requirement for prospective IRB review.

Ordinarily, the investigator must obtain the informed consent of the subject or the subject’s legally authorized representative for such an emergency use, except as described in Section III.7.

III.7. Emergency Use of a Test Article Without Informed Consent

An exception under FDA regulations at 21 CFR 50.23 permits the emergency use of an investigational drug, device or biologic without informed consent where the Investigator and



IRB STANDARD OPERATING PROCEDURES

an independent physician who is not otherwise participating in the clinical investigation certify in writing all four of the following specific conditions:

- (1) The subject is confronted by a life-threatening situation necessitating the use of the test article;
- (2) Informed consent cannot be obtained because of an inability to communicate with, or obtain legally effective consent from, the subject;
- (3) Time is not sufficient to obtain consent from the subject's legally authorized representative (if your institution allows surrogate consent);
- (4) No alternative method of approved or generally recognized therapy is available that provides an equal or greater likelihood of saving the subjects life.

If time is not sufficient to obtain the independent physician determination before use of the test article, the actions of the Investigator must be reviewed and evaluated in writing by an independent physician within 5 working days. The emergency use must be reported to the IRB within 5 working days using the Emergency Use Notification Form ([Appendix 39](#)). This reporting must not be construed as an approval for the emergency use by the IRB.

Although the FDA regulations allow for an exemption from obtaining consent for the use of test article in a life-threatening situation, the BRANY IRB requires prior notification, if possible, of the investigator's intent to invoke the exception to obtain consent, so the IRB Chairperson can review the circumstances and determine if the exception is in compliance with FDA regulations.

Such exceptions to the requirement to obtain consent must be reported to the IRB within five working days. IRB staff will forward such report to the IRB Chair to determine if the exception met the regulatory requirements. The IRB Chairman will complete the IRB Checklist –Emergency Use ([Appendix 38](#)). Information pertaining to such exception will be communicated to the full committee on the agenda for the next convened IRB meeting. This reporting must not be construed as an approval for the emergency use by the IRB. The IRB will notify the appropriate institutional liaison of the exception.

III.8. Exception From Informed Consent (EFIC) for Planned Emergency Research

Planned emergency research applications may or may not be subject to FDA regulations. Research that is not subject to FDA regulations will be reviewed under the DHHS Emergency Research Consent Waiver effective November 1, 1996.

For research that is subject to requirements of the **Department of Defense**, an exception from consent in emergency medicine research is prohibited unless a waiver is obtained from the Secretary of Defense.

The FDA allows for research with human subjects employing experimental emergency intervention (i.e. use of non-approved drug or device) where informed consent requirements are waived, provided the IRB, clinical investigators and Sponsors meet specific requirements as outlined in 21CFR50.24 and FDA Guidance. Planned emergency research



IRB STANDARD OPERATING PROCEDURES

should not be confused with emergency interventions administered in a standard patient-care setting (e.g. administration of an experimental drug for a patient in the emergency room at a hospital) by a physician; where IRB review and oversight is not applicable.

III.8.a. Requirements

BRANY IRB with the concurrence of a licensed physician who is a member of or consultant to the IRB and who is not otherwise participating in the clinical investigation must find and document (21CFR50.24(a)):

- (1) The application clearly identifies the protocols that will include participants who are unable to consent.
- (2) Protocols using the exception from informed consent (EFIC) procedures are performed under a separate IND or IDE application that clearly identifies the protocol(s) as “EFIC” protocol(s), regardless of whether an IND or IDE already exists (21CFR50.24(d)).
- (3) The human subjects are in a life-threatening situation, available treatments are unproven or unsatisfactory, and the collection of valid scientific evidence, which may include evidence obtained through randomized placebo-controlled investigations, is necessary to determine the safety and effectiveness of particular interventions.
- (4) Obtaining informed consent is not feasible because:
 - (i) The subjects will not be able to give their informed consent as a result of their medical condition;
 - (ii) The intervention under investigation must be administered before consent from the subjects' legally authorized representatives is feasible; and
 - (iii) There is no reasonable way to identify prospectively the individuals likely to become eligible for participation in the clinical investigation.
- (5) Participation in the research holds out the prospect of direct benefit to the subjects because:
 - (i) Subjects are facing a life-threatening situation that necessitates intervention;
 - (ii) Appropriate animal and other preclinical studies have been conducted, and the information derived from those studies and related evidence support the potential for the intervention to provide a direct benefit to the individual subjects; and



IRB STANDARD OPERATING PROCEDURES

- (iii) Risks associated with the investigation are reasonable in relation to what is known about the medical condition of the potential class of subjects, the risks and benefits of standard therapy, if any, and what is known about the risks and benefits of the proposed intervention or activity.
- (6) The clinical investigation could not practicably be carried out without the waiver.
- (7) The proposed investigational plan defines the length of the potential therapeutic window based on scientific evidence, and the investigator has committed to attempting to contact a legally authorized representative for each subject within that window of time and, if feasible, to asking the legally authorized representative contacted for consent within that window rather than proceeding without consent. The investigator will summarize efforts made to contact legally authorized representatives and make this information available to BRANY IRB at the time of continuing review.
- (8) BRANY IRB has reviewed and approved informed consent procedures and an informed consent document consistent with 50.25. These procedures and the informed consent document are to be used with subjects or their legally authorized representatives in situations where use of such procedures and documents is feasible. BRANY IRB has reviewed and approved procedures and information to be used when providing an opportunity for a family member to object to a subject's participation in the clinical investigation consistent with paragraph (7)(v) of this section.
- (9) Additional protections of the rights and welfare of the subjects will be provided, including, at least:
 - (i) Consultation (including, where appropriate, consultation carried out by the IRB) with representatives of the communities in which the clinical investigation will be conducted and from which the subjects will be drawn;
 - (ii) Public disclosure to the communities in which the clinical investigation will be conducted and from which the subjects will be drawn, prior to initiation of the clinical investigation, of plans for the investigation and its risks and expected benefits;
 - (iii) Public disclosure of sufficient information following completion of the clinical investigation to apprise the community and researchers of the study, including the demographic characteristics of the research population, and its results;
 - (iv) Establishment of an independent data monitoring committee to exercise oversight of the clinical investigation; and
 - (v) Procedures are in place to inform, at the earliest feasible opportunity, each participant, or if the participant remains



IRB STANDARD OPERATING PROCEDURES

incapacitated, a legally authorized representative of the participant, of the participant's inclusion in the clinical investigation, the details of the investigation and other information contained in the consent document.

- (vi) If obtaining informed consent is not feasible and a legally authorized representative is not reasonably available, the investigator has committed, if feasible, to attempting to contact within the therapeutic window the subject's family member who is not a legally authorized representative to inform them of the participant's inclusion in the clinical investigation, of the details of the investigation and other information contained in the consent document, and asking whether he or she objects to the subject's participation in the clinical investigation.

The investigator will summarize efforts made to contact family members and make this information available to the IRB at the time of continuing review. If the subject is enrolled without providing consent, and a legally acceptable representative is not present to provide consent, the legally acceptable representative will be informed about the clinical trial as soon as possible and will provide consent if the subject wishes to continue,

- (vii) There is a procedure to inform the participant, or if the participant remains incapacitated, a legally authorized representative of the participant, or if such a representative is not reasonably available, a family member, that he or she might discontinue the participant's participation at any time without penalty or loss of benefits to which the participant is otherwise entitled.
- (viii) If a legally authorized representative or family member is told about the clinical investigation and the participant's condition improves, the participant is also to be informed as soon as feasible.
- (ix) If a participant is entered into a clinical investigation with waived consent and the participant dies before a legally authorized representative or family member can be contacted, information about the clinical investigation is to be provided to the participant's legally authorized representative or family member, if feasible.

If the IRB determines that it cannot approve a clinical investigation because the investigation does not meet the criteria in the exception or because of other relevant ethical concerns, the IRB will document its findings and provide these findings promptly (no longer than within 30 days) in writing to the clinical investigator and to the sponsor of the clinical investigation.

When research is not subject to FDA regulations, but follows DHHS regulations, BRANY IRB finds, documents, and reports to DHHS that the following conditions have been met relative to the research:



IRB STANDARD OPERATING PROCEDURES

- The IRB found and documented that the research is not subject to regulations codified by the FDA at 21 CFR 50.
- The research participants are in a life-threatening situation, available treatments are unproven or unsatisfactory, and the collection of valid scientific evidence, which may include evidence obtained through randomized placebo-controlled investigations, is necessary to determine the safety and effectiveness of particular interventions.
- Obtaining consent is not feasible because:
 - The participants are not able to give their consent as a result of their medical condition.
 - The intervention involved in the research is administered before consent from the participants' legally authorized representatives is feasible.
 - There is no reasonable way to identify prospectively the individuals likely to become eligible for participation in the research.
- Participation in the research held out the prospect of direct benefit to the participants because:
 - Participants are facing a life-threatening situation that necessitated intervention.
 - Appropriate animal and other preclinical studies have been conducted, and the information derived from those studies and related evidence supported the potential for the intervention to provide a direct benefit to the individual participants.
 - The risks associated with the research are reasonable in relation to what is known about the medical condition of the potential class of participants, the risks and benefits of standard therapy, if any, and what is known about the risks and benefits of the proposed intervention or activity.
- The research could not practicably be carried out without the waiver.
- The proposed research protocol defines the length of the potential therapeutic window based on scientific evidence, and the investigator has committed to attempting to contact a legally authorized representative for each participant within that window of time and, if feasible, asking the legally authorized representative contacted for consent within that window rather than proceeding without consent. The investigator will summarize efforts made to contact representatives and make this information available to the IRB at the time of continuing review.
- The IRB has reviewed and approved consent procedures and a consent document in accord with 45 CFR 46.116 and 46.117.
 - These procedures and the consent document are to be used with participants or their legally authorized representatives in situations where use of such procedures and documented is feasible.
 - The IRB has reviewed and approved procedures and information to be used when providing an opportunity for a family member to object to a participant's participation in the research consistent with the paragraph of this waiver.
- Additional protections of the rights and welfare of the participants are provided, including, at least:
 - Consultation (including, where appropriate, consultation carried out by the IRB) with representatives of the communities in which the research is conducted and from which the participants are drawn.



IRB STANDARD OPERATING PROCEDURES

- Public disclosure to the communities in which the research is conducted and from which the participants are drawn, prior to initiation of the research, of plans for the research and its risks
- and expected benefits.
- Public disclosure of sufficient information following completion of the research to apprise the community and researchers of the study, including the demographic characteristics of the research population, and its results.
- Establishment of an independent data monitoring committee to exercise oversight of the research.
- If obtaining consent is not feasible and a legally authorized representative is not reasonably available, the investigator has committed, if feasible, to attempting to contact within the therapeutic window the participant's family member who is not a legally authorized representative, and asking whether he or she objects to the participant's participation in the research.
 - The investigator will summarize efforts made to contact family members and make this information available to the IRB at the time of continuing review.
 - Procedures are in place to inform, at the earliest feasible opportunity, each participant, or if the participant remained incapacitated, a legally authorized representative of the participant, or if such a representative is not reasonably available, a family member, of the participant's inclusion in the research, the details of the research and other information contained in the consent document.
 - There is a procedure to inform the participant, or if the participant remained incapacitated, a legally authorized representative of the participant, or if such a representative is not reasonably available, a family member, that he or she may discontinue the participant's participation at any time without penalty or loss of benefits to which the participant is otherwise entitled.
 - If a legally authorized representative or family member is told about the research and the participant's condition improves, the participant is also informed as soon as feasible.
 - If a participant is entered into research with waived consent and the participant dies before a legally authorized representative or family member can be contacted, information about the research is provided to the participant's legally authorized representative or family member, if feasible.
 - For the purposes of this waiver "family member" means any one of the following legally competent persons: spouses; parents; children (including adopted children); brothers, sisters, and spouses of brothers and sisters; and any individual related by blood or affinity whose close association with the participant is the equivalent of a family relationship

III.8.b. Implementation of IRB requirements in accordance with 21CFR50.24(a)(7)

(1) Consultation with Community Representatives

50.24(a)(7)(i) – Consultation with community representatives should be conducted by



IRB STANDARD OPERATING PROCEDURES

the principal investigator of the EFIC protocol. The protocol should clearly identify the community/communities in which the research will take place, the target research population within those communities, the community representatives the PI has met or will be meeting with (e.g. community board president), and the setting and frequency in which the PI has met or will be meeting with the community representatives (e.g. monthly at community board meetings). The PI should provide a summary of meeting(s) with the community representatives to BRANY IRB for review. The PI can arrange their meetings with community representatives prior to or in parallel with IRB submission.

BRANY IRB will review and determine if the consultation(s) with community representatives are sufficient for the EFIC study. BRANY IRB may choose to conduct its own consultation with community representatives if it feels the PI's summary lacks sufficient information for review of the protocol. BRANY IRB may elect to invite community representatives to its IRB meeting to discuss the EFIC protocol and implications it may have on the respective community. For example, if the research will take place in East Harlem in New York City, the IRB may invite members of clergy from the local churches to an IRB meeting to discuss the prospective research, as the members of clergy will likely have sufficient knowledge of their respective neighborhoods.

Please note the FDA regulations do not specifically define a "community representative." Although "community representatives" are likely individuals that have a good knowledge of their respective neighborhoods and the people that live in those neighborhoods, it is up to the IRB to determine whether the members whom the PI is meeting with are sufficient for the study.

(2) **Prior Public Disclosure**

50.24(a)(7)(ii) – Public disclosure of the EFIC protocols must be conducted PRIOR to starting the research. The PI should present the details of the planned research at community settings appropriate to the target population (e.g. community board meetings, local churches, etc). The PI must provide BRANY IRB with a protocol that clearly outlines his/her plans for public disclosure: the information (planned procedures, risks, benefits, etc.) that will be disclosed, procedures for disclosure, and the setting and frequency in which this disclosure will take place.

BRANY IRB will review the PI's plans for the public disclosure and determine if they are sufficient and meet human research protection requirements. After BRANY IRB determines the proposed plans for disclosure are sufficient, the PI can then disclose the information in accordance with the IRB-approved plan. The PI should accurately document the discussion and any questions and concerns expressed by individuals present during this public disclosure. The PI will then need to provide a report of this disclosure to BRANY IRB for review. If BRANY IRB is not satisfied with the report, the IRB will need to outline specific details and requirements the PI will need to address in order to satisfy the IRB's concerns. This report must be reviewed and approved, in addition to the remainder of the protocol, prior to study implementation by the PI.

(3) **Disclosure to Public Post-Study Completion**



IRB STANDARD OPERATING PROCEDURES

50.24(a)(7)(iii) – After the EFIC study is completed, a summary of the study must be disclosed to the public. This summary must include sufficient information about the study, including, but not limited to, demographic information of the study population and the results from the study. The summary can also include any adverse events related to administration of the study intervention and progress of some of the research participants that may have benefited from the study intervention. The PI should submit the summary to BRANY IRB for review prior to disclosure in a public setting.

BRANY IRB will review and determine if the summary is sufficient for disclosure to the public. If BRANY IRB feels the summary is not sufficient, it will provide feedback to the PI indicating required revisions or additional information.

NOTE: FDA regulations do not specifically define what is considered “sufficient information” for this disclosure; BRANY IRB will make this determination.

(4) **Independent Data monitoring Committee**

50.24(a)(7)(iv) – The PI, prior to or in consultation with BRANY IRB, will need to establish an independent data monitoring committee (DMC) that will provide proper oversight for the study. This DMC must include physician members that are not part of the research personnel, are familiar with the study population and study interventions, and do not have any interests in the study or study drug/device that is or have the potential to be a conflict of interest. BRANY IRB will review the composition of the DMC and determine if the members are appropriate and have sufficient expertise to perform the required functions.

The DMC should meet regularly to address the safety concerns of the study and study population (e.g. monthly or bimonthly). The DMC will have the authority to recommend continuing the study, stopping the study, or stopping study interventions with a specific subject if they feel the welfare of that subject is or could be compromised by continuing the study. The PI must provide the DMC’s summaries and recommendations to BRANY IRB for review and acknowledgement.

(5) **Plans for Obtaining Consent When Feasible**

50.24(a)(7)(v) – The PI will need to provide BRANY IRB with a description of the plans for contacting a subject’s family member (who is not a court-appointed legally authorized representative or health care proxy) for permission to include the subject in the study if the PI finds that the subject could directly benefit from participation in the study and the PI cannot feasibly obtain informed consent from the subject and the subject’s legally authorized representative is not reasonably available.

BRANY IRB must review the PI’s plans for enrollment of such subjects prior to the start of the study. The PI must also provide a summary of his or her efforts to BRANY IRB for review when such subjects are enrolled.

NOTE: Exception from Informed Consent for Planned Emergency Research is prohibited for **Department of Defense** protocols unless a waiver is obtained from the Secretary of Defense.



IRB STANDARD OPERATING PROCEDURES

III.8.c. References

- (1) FDA EFIC Regulations: 21CFR50.24
- (2) FDA Guidance for EFIC for Planned Emergency Research:
<http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM249673.pdf>
- (3) DHHS Informed Consent Requirements in Emergency Research:
<http://www.hhs.gov/ohrp/policy/hsdc97-01.html>

III.9. Additional Committee Review for IRB Approved Projects

Some institutions may require that BRANY IRB approved projects be submitted for an additional review by the institution's internal research committee or Institutional Review Board. **It is the responsibility of the investigator to obtain these approvals prior to initiating research.** BRANY IRB provides IRB documentation and/or reports of ongoing research under its auspices to institutional liaisons as requested to facilitate communication and allow for integration of BRANY IRB review with institutional procedures and requirements.

EXAMPLES:

III.9.a. The New York Harbor Health Care System (VA Institutions)

Requires that the VA IRB review and approve all research.

III.9.b. The Health and Hospitals Cooperation (HHC) Public Hospitals

Require approval from the HHC central office at 125 Worth Street, NY, NY, 10013. Individual HHC institutions may have subcommittees that must approve all research at their institution.

III.9.c. BioSafety Committee

Studies that involve the use of any biohazardous materials (i.e. gene therapy) will require review and approval by a BioSafety Committee.

III.9.d. NCI Designated Centers

Require approval by the cancer committee prior to initiation of research.

III.9.e. GCRC

Require approval of GCRC research committee.

III.9.f. Radiation Safety

Projects involving radiation may require the approval of the radiation safety committee.



IRB STANDARD OPERATING PROCEDURES

III.9.g. Pharmacy Committee

Projects involving agents to be dispensed via the pharmacy may require the approval of a pharmacy committee.

III.9.h. Cooperative Research Projects

In the conduct of cooperative research projects, each institution is responsible for safeguarding the rights and welfare of human subjects. Investigators should consult their institution's policy regarding cooperative research to determine whether they may use joint review and rely on another qualified IRB to avoid duplication of effort in keeping with 21CFR56.114 and 45CFR46.114. A written agreement between the cooperating institutions should be implemented to describe how the respective IRBs will relate to each other, i.e., whether one IRB will act on behalf of all others in reviewing and overseeing the research, or whether each institution will have responsibility for local oversight.

III.9.i. Multi-Center Research

III.9.i.1. Designation of BRANY IRB

The BRANY IRB reviews research for organizations that have designated BRANY IRB as an IRB of record for their Institution. This designation can be made by amending the organization's Federalwide Assurance (FWA), if the Institution has an IRB that is registered with the Office of Human Research Protections (OHRP), or if the organization does not have an IRB, by written agreement between the organization and the BRANY IRB. The written agreement will document each party's role and responsibilities, and confirm the authority of the IRB to oversee one or multiple research projects for the organization. An individual at the organization with sufficient authority to bind the organization to the terms of the agreement must execute such agreements. While the BRANY IRB will be responsible for oversight and continuing review of the research, the Investigator and/or organization retain the responsibility for the conduct of the study.

When an Institution that has an IRB chooses to designate the BRANY IRB as an IRB of record, the Institution should document in its policies and procedures the scope of studies subject to review by the BRANY IRB. The BRANY IRB cannot become the IRB of record for studies within that defined scope unless the Institution and the Institution's IRB agree.

Investigators will be asked to provide information regarding the designation of the BRANY IRB in the Research Application submitted with a project for review. IRB staff will confirm that the appropriate agreement is in place prior to IRB review.

III.9.i.2. Responsibilities for a Lead Investigator in a Multi-Center Study



IRB STANDARD OPERATING PROCEDURES

When the BRANY IRB reviews research for which the investigator or the organization is responsible for the overall conduct of the study, the BRANY IRB will expect that the lead investigator/organization will be responsible to obtain and manage the information obtained from the multi-center research that might be relevant to participant protections, including but not limited to:

- Unanticipated problems involving risks to subjects or others
- Interim results
- Protocol Modifications

The investigator/organization is required to promptly provide this information to the IRB for review and processing.

At the time the investigator/organization submits the research for review, the BRANY IRB will require that a detailed plan for managing such information be included with the application for review. The IRB will consider the appropriateness of this plan at the time of initial review (documented via the Reviewer Checklist – [Appendix 6](#)). If necessary, the IRB may require modifications. Any subsequent changes to the original plan must be communicated to the BRANY IRB.

For Department of Defense regulated multi-center research, a formal agreement between organizations is required to specify the roles and responsibilities of each party.



IRB STANDARD OPERATING PROCEDURES

IV. INFORMED CONSENT

IV.1. Investigations Involving Human Subjects and Informed Consent

IV.1.a. Informed Consent:

No investigator may involve a human being as a subject in research until the investigator has obtained the approval of the BRANY IRB and has obtained the legally effective informed consent of the subject or the subject's legally authorized representative, except when a waiver is allowable under applicable FDA/OHRP guidelines. The consent process begins as soon as a potential research subject is approached or contacted about participation in a research project.

Consent may be obtained by the Principal Investigator, Research Coordinator or another member of the Research staff designated by the Principal Investigator. All study personnel authorized to obtain informed consent must provide evidence of training in human subject protections and a financial conflict of interest in research disclosure form.

Informed consent may only be sought under circumstances that provide the subject (or authorized representative) with sufficient opportunity to consider whether or not to participate in the research and that minimize the possibility of coercion or undue influence (45 CFR 46.116). The informed consent information must be presented in language that is understandable to the subject (or representative). The BRANY IRB recommends that consent documents be written in language understandable to individuals with an approximate sixth to eighth grade education. (See [Appendix 5: Glossary of Lay Terms for Use in Preparing Informed Consent Documents](#) and [Appendix 17: Risks and Procedures – Lay Terminology](#)) The informed consent process may not include any exculpatory language through which the subject or representative is made to waive, or appear to waive, any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, or the institution or its agents from liability for negligence. Informed consent must be obtained prior to initiation of any clinical screening procedures that are performed solely for the purposes of determining eligibility for research.

For **classified research** subject to the requirements of the **Department of Defense**, the IRB shall determine whether potential human subjects need access to classified information to make a valid, informed consent decision.

IV.1.b. IRB's Responsibilities

The BRANY IRB shall review the information given to the subjects as part of the informed consent to ascertain that the subject is informed according to the general requirements for informed consent as specified in 45 CFR 46, and 21 CFR 50.

IV.1.c. Consent Monitoring

In evaluating the adequacy of informed consent procedures, the IRB may require special monitoring of the consent process by an auditor, an individual who is not involved in the research, to ensure that there is no coercion or undue influence. Situations in which the



IRB STANDARD OPERATING PROCEDURES

IRB might consider observing the consent process as a method to protect subjects may include:

- Studies Involving Potentially Vulnerable Populations
- Studies which the IRB considers to be high risk
- Investigator's that are new to the BRANY IRB
- Situations in which the Investigator fails to provide appropriate Informed Consent documents as required at the time of continuing review (see BRANY IRB SOP III.1.c)

If the IRB has concerns, at any time during the course of a research project, that the informed consent process is not being conducted appropriately, they may require consent monitoring.

Mechanisms by which the auditor may conduct consent monitoring include:

- In person observation at the research site.
- Telephone discussion with subject.
- Review of Investigator's documentation of the informed consent process.

IV.1.d. Principal Investigator's Responsibilities

When any research project or clinical investigation is undertaken that involves human subjects, the Principal Investigator is required to observe the following:

- (1) The BRANY IRB must review the research prior to initiation. Refer to the Research Application ([Appendix 11](#)) for submission instructions.
- (2) When BRANY IRB has not approved a waiver of the requirement to obtain consent, informed consent as approved by the BRANY IRB will be obtained from the human subject (or the subject's legally authorized representative, if consent by a legally authorized representative has been approved by the IRB).
- (3) The written informed consent form and any other written information to be provided to subjects should be revised whenever important new information becomes available that may be relevant to the subject's consent, including new information that may affect the risks or benefits to subjects or a subject's willingness to continue participation in the research. Any revised written informed consent form or other revised written information to be provided to subjects should receive the IRB's approval in advance of use.

The subject or the subject's legally authorized representative should be informed in a timely manner if new information becomes available that may be relevant to the subject's willingness to continue participation in the trial. The communication of this information should be documented.



IRB STANDARD OPERATING PROCEDURES

IV.1.d.1. Re-Consent

Subjects may need to be re-consented due to changes in their status (i.e., previously enrolled by proxy and now able to consent on their own behalf) or due to changes in the protocol and/or consent form as follows:

- The protocol and/or consent form has been modified since the subject enrolled and the changes are more than administrative (i.e. the information which has been added/deleted may have an impact on risk to subjects and/or their willingness to participate).
- The subject was initially enrolled in a study by parents, a legally authorized representative or a research proxy because:
 - The subject was a minor at the time of entry into a study and has since reached the age of 18 and can now consent on his/her own behalf, or
 - The subject was incapacitated at the time of enrollment and has regained capacity to consent on his/her own behalf.

IV.1.d.1.1. Re-consent due to modifications

If the modifications are minor (see III.1.d.3. Expedited Review of Minor Changes in Previously Approved Research), including typographical errors or basic reformatting, re-consent is most likely not needed or re-consent may be accomplished by verbally informing subjects of the change with documentation in the medical record/study subject record that such notification took place.

If the modifications are more than minor and/or could affect the subject's willingness to continue participation, the IRB requires that research subjects be re-consented. It may be appropriate to provide the subject with an addendum to the original consent form that provides the new information, or to revise the full consent form. If an addendum is used, it must clearly state that the information in the original consent form is still current and valid, and that the information in the addendum is supplementary.

IRB approval letters will indicate whether or not re-consent is necessary and the method that should be used for re-consent. This information will also be documented in the IRB record.

IV.1.e. General Issues in Informed Consent Documents and Process

Clinical Investigators often find it confusing and awkward to make the distinction between the risks, benefits and purpose of a research study and those of the therapy that is being studied.

In virtually all-therapeutic trials, there are purposes and risks that are the *result of data gathering and hypothesis testing*, rather than the result of giving good quality care.



IRB STANDARD OPERATING PROCEDURES

The patient/subject is entitled to have some sense of this, to know how much risk, expense or discomfort is being borne for the sake of the investigation rather than for his or her own sake.

IV.1.f. Consent Form Criteria

Informed consent is not a single event or just a form to be signed - it is an educational process that takes place between the investigator and prospective subject

The basic elements of the consent process include:

- Full disclosure of the nature of the research and the subject's participation,
- Adequate comprehension on the part of potential subjects, and
- The subject's voluntary choice to participate

Informed consent is not valid unless the consentor understands the information that has been provided. It is the responsibility of each investigator to do what he/she can to enhance each prospective subject's comprehension of the information.

The investigator must consider the nature of the proposed research population, the type of information to be conveyed, and the circumstances under which the consent process will take place in determining the appropriate way to present the information. Investigators must also be cognizant of the fact that consent is an ongoing process. Subjects have the right to withdraw at any time and should continue to have their questions answered and be informed of any changes in the research that may impact their decision to remain in the a study. If a subject chooses to withdraw from a study early, they should be reminded that data collected to the point of withdrawal remains part of the study database and may not be removed. An investigator may choose to ask the subject permission to provide continued follow-up and further data collection subsequent to their withdrawal from the interventional portion of the research, and the investigator must obtain the subject's consent to do so. It is expected that the investigator's discussion with the subject will distinguish between study-related interventions and standard care procedures. If a participant withdraws from the interventional portion of a study and does not consent to continued follow-up of associated clinical outcome information, the researcher must not access for purposes related to the study the participant's medical record or other confidential records requiring the participant's consent. However, a researcher may review study data related to the participant collected prior to the participant's withdrawal from the study, and may consult public records, such as those establishing survival status.

If the BRANY IRB approved consent form does not already address this information, a consent form revision (or consent addendum) must be submitted for IRB review prior to implementation.

Consent is a legal concept and only legally competent adults can give consent. In most cases, children cannot give consent - only parents or legal guardians can give consent for children to participate in research.



IRB STANDARD OPERATING PROCEDURES

The “deliberate objection” of a child subject should be construed as a veto of the consent of a parent or guardian, whether that objection is verbal or non-verbal. In order to be valid, consent must be freely given - that means free from all coercion or undue influence. However, in rare instances, the IRB may waive the assent of a child in accordance with Federal regulations. In addition to overt coercion, the investigator should be sensitive to more subtle forms of coercion such as social pressure, requests from authority figures, and undue incentive for participation.

An investigator shall seek consent only under the following circumstances:

- The potential subject has the legal and mental capacity to give consent; if not, consent must be obtained from his/her legally authorized representative.
- Sufficient opportunity is provided to consider whether or not to participate to the prospective subject, or his/her representative
- The possibility of coercion or undue influence is minimized
- The information that is given to the prospective subject, or his/her representative, is in language understandable to the subject or representative (this applies to both the written informed consent form and the discussion) and
- The subject or his/her representative, is not made to waive or appear to waive any of his/her legal rights, or release or appear to release the investigator, the sponsor, the institution or its agents from liability or negligence

It is recommended that consent forms meet four criteria:

- (1) Be brief, but have complete information
- (2) Be readable and understandable to most people
- (3) Be in a format that helps people comprehend and remember the information
- (4) Serve as a script for the face-to-face discussions with the potential subjects

Format can help comprehend and remember complex material. Good format uses:

- Headings
- Indents
- Bolded types
- Lists
- Extra spacing between sub-topics
- Repetition
- Reasonable size type
- Plenty of margins and empty space in general



IRB STANDARD OPERATING PROCEDURES

IV.1.g. Documentation of Informed Consent

To approve research, the IRB must determine that informed consent will be appropriately documented (45 CFR 46.117(a)), unless documentation can be waived (45 CFR 46.117(c)). Consent will be documented through use of a written consent document that incorporates all of the required elements of informed consent as described below. If subjects agree to participate, the subjects should sign and date the consent document in the appropriate place on the form in the presence of the person obtaining consent. A consent form will be considered properly executed when signed and dated by both the subject and the person obtaining consent. The subject should be given a copy of the consent form for his/her records. The original completed, signed consent form must be retained and included in the PI's research records as part of the essential documents of the study. All subjects who sign a consent form are considered to have entered the study. The PI must retain all consent forms even if subjects are later withdrawn for any reason or do not actually participate in the project. A sample informed consent form is attached as [Appendix 19](#).

IV.1.h. Waiver of Documentation of Consent

Federal regulations require that research subjects sign a consent document (45 CFR 46.117). The IRB may waive the requirement for the subject's signature on a consent document, only under limited circumstances (45 CFR 46.117). The IRB is not obligated to approve a request for a waiver of signed consent.

Signed consent may only be waived in those situations where either:

- (a) the research presents no more than minimal risk of harm to the subject; **AND** the research involves no procedure for which written consent is normally required outside of the research context **OR**
- (b) the consent document would be the **ONLY** identifiable link between the subject and the research **AND** there is a risk of harm to the subject if information regarding the subject's participation were to be inadvertently or lawfully released.

In order for the IRB to consider a request for a waiver of informed consent, the investigator must provide the IRB with written summary of the information to be provided to the subject. The IRB will review, verify and document that the waiver request (including the written summary of the information to be provided to the subject) meets regulatory requirements and that such request is applicable to the proposed research. When granting waivers of the requirement to obtain written documentation of the consent process, the IRB will consider whether the researcher will be required to provide participants with a written statement regarding the research.

A waiver of signed consent does not exempt an investigator from obtaining informed consent. Investigators may apply for a waiver of consent using the form attached as [Appendix 29](#).

Waiver of parental/guardian permission for research involving children will be considered in accordance with Section V.1.b.5.(c) of this policy.



IRB STANDARD OPERATING PROCEDURES

IV.1.i. Basic Elements of Informed Consent

In seeking informed consent the following information shall be provided to each subject:

- (1) A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental;
- (2) A description of any reasonably foreseeable risks or discomforts to the subject;
- (3) A description of any benefits to the subject or to others which may reasonably be expected from the research;
- (4) A disclosure of appropriate alternative procedures or courses of treatment, if any, that are available to the subject;
- (5) A statement describing the extent to which confidentiality of records identifying the subject will be maintained.
- (6) A statement describing the whether any compensation and an explanation as to whether any medical treatment are available in the event of research-related injury, and if so, what they consist of or where further information may be obtained. This applies to for research involving greater than minimal risk. (NOTE: For research subject to **Department of Defense** requirements, this disclosure must follow the requirements of the DoD component.)
- (7) An explanation of whom to contact for answers to questions about the research and the research subject's rights, and whom to contact in the event of a research-related injury to the subject;
- (8) A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to the subject, and that the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

IV.1.j. Additional Elements of Informed Consent

When appropriate, one or more of the following elements of information shall also be provided to each subject (a Sample Informed Consent Form is attached as [Appendix 19](#)):

- (1) A statement that the particular treatment of procedure might involve risks to the subject which are currently unforeseeable [required if the research involved investigational drugs/devices or when the research involved procedures whose risks were not well known];
- (2) A statement that if the participant was or became pregnant, the particular treatment or procedure might involve risks to the embryo or fetus, which were



IRB STANDARD OPERATING PROCEDURES

currently unforeseeable [required if the research involved pregnant women or women of child bearing potential and involved procedures whose effects on fetuses were not well known];

- (3) Anticipated circumstances under which the subject's participation may be terminated by the investigator without the subject's consent; [required for long term studies];
- (4) Any additional costs to the subject that may result from participation in the research; [required when the research might involve additional costs to the participant];
- (5) The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject; [required when withdrawal from the research would have adverse consequences];
- (6) A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject; [required for all studies involving more than minimal risk];
- (7) The approximate number of subjects involved in the study; [required for all studies];
- (8) For applicable clinical trials, as defined in 42 U.S.C. 282(j)(1)(A), such as:
 - (a) Trials of Drugs and Biologics: controlled clinical investigations, other than Phase 1 investigations, of a product subject to FDA regulation (not generics)
 - (b) Trials of Devices: Controlled trials with health outcomes of devices subject to FDA regulation, other than small feasibility studies, and pediatric postmarket surveillance

The following statement must be added to the informed consent document:

"A description of this clinical trial will be available on <http://www.ClinicalTrials.gov>, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time."

- (9) For **classified research** subject to the requirements of the **Department of Defense**:
 - (a) Identification of the Department of Defense as the supporting institution of the research, unless the research involves no more than minimal risk. The Secretary of Defense may grant an exception to this requirement on the grounds that providing this information could compromise intelligence sources or methods.



IRB STANDARD OPERATING PROCEDURES

- (b) A statement that the research involving human subjects is classified and an explanation of the impact of the classification.
- (10) And such other information that the BRANY IRB recommends as necessary to inform and/or protect subjects.

IV.2. Waiver or Alteration of Informed Consent Requirements

IV.2.a. Minimal Risk Research

Federal regulations (45 CFR 46.116) allow the IRB to approve a consent procedure that does not include or that alters some or all of the required elements of informed consent, or to waive the requirement to obtain informed consent altogether. A waiver of informed consent may be granted only when **ALL 6** of the following are applicable:

- (1) No more than minimal risk to the subject is involved; and
- (2) The research could not practicably be carried out without the waiver or alteration (this does not mean mere inconvenience), and
- (3) The waiver or alteration will not adversely affect the rights and welfare of the subject, and
- (4) The subjects will be provided with additional pertinent information after participation, whenever appropriate, and
- (5) The research is not subject to FDA regulations.
- (6) The research is not **classified research** subject to the requirements of the **Department of Defense (DoD)**.

The form for requesting IRB consideration of waiver or alteration of consent is attached as [Appendix 29](#).

IV.2.b. The FDA's Requirements for Waiver of Informed Consent

The FDA (21 CFR 50.23) permits entry of a subject into a research project without informed consent providing that both the investigator and a physician who is not otherwise participating in the IRB approved clinical investigation certify in writing that **all** of the following pertain:

- (1) The subject is confronted by a life-threatening situation necessitating the use of the investigational drug or device; and
- (2) Informed consent cannot be obtained from the subject because of an inability to communicate with or obtain legally effective consent from the subject (inability to



IRB STANDARD OPERATING PROCEDURES

communicate means that the subject is in a coma or a state of confusion, not because of the subject's inability to speak a particular language); and

- (3) Time is insufficient to obtain a consent from the subject's legal representative; and
- (4) No alternative method of approved or generally recognized therapy is available that provides an equal or greater likelihood of saving the subject's life.

If an investigator believes that immediate use of the investigational drug or device is essential to preserve the subject's life, and timely certification from a physician who is not participating in the research study cannot be obtained, the investigator may use the drug or device, but it is essential that a physician who is not otherwise participating in the research evaluate and review in writing, the use of the test article. The PI must submit the certification or the evaluation by the non-participating physician to the IRB within five working days after the test article's use. This information will be reviewed by the IRB Chairperson and will be presented to the full IRB at its next convened meeting.

IV.2.c. Waiver of Informed Consent for Department of Defense Supported Research

Research involving a human being as an experimental subject that also proposes to request a waiver of the requirement to obtain consent is subject to additional approval by the Department of Defense component involved in the research (see Department of Defense Instruction 3216.02 section 4.2.2).

See section II.2.a. of this policy for definitions of "**Experimental Subject**" and "**Research involving a human being as an experimental subject.**"

IV.3. Criteria for Obtaining Informed Consent

IV.3.a. Categories of Investigational Research that are Exempt from Subject Consent

- (1) Research conducted in established or commonly accepted educational settings, involving normal education practices, such as:
 - (a) Research on regular and special education instructional strategies, or
 - (b) Research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.
- (2) Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, or observation of public behavior, unless:
 - (a) Information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects, and



IRB STANDARD OPERATING PROCEDURES

- (b) Any disclosure of the human subject's response outside the research could reasonably place the subject at risk of criminal or civil liability or be damaging to the subject's financial standing, employability, or reputation.
- (3) Research involving the use of special educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior that is not exempt above if:
 - (a) The human subjects are elected or appointed public officials or candidates for public office; or
 - (b) Federal statutes require without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.
- (4) Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or the information is recorded by the investigator in such a manner that subject's cannot be identified, directly or through identifiers linked to the subjects.
- (5) Research and demonstration projects which are conducted by or subject to the approval of the funding agency head and which are designed to study, evaluate, or otherwise examine:
 - (a) Public benefit or service programs,
 - (b) Procedures for obtaining benefits or services under those programs;
 - (c) Possible changes in or alternatives to those programs or procedures; or
 - (d) Possible changes in methods or levels of payment for benefits or services under those programs.
- (6) Certain taste and food quality evaluation and consumer acceptance studies.

The form for requesting IRB consideration of waiver or alteration of consent is attached as [Appendix 29](#).

IV.3.b. Limited English Proficient Subjects

Limited English proficient participants should not be systematically excluded from research because of inconvenience in translating informed consent documents. In accordance with the principle of justice outlined in The Belmont Report, it is incumbent upon investigators to ensure that no subject is unfairly excluded from participation in potentially beneficial research that involves greater than minimal risk, including LEP Subjects. Research that is greater than minimal risk and that has the potential to benefit subjects shall not be limited to English speaking subjects.



IRB STANDARD OPERATING PROCEDURES

IV.3.c. When Investigator Anticipates a Limited English Proficient Population

If the investigator anticipates enrolling subjects with limited English proficiency (“LEP Subjects”) (e.g., the investigator’s practice is in an area with a known population of foreign-language speaking persons), the investigator must obtain an informed consent form (“ICF”) translated into the language(s) of the anticipated LEP population (comprising approximately 1% or more of the eligible subject population), with such translation being approved by the Institutional Review Board. The IRB may rely on a certified translator, or a translation performed by an individual reasonably believed by the IRB to be competent to provide it. Researchers and sponsors that are uncertain about the appropriateness of a translator should inquire with IRB before moving forward with such translation.

Any subsequent revisions to the informed consent document must also be translated and submitted for IRB review.

The BRANY IRB does not allow the use of “Short Form” consent form when the limited English proficient population is anticipated, unless the translated informed consent document is in progress but not available at the time the potential subject presents.

IV.3.d. When Investigator Encounters a Non-English Speaking Subject Whose Primary Language Was Not Anticipated (e.g., rarely-encountered foreign languages)

If investigators enroll subjects without a BRANY IRB approved written translation, a "short form" written consent document, in a language the subject understands, should be used to document that the elements of informed consent required by 21 CFR 50.25 were presented orally to the subject or the subject's legally authorized representative. When this method is used, the IRB shall determine:

- The consent document states that the elements of disclosure required by the regulations have been presented orally to the participant or the participant’s legally authorized representative.
- The written summary embodies the basic and required additional elements of disclosure.
- There shall be a witness to the oral presentation. The witness shall be conversant in both English and the language of the participant.

Also, the IRB shall approve a written summary of what is to be said to the subject or the representative. Only the short form itself is to be signed by the subject or the representative. However, the witness shall sign both the short form and a copy of the summary, and the person actually obtaining the consent shall sign a copy of the summary. A copy of the summary shall be given to the subject or the representative in addition to a copy of the short form.



IRB STANDARD OPERATING PROCEDURES

The investigator must thereafter pursue a written translation of the ICF and HIPAA authorization in the language that the LEP Subject understands, unless doing so would constitute an undue or excessive burden, or unless the LEP subject is illiterate or the LEP Subject's primary language is non-written.

IV.3.d.1. Ongoing Translation For All Limited English Proficient Subjects Enrolled in Research

The investigator must ensure that an appropriate, certified translator is available at study visits and throughout the study to assist in confirming the subject's ongoing consent, and to enable communication with the LEP Subject.

IV.3.e. Illiterate Subjects

When the investigator encounters an illiterate subject who understands English, the ICF and HIPAA authorization may be read to the subject, and the subject may make a "mark" on the subject signature line if he/she is unable to sign his/her name. The consent process must be witnessed, and the ICF and HIPAA authorization should be signed by the witness and by the person conducting the informed consent discussion. The BRANY IRB will consider whether appropriate additional safeguards are required when enrollment of an illiterate subject is anticipated, as such subjects may be vulnerable to coercion and undue influence. The investigator must consider on a case-by-case basis whether the prospective illiterate subject has an appropriate understanding of the research based on the consent discussion.

IV.3.f. Consent Issues for Phase I studies

In studies where subjects may be observed for extended periods of time by a member of the research staff or a medical monitor, such actions must be clearly stated in the informed consent document. The process of informed consent is especially important in Phase I trials because the subjects participating in the research may not benefit from participation in any way.

IV.4. Health Insurance Portability and Accountability Act of 1996 (HIPAA)

The requirements mandated by the Health Insurance Portability and Accountability Act of 1996 (HIPAA) should be addressed in a separate authorization form, or incorporated into the informed consent document (see [Appendix 18](#): HIPAA Authorization Template Language). Under HIPAA requirements, subjects must authorize the use and disclosure of their protected health information (PHI).

Authorization elements required for HIPAA compliance include:

- Description of information to be used or disclosed
- Persons authorized to use and disclose information



IRB STANDARD OPERATING PROCEDURES

- Persons authorized to receive information
- Purpose of the requested use or disclosure of information
- Redisclosure of information
- Expiration of authorization
- Right to withdraw authorization
- Right of refusal

Refer to the Section VII for additional policies and procedures regarding HIPAA.



IRB STANDARD OPERATING PROCEDURES

V. SPECIAL CONSIDERATIONS IN IRB REVIEW

V.1. Potentially Vulnerable Subject Groups

The IRB must give special consideration to protecting the welfare of particularly vulnerable subjects, such as children, elderly, prisoners, pregnant women, handicapped, mentally disabled persons, subjects enrolled in clinical trials in an emergent care setting, economically or educationally disadvantaged persons, or any other group the IRB may deem as a vulnerable population. If vulnerable subjects are to be recruited and subsequently enrolled into a research project they must, of course, be provided all of the protections that are required for every other research subject. OHRP requires that additional, even more rigorous protections be provided for those who are vulnerable:

- If research involves pregnant women, fetuses, or neonates the IRB follows Subpart B of the DHHS regulations or equivalent protections as allowed by law.
- If research involves children as participants the IRB follows Subpart D of the DHHS or equivalent protections as allowed by law.
- If research involves adults unable to consent the IRB considers specific criteria for approval of such research that provides additional safeguards to protect their rights and welfare.

The investigator must determine if the safeguards afforded to all subjects enrolled in a particular clinical trial are sufficient to protect vulnerable subjects. If the investigator determines that additional safeguards are necessary to protect vulnerable subjects, these additional safeguards must be described and submitted to the IRB with the research application. The IRB must determine whether the safeguards described in the research application and protocol are appropriate or whether additional safeguards will be required.

The IRB is also required to ensure that it has adequate representation on the Board to consider research involving these vulnerable populations in a satisfactory manner. When the IRB reviews a project involving vulnerable populations, the IRB Coordinator(s) will ensure that one or more individuals who are knowledgeable about or experienced in working with such participants will be present at the IRB meeting, or will be available to provide consultation to the designated IRB reviewer when the submission qualifies for expedited review. When necessary the IRB will seek legal counsel for guidance on the definitions below when state and/or local laws may apply. For research involving potentially vulnerable subject groups, determinations of exempt status will be made by the BRANY IRB according to Section II.2.c of this policy.

V.1.a. Elements to Consider in Reviewing Research Involving Vulnerable Subjects

The IRB will pay special attention to the following specific elements of the research plan when reviewing research involving vulnerable subjects:

- (1) Strategic issues include inclusion and exclusion criteria for selecting and recruiting participants; informed consent and willingness to volunteer; coercion and undue influence; and confidentiality of data.



IRB STANDARD OPERATING PROCEDURES

- (2) The IRB will carefully consider group characteristics for the specific protocols, such as economic, social, physical, and environmental conditions, to ensure that the research incorporates additional safeguards for vulnerable subjects.
- (3) The IRB will not permit investigators to over-select or exclude certain groups based on perceived limitations or complexities associated with those groups. For example, it is not appropriate to target prisoners as research subjects merely because they are a readily available captive population. (Note, the BRANY IRB does not routinely review research involving prisoners.)
- (4) The IRB will be knowledgeable about applicable state or local laws that bear on the decision-making abilities of potentially vulnerable populations (e.g. State statutes related to competency to consent for research, emancipated minors, legally authorized representatives, the age of majority for research consent, and the waiver of parental permission for research). In New York State, those under the age of 18 that are considered to be emancipated by New York State may be able to consent to research participation for themselves. The BRANY IRB will consider the inclusion of emancipated minors in research on a case-by-case basis. Consultation on such matters will be sought whenever needed from BRANY legal counsel.
- (5) Research studies that plan to involve any potentially vulnerable populations will have adequate procedures in place for assessing and ensuring the subjects' capacity, understanding, and informed consent or assent. The IRB will require that such procedures are included in the research plan. In some cases it may be possible for researchers to enhance the understanding for potentially vulnerable subjects. Examples include requiring someone not involved in the research to obtain the consent, the inclusion of a consent monitor, a subject advocate, interpreter for hearing impaired subjects, translation of informed consent forms into languages the subjects understand, and reading the consent form to subjects slowly and ensuring their understanding paragraph by paragraph.
- (6) The IRB may require additional safeguards to protect potentially vulnerable populations. For instance, the IRB may require that someone from the IRB oversee the consent process, or that a waiting period be established between initial contact and enrollment to allow time for discussion and questions.

V.1.b. Research Involving Children – Special Considerations

The IRB follows the requirements specified in Subpart D for research involving children.

V.1.b.1. Definition of Terms Relevant to This Area of Research

“**Assent**” means affirmative agreement (usually from a child) to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent.

“**Children**” are persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law or the



IRB STANDARD OPERATING PROCEDURES

jurisdiction in which the research will be conducted. A person is deemed to be a “child” in New York State if he is under 18 years old (age of majority is reached the day prior to the individual’s birth date). State laws may vary with regard to the definition of “child”. The BRANY IRB will seek legal consult on this matter when reviewing research for investigators in states other than New York.

“**Guardian**” means an individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care. In New York State, a guardian is appointed either by parent pursuant to a designation, deed of guardianship or will approved by a Family Court or Surrogate’s Court judge; or by a Family Court or Surrogate’s Court judge pursuant to a letter or order of guardianship. State laws may vary with regard to the definition of “child”. The BRANY IRB will seek legal consult on this matter when reviewing research for investigators in states other than New York.

“**Parent**” means a child’s biological or adoptive parent.

“**Permission**” means the agreement of parent(s) or guardian to the participation of their child or ward in research.

When reviewing research that involves children as participants, the BRANY IRB will use the definitions above when determining who is a “child” and who is a “guardian”.

The BRANY IRB is charged with additional responsibilities when reviewing research activities involving children as subjects. The BRANY IRB must consider the degree of risk and potential benefit to the individual subject, in accordance with 45 CFR 46 Subpart D. The IRB Coordinator will ensure that the IRB determines and documents the applicable degree of risk described below.

V.1.b.2. Degrees of Risk

- (a) **Minimal Risk** (Research not involving greater than minimal risk):
 - (i) Minimal risk is defined as a risk where the probability and magnitude of harm or discomfort anticipated in the proposed research are not greater, in and of themselves, than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.
 - (ii) In order to approve minimal risk the research, the BRANY IRB must determine that adequate provisions are made for soliciting the assent of the children and the permission of at least one parent or guardian. The IRB may, at its discretion, require permission of both parents.
- (b) **Greater Than Minimal Risk with Benefits to the Subject** (Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subject):



IRB STANDARD OPERATING PROCEDURES

In order to approve such research, the BRANY IRB must determine that:

- (i) The risk is justified by the anticipated benefit to the subject,
- (ii) The relation of the anticipated benefit to the risk is at least as favorable to the subject as that presented by available alternative approaches,
- (iii) Adequate provisions are made for soliciting the assent of the children and permission of at least one parent/guardian. The IRB may, at its discretion, require permission of both parents.

- (c) **Greater Than Minimal Risk with NO Benefits to the Subject** (Research involving greater than minimal risk and no prospect of direct benefit to the individual subject, but likely to yield generalizable knowledge about the subject's disorder or condition):

The BRANY IRB shall determine that:

- (i) More than minimal risk to children is presented by an intervention or procedure that does not hold out the prospect of direct benefit for the individual participant, or by a monitoring procedure which is not likely to contribute to the well-being of the participant,
- (ii) The risk represents a minor increase over minimal risk,
- (iii) The intervention or procedure presents experiences to the subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social or educational situations.
- (iv) The intervention or procedures is likely to yield generalizable knowledge about the subject's disorder or condition which is of vital importance for the understanding and amelioration of the subject's condition; and
- (v) Adequate provisions are made for soliciting assent of the children and permission of both parents or guardian.

- (d) **High Risk** (Research not otherwise approvable which presents an opportunity to understand, prevent or alleviate a serious problem affecting the health or welfare of children):

Research that does not meet the above criteria may be conducted only if the BRANY IRB determines that:

- (i) The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children, in which case the



IRB STANDARD OPERATING PROCEDURES

assent of the children and the permission of both parents or guardian are to be obtained;

- (ii) The federal agency approves the research, after consultation with a panel of experts in pertinent disciplines (e.g. Science and medicine, education, ethics, law), and following opportunity for public review and comment, had determined either:
 1. That the research in fact satisfies the conditions of 45 CFR 46.404, 45 CFR 46.405, OR 45 CFR 46.406, as applicable, or
 2. The following:
 - a. The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children;
 - b. The research will be conducted in accordance with sound ethical principles;
 - c. Adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians, as set forth in 45 CFR 46.408.

V.1.b.3. Children Who Are Wards of the State or Other Agency, Institution or Entity

Children who are wards of the State can be included in research under items (c) and (d) above only if BRANY IRB determines such research is:

- (a) Related to their status as wards; or
- (b) Conducted in schools, camps, hospitals, institution, etc., in which the majority of the children involved are not wards.

For research approved by the BRANY IRB involving wards and within the categories listed above, the IRB shall require the appointment of an advocate for each child (in addition to the child's guardian), who has the experience to act in the best interest of the child for the duration of the child's participation in the research, and is not in any way (except in the role as advocate or member of the IRB) associated with the research, investigator, or guardian. The IRB Coordinator will ensure the above IRB determinations are made and documented.



IRB STANDARD OPERATING PROCEDURES

V.1.b.4. Justification of Exclusion of Children

Children should be included in all research involving human subjects unless one of more of the following exclusionary circumstances can be fully justified:

- (a) The research topic to be studied is irrelevant to children
- (b) There are laws or regulations barring the inclusion of children in the research
- (c) The knowledge being sought in the research is already available for children or will be obtained from another ongoing study, and an additional study will be redundant
- (d) A separate, age specific study in children is warranted and preferable.
Examples include:
 - (i) The relative rarity of the condition in children, as compared to adults;
 - (ii) The number of children is limited because the majority are already accessed by a nationwide pediatric disease research network;
 - (iii) Issues of study design preclude direct applicability of hypotheses and/or interventions to both adults and children (including different cognitive, developmental, or disease stages or different age related metabolic processes)
- (e) Insufficient data are available in adults to judge potential risk in children
- (f) Study designs aimed at collecting additional data on pre enrolled adult study participants (e.g., longitudinal follow up studies that did not include data on children)
- (g) Other special cases justified by the investigator.

V.1.b.5. Requirements for Permission by Parents or Guardians and for Assent by Children

According to 45 CFR 46.408, requirements for permission by Parents or Guardians and for assent by children are as follows:

(a) **Assent**

Provision must be made for soliciting the assent of children when in the judgment of the IRB the children are capable of providing assent.



IRB STANDARD OPERATING PROCEDURES

- (i) It is important to note that failure to object to participate as a research subject cannot be construed as assent. The assent guidelines (detailed below) should be reviewed to determine the requirements for obtaining assent.
- (ii) When applicable, an Assent form (see [Appendix 20: Sample Assent Form and Preparation Guidelines](#)) must be completed to document that assent was freely obtained and without any coercion or undue influence. Investigators must maintain each signed Assent form on file along with the consent document that was signed by the parents or guardian and other research records relevant to the individual research subject.

(b) Parental Permission

Provision must be made for soliciting the permission of each child's parents or guardian and the permission must be documented in the consent document.

- (i) The IRB may require permission of only one parent if the research involves no greater than minimal risk or involves greater than minimal risk but presents the prospect of direct benefit to the individual subjects.
- (ii) If the research involves greater than minimal risk and offers no prospect of direct benefit to individual subjects or the research is not otherwise approvable but presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children, permission **must** be obtained from both parents, unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.

(c) Waiver of Parental Consent

Under very special circumstances the IRB may waive the requirement for parental consent. Waivers can only be granted for conditions or for a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects (e.g. neglected or abused children), if an appropriate mechanism for protecting the child is provided, the research must not be FDA-regulated, and if the waiver is not inconsistent with Federal, State, or Local law. Waivers will be granted in accordance with 45 CFR 46.116(c) or 45. CFR 46.116(d) (see Section IV.1.h. of this policy).

V.1.b.6. Obtaining Assent

In response to the Federal regulations regarding the enrollment of children as research subjects, the IRB has established the following guidelines for obtaining the



IRB STANDARD OPERATING PROCEDURES

assent of children. It is the intent of the regulations and guidelines to protect the child-subject against unwilling or unwitting exposure to situations of risk.

All pediatric research subjects should be fully informed about a research study, in language appropriate for their age, maturity and previous experiences, whether assent is to be requested or not. This information can be provided verbally and should include all tests and procedures to be performed, frequency of interventions, duration of participation in the study, risks, discomforts and potential benefits. The child should be encouraged to ask questions, all of which should be answered.

In addition, when the research involves greater than minimal risk and offers no prospect of direct benefit to individual subjects or the research is not otherwise approvable but presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children, the BRANY IRB shall determine that adequate provisions are made for soliciting the assent of the children and will require the Principal Investigator to obtain assent when in their judgment the children are capable of providing assent. To make this judgment, the Principal Investigator must consider the ages, maturity, and psychological state of each child. However, depending on the study, the BRANY IRB may set specific requirements for when assent must be obtained.

BRANY IRB will determine whether assent is a requirement of:

(a) All Children

- The IRB will determine whether assent must be documented, and if so, the process to document assent.

(b) Some children

- The IRB will determine whether assent must be documented, and if so, the process to document assent.
- The IRB will determine which children will not be required to assent.

(c) None of the children.

When the IRB determines that assent is not a requirement for some or all children (see b. and c. above), the IRB will determine one or more of the following:

- The children are not capable of providing assent based on the age, maturity, or psychological state.
- The capability of the children will be so limited that they could not reasonably be consulted or that the intervention.
- The research holds out a prospect of direct benefit that is important to the health or well-being of the children and was available only in the context of the research.
- The assent could be waived using the criteria for waiver of informed consent.



IRB STANDARD OPERATING PROCEDURES

These determinations regarding assent will be documented on the Reviewer's Checklist and in the meeting minutes.

V.1.b.7. Waiver of Assent

The BRANY IRB may waive the assent requirement under circumstances in which consent requirements are waived, in accordance with 45 CFR 46.408. If the IRB determines that the capability of some or all of the children is so limited that they cannot reasonably be consulted or that the intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the children and is available only in the context of the research, the assent of the children is not a necessary condition for proceeding with the research. Even where the IRB determines that the subjects are capable of assenting, the IRB may still waive the assent requirement under the same circumstances in which consent may be waived. If an investigator believes that assent is not appropriate, a waiver must be specifically requested, described, and justified in the protocol.

V.1.b.8. Documentation of Assent

For research where assent is required, the BRANY IRB will determine whether and how it is to be documented. A third party unrelated to the family must witness the assent process. If Institution provides for additional safeguards, such measures may be employed. While federal regulations do not require that the subject, upon maturity, sign the adult consent form, the IRB recommends that this be done to respect the subject's autonomy.

V.1.b.9. Proposed Reimbursement for Child Subjects

In reviewing pediatric research, the IRB must consider the appropriateness of the payment to the parents/guardian, as well as to the child, if any. Reimbursements must not represent an undue influence either to the parents or the children, and must be reasonable in relation to the visits involved in the research.

V.1.b.10. Emancipated Minors

As noted above, "children" are persons who have not attained the legal age for consent to treatments or procedures involved in research under the applicable law or the jurisdiction in which the research will be conducted. However, persons who have not yet attained the age of legal majority as defined by state or local law (18 years of age in New York), but who are entitled to treatment as if they had by virtue of assuming adult responsibilities, such as marriage, or procreation are considered emancipated minors.

While emancipated minors do not meet the DHHS and FDA regulatory definitions of "child", the BRANY IRB will review and process projects that plan to include emancipated minors in accordance with 45 CFR 46, subpart D requirements as described above. Since state and local law may vary in this regard, the BRANY IRB will seek legal consult on this matter when reviewing research for investigators in states other than New York.



IRB STANDARD OPERATING PROCEDURES

Individuals who are considered emancipated minors by state or local law may be able to consent to research participation for themselves. The IRB shall consider the inclusion of emancipated minors in research, absent parental or guardian consent, on a case-by-case basis. The IRB shall consider the subject's ability to comprehend what is being proposed, and the intervention or procedure involved in the research must offer a prospect of direct benefit that is important to the health or well-being of the emancipated minor and is not available outside the context of the research protocol.

V.1.c. Research Involving Pregnant Women, Fetuses and Neonates

V.1.c.1. Definition of Terms Relevant to This Area of Research

- (1) **“Dead Fetus”** means a fetus after delivery, which exhibits neither heartbeat, spontaneous respiratory activity, spontaneous movement of voluntary muscles, nor pulsation of the umbilical cord (if still attached).
- (2) **“Delivery”** means complete separation of the fetus from the woman by expulsion or extraction or any other means.
- (3) **“Fetus”** means the product of conception from the time of implantation (as evidenced by any of the presumptive signs of pregnancy, such as missed menses, or a medically acceptable pregnancy test) until a determination is made, following expulsion or extraction of the fetus, that it is viable.
- (4) **“Neonate”** means newborn.
- (5) **“Nonviable”** neonate means a fetus after delivery that, although living, is not viable.
- (6) **“Pregnancy”** encompasses the period of time from confirmation of implantation (through any of the presumptive signs of pregnancy, such as missed menses, or by a medically acceptable pregnancy test), until delivery.
- (7) **“Viable”** as it pertains to the fetus means being able, after either spontaneous or induced delivery, to survive (given the benefit of available medical therapy) to the point of independently maintaining heart beat and respiration. If a fetus is viable after delivery, then it is a child as defined by 46.402(a) & Subpart D is applicable.

***Note:** In New York State, any person who is pregnant, regardless of age, may give effective consent for medical, dental, health and hospital services relating to prenatal care (NYS Public Health Law, Section 2504).

V.1.c.2. Research Involving Pregnant Women or Fetuses

Pregnant women or fetuses may be involved in research if the IRB determines all of the following conditions are met:



IRB STANDARD OPERATING PROCEDURES

- (a) Where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies, including studies on nonpregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses;
- (b) The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus; or, if there is no such prospect of benefit, the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge which cannot be obtained by any other means;
- (c) Any risk is the least possible for achieving the objectives of the research;
- (d) The consent of the mother is obtained in accordance with the regulations.
- (e) If the research holds out the prospect of direct benefit to the pregnant woman, the prospect of a direct benefit both to the pregnant woman and the fetus, or no prospect of benefit for the woman nor the fetus when risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means, her consent is obtained in accord with the informed consent provisions of 45 CFR 46 Subpart A;
- (f) If the research holds out the prospect of direct benefit solely to the fetus then the consent of the father is obtained in accord with the informed consent provisions of 45CFR46 Subpart A, except that the father's consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity or the pregnancy resulted from rape or incest.
- (g) Each individual providing consent under paragraph (d) or (e) of this section is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate;
- (h) For children as defined in 45 CFR 46.402(a) who are pregnant, assent and permission are obtained in accord with the provisions of 45 CFR 46 Subpart D;
- (i) No inducements, monetary or otherwise, will be offered to terminate a pregnancy;
- (j) Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy; and
- (k) Individuals engaged in the research will have no part in determining the viability of a neonate.

The IRB Coordinator is responsible for ensuring the above determinations are made and documented by the IRB.



IRB STANDARD OPERATING PROCEDURES

V.1.c.3. Research Involving Neonates

V.1.c.3.1. Neonates of Uncertain Viability and Nonviable Neonates

Neonates of uncertain viability and nonviable neonates may be involved in research if the IRB determines all of the following conditions are met:

- (a) Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates.
- (b) Each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the neonate.
- (c) Individuals engaged in the research will have no part in determining the viability of a neonate.
- (d) The legally effective consent of either parent of the neonate is obtained in accordance with the regulations.
 - (A) If neither parent is able to consent because of unavailability, incompetence, or temporary incapacity, the legally effective consent of either parent's legally authorized representative is obtained.
 - (B) The consent of the father or his legally authorized representative does not have to be obtained if the pregnancy resulted from rape or incest.

The IRB Coordinator is responsible for ensuring the above determinations are made and documented by the IRB.

V.1.c.3.2. Neonates of Uncertain Viability

Until it has been ascertained whether or not a neonate is viable, a neonate may not be involved in research unless the following additional conditions have been met:

- (A) The IRB determines that:
 - (i) The research holds out the prospect of enhancing the probability of survival of the neonate to the point of viability, and any risk is the least possible for achieving that objective, or
 - (ii) The purpose of the research is the development of important biomedical knowledge which cannot be obtained by other means and there will be no added risk to the neonate resulting from the research; and



IRB STANDARD OPERATING PROCEDURES

- (B) The legally effective informed consent of either parent of the neonate or, if neither parent is able to consent because of unavailability, incompetence, or temporary incapacity, the legally effective informed consent of either parent's legally authorized representative is obtained in accord with subpart A of this part, except that the consent of the father or his legally authorized representative need not be obtained if the pregnancy resulted from rape or incest.

The IRB Coordinator is responsible for ensuring the above determinations are made and documented by the IRB.

V.1.c.3.3. Nonviable Neonates

After delivery nonviable neonates may not be involved in research unless the IRB determines all of the following additional conditions are met:

- (a) Vital functions of the neonate will not be artificially maintained;
- (b) The research will not terminate the heartbeat or respiration of the neonate;
- (c) There will be no added risk to the neonate resulting from the research;
- (d) The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means; and
- (e) The legally effective informed consent of both parents of the neonate is obtained in accord with subpart A of this part, except that the waiver and alteration provisions of 45 CFR 46.116(c) and (d) do not apply. However, if either parent is unable to consent because of unavailability, incompetence, or temporary incapacity, the informed consent of one parent of a nonviable neonate will suffice to meet the requirements of this paragraph (c)(5), except that the consent of the father need not be obtained if the pregnancy resulted from rape or incest. The consent of a legally authorized representative of either or both of the parents of a nonviable neonate will not suffice to meet the requirements of this paragraph (c)(5).

The IRB Coordinator is responsible for ensuring the above determinations are made and documented by the IRB.

V.1.c.3.4. Viable neonates

A neonate, after delivery, that has been determined to be viable may be included in research only to the extent permitted by and in accord with the requirements of subparts A and D of 45 CFR 46.



IRB STANDARD OPERATING PROCEDURES

V.1.c.4. Research Involving, After Delivery, the Placenta, the Dead Fetus or Fetal Material

- (a) Research involving, after delivery, the placenta; the dead fetus; macerated fetal material; or cells, tissue, or organs excised from a dead fetus, shall be conducted only in accord with any applicable federal, state, or local laws and regulations regarding such activities.
- (b) If information associated with material described in paragraph (a) of this section is recorded for research purposes in a manner that living individuals can be identified, directly or through identifiers linked to those individuals, those individuals are research subjects and all pertinent subparts of this part are applicable.

V.1.c.4.1. Dead Fetus, Fetal Material or the Placenta

- (a) Non viable fetuses may only be involved in research if:
 - (i) Vital functions are not maintained
 - (ii) Research won't terminate heart beat or respiration
 - (iii) No risk resulting from research
 - (iv) The purpose of the research is for the development of important biomedical knowledge not obtainable by other means.
 - (v) Both parents must consent unless one is unavailable, incompetent or temporarily incapacitated. A legally authorized representative of one or both parents will not suffice.

V.1.c.5. Obtaining Consent from Women in Labor

V.1.c.5.1. Obtaining Consent in Advance

If research is to be performed while a woman is in active labor, efforts should be made to obtain written informed consent during a prenatal visit, if possible. At the time the research procedures will be carried out, the patient should be reminded of her consent to the procedure. Those selected should be given relevant information again, and afforded the opportunity to ask questions or to withdraw. Both advanced consent and that obtained at the time of the research should be documented in writing.

V.1.c.5.2. Not Obtaining Consent in Advance

The following procedures should be followed for women in active labor when the research procedure carries a significant degree of risk:



IRB STANDARD OPERATING PROCEDURES

The pregnant woman should be approached for her informed consent

Consent should also be asked of a second person, typically her husband, father of the baby or woman's mother, or close relative accompanying her.

If a second person is not available, the research may still be carried out. It will be the determination of the researcher if the patient has capacity to grant valid, informed consent while in active labor.

(NOTE: If the anticipated risks are low, only the consent of the pregnant woman is needed. This degree should be determined by the IRB at the time of initial review of the study protocol.)

V.1.d. Prisoners

The BRANY IRB does not routinely review research involving prisoners. When the IRB reviews research that involves prisoners, the research must be reviewed at a convened meeting. The majority of the board (exclusive of prisoner members) shall have no association with the prison involved and at least one member of the board shall be a prisoner or a prisoner advocate, in keeping with 45CFR46.304. The IRB Coordinator(s) will ensure that one or more individuals who were prisoners or prisoner representatives will be present at the IRB meeting at which the research involving prisoners is reviewed. If the prisoner representative is not present, research involving prisoners cannot be reviewed or approved.

The prisoner representative must review research involving prisoners, focusing on the requirements in Subpart C or equivalent protections.

- The prisoner representative will receive all review materials pertaining to the research (same as primary reviewer)
- The prisoner representative may attend the meeting by phone, video-conference, or webinar, as long as the representative is able to participate in the meeting as if they were present in person at the meeting.
- The prisoner representative must present his/her review either orally or in writing at the convened meeting of the IRB when the research involving prisoners is reviewed.
- Modifications will be reviewed by the convened IRB, using the same procedures for initial review including the responsibility of the prisoner representative to review the modification and participate in the meeting (as described above).
- Continuing review will be reviewed by the convened IRB, and must use the same procedures for initial review including the responsibility of the prisoner representative to review the continuing review materials and participate in the meeting (as described above).



IRB STANDARD OPERATING PROCEDURES

- If Subpart C is applicable either by funding requirement or voluntarily (e.g. Subpart C box is checked on the FWA) research involving prisoners cannot be deemed exempt. If Subpart C is not applicable, research using data, samples, or materials that involves prisoners or that may involve prisoners but qualifies for an exemption may be granted an exemption. It must be determined that an exemption is appropriate for the prison population being studied. The prisoner representative may be consulted for exempt determinations involving prisoners, but this consultation is not required. An exemption may not be granted if the research involves interaction with prisoners (including obtaining informed consent).

For prisoners, “minimal risk” means the probability and magnitude of physical or psychological harm that is normally encountered in the daily lives, or in the routine medical, dental, or psychological examination of healthy persons.

Only research studies meeting one of four categories described below may be approved to include prisoners as research participants (NOTE: When subject to the requirements of the Department of Defense, research involving detainees or prisoners of war is prohibited):

Category A

Studies of the possible causes, effects, and processes of incarceration, and of criminal behavior, provided that the study presents no more than minimal risk and no more than inconvenience to the participants;

Category B

Studies of prisons as institutional structures or of prisoners as incarcerated persons, provided that the study presents no more than minimal risk and no more than inconvenience to the participants;

Category C

Research on conditions particularly affecting prisoners as a class (for example, vaccine trials and other research on hepatitis which is much more prevalent in prisons than elsewhere; and research on social and psychological problems such as alcoholism, drug addiction, and sexual assaults) provided that the study may proceed only after the Secretary of the Department of Health & Human Services (DHHS) has consulted with appropriate experts including experts in penology, medicine, and ethics, and published notice, in the Federal Register, of the intent to approve such research; or

Category D

Research on practices, both innovative and accepted, which have the intent and reasonable probability of improving the health or well-being of the participant. In cases in which those studies require the assignment of prisoners in a manner consistent with protocols approved by the IRB to control groups which may not benefit from the research, the study may proceed only after the Secretary of



IRB STANDARD OPERATING PROCEDURES

DHHS has consulted with appropriate experts, including experts in penology, medicine, and ethics, and published notice, in the Federal Register, of the intent to approve such research.

Additional Category for Research Subject to Department of Defense Requirements

Epidemiological research is also allowable when the IRB determines and documents:

- Prisoners are not a particular focus of the research.
- The research describes the prevalence or incidence of a disease by identifying all cases or studies potential risk factor association for a disease.
- The research presents no more than minimal risk.
- The research presents no more than an inconvenience to the participant.

In addition to the other responsibilities described in the section for the use of prisoners, the IRB can only approve research studies if it finds that:

- (1) Any possible advantages accruing to the prisoner through his or her participation in the research, when compared to the general living conditions, medical care, quality of food, amenities and opportunity for earnings in the prison, are not of such a magnitude that his or her ability to weigh the risks of the research against the value of such advantages in the limited choice environment of the prison is impaired;
- (2) The risks involved in the research are commensurate with risks that would be accepted by non-prisoner volunteers;
- (3) Procedures for the selection of participants within the prison are fair to all prisoners and immune from arbitrary intervention by prison authorities or prisoners. Unless the principal investigator provides to the Board justification in writing for following some other procedures, control participants must be selected randomly from the group of available prisoners who meet the characteristics needed for that particular research study;
- (4) The information is presented in a language and reading level that is understandable to the participant population;
- (5) Adequate assurance exists that parole boards will not take into account a prisoner's participation in the research in making decisions regarding parole, and each prisoner is clearly informed in advance that participation in the research will have no effect on his or her parole; and



IRB STANDARD OPERATING PROCEDURES

- (6) Where the IRB finds there may be a need for follow-up examination or care of participants after the end of their participation, adequate provision has been made for such examination or care, taking into account the varying lengths of individual prisoners' sentences, and for informing participants of this fact.

If a study utilizing prisoners as research participants is federally funded, the IRB director or a designee of the IRB director will send a letter to the DHHS Secretary through the Office for Human Research Protections (OHRP) indicating BRANY IRB has approved a study that will include prisoners in accordance with 45 CFR part 46 Subpart C. The research may not begin until written approval is received from OHRP on behalf of the DHHS Secretary confirming that the proposed research involves solely one of the permissible categories.

V.1.d.1. Subjects Who Become Prisoners After Enrollment in Research

When a subject becomes a prisoner or is detained after enrollment in a research study, the Investigator must notify the IRB as soon as possible after becoming aware of the situation. If the research project was not reviewed and approved by the IRB in accordance with the requirement of 45 CFR part 46 Subpart C, all research activity for the incarcerated prisoner/subject must cease until the requirements of Subpart C can be satisfied. If it is in the best interest of the subject to remain in the research study while incarcerated, the IRB Chair may make a determination to allow the subject to continue in the research until the requirements of Subpart C can be satisfied.

Upon notification that a subject enrolled in a research project has become a prisoner, the IRB will promptly re-review the protocol in accordance with the requirements of Subpart C if the Investigator wants to have the subject continue in the research.

V.1.e. Research Involving Psychiatric Populations

V.1.e.1. Definition of Terms Relevant to This Area of Research

- (1) **Cognitively Impaired:** Having a psychiatric disorder (e.g., psychosis, neurosis, personality or behavior disorders), an organic impairment (e.g., dementia) or a developmental disorder (e.g., mental retardation) that affects cognitive or emotional functions to the extent that capacity for judgment and reasoning is significantly diminished. Others, including persons under the influence of or dependent on drugs or alcohol, those suffering from degenerative diseases affecting the brain, terminally ill patients, and persons with severely disabling physical handicaps, may also be compromised in their ability to make decisions in their best interests.
- (2) **Competence:** Technically, a legal term, used to denote capacity to act on one's own behalf; the ability to understand information presented, to appreciate the consequences of acting (or not acting) on that information, and to make a choice. (See also: Incompetence, Incapacity.) Competence may fluctuate as a function of the natural course of a mental illness, response to treatment, effects of medication, general physical health, and other factors. Therefore, mental



IRB STANDARD OPERATING PROCEDURES

status should be re-evaluated periodically. As a designation of legal status, competence or incompetence pertains to adjudication in court proceedings that a person's abilities are so diminished that his or her decisions or actions (e.g., writing a will) should have no legal effect. Such adjudications are often determined by inability to manage business or monetary affairs and do not necessarily reflect a person's ability to function in other situations.

- (3) **Decisionally Impaired:** State of diminished mental capacity that interferes with the ability to make sound, informed judgments regarding medical treatment, or, in the context of research, regarding participation in research studies.
- (4) **Health Care Proxy:** Someone a person appoints to make health care decisions on his/her behalf in the event that he/she becomes unable to make those decisions for him/herself. See New York Health Care Proxy Law. Under the NY State Health Care Proxy Statute, the act of executing a new proxy automatically voids any prior proxies. Therefore, it is recommended that investigators advise subjects who are signing a "health care proxy for research" to name the same person that they have chosen as a health care proxy for clinical care.
- (5) **Incapacity:** Refers to a person's mental status and means inability to understand information presented, to appreciate the consequences of acting (or not acting) on that information, and to make a choice. Often used as a synonym for incompetence.
- (6) **Incompetence:** Technically, a legal term meaning inability to manage one's own affairs. Often used as a synonym for incapacity.
- (7) **Legally Authorized Representative (LAR):** FDA regulation 21 CFR 50.3 and DHHS regulation 45 CFR 102(c) define a legally authorized represent as an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research. However, State and local law would control over the regulations stated above. If a subject is medically incapable and/or legally incompetent, then a legally authorized representative, as determined under state or local law, must consent on the subject's behalf. A legally authorized representative may be a parent or legal guardian of a child, someone having durable power of attorney for health care (a health care proxy) for the subject, or some other court order authorizing him/her to be the legal representative. When reviewing research for which an investigator seeks the use of a legally authorized representative, the BRANY IRB will apply this definition when determining who can serve as a "Legally Authorized Representative". Since state and local law may vary in this regard, the BRANY IRB will seek legal consult on this matter when reviewing research for investigators in states other than New York.



IRB STANDARD OPERATING PROCEDURES

V.1.e.2. Physician's Responsibilities

For individuals who may have diminished mental capacity there must be an assessment of the subject's capacity to consent to participate prior to enrolling the subject in the study. For all subjects in studies involving individuals with psychiatric illness affecting competency, the assessment should be undertaken by a physician not associated with the study and whose professional training and credentials are suitable given the nature of the subject's illness and the nature of the study. This physician must be completely independent from the study and the physician's name should not appear as an author on any published paper reporting on the study as that might lead to the appearance of a conflict. Factors to be considered in assessing capacity include: the prospective subject's medical condition, the voluntariness of the subject's consent in light of the subject's hospitalization or relationship with the physicians conducting the study, as well as the subject's ability to assess the information provided to him/her and make informed and knowing decisions. In the event the subject lacks capacity to consent to participate, an individual legally authorized to consent on behalf of the subject must give consent.

V.1.e.3. Specially Trained Psychiatric In-Patients

Research staff and others involved should be specially trained. They should be knowledgeable about details of the protocol, including recruitment of subjects, potential risks to subjects, and the subjects' right to withdraw at any time.

It is necessary to contact the in-patients' psychiatrist before beginning recruitment. The psychiatrist should determine if it is in the subject's best interest to be enrolled in the study.

If it is decided that the patient should be enrolled, the subject's psychiatrist should be involved in the process of explaining the research that is being carried out to the patient. Furthermore, the patients should be told that a research coordinator or principal investigator in connection with the research will be approaching them.

V.1.f. Surrogate Consent with Subjects Incompetent or Unable to Give Consent or Emancipated Minors who are not Children

The IRB guidelines relative to surrogate permission are as follows:

V.1.f.1. Individuals Who May Serve As Surrogates

In the absence of a court appointed guardian who is specifically given authorization to consent to participation in research for individuals who do not have capacity to consent for him/herself, the participation of such subjects in research projects can only take place if consent can be obtained from a surrogate. Institutional policies vary with respect to who may be used as a surrogate for consent in research. Accordingly, Investigators are instructed to follow the policies of their respective institutions/practice and applicable state and local law with regard to who may act as the surrogate.



IRB STANDARD OPERATING PROCEDURES

In all forms of research in which surrogate consent will be utilized it is essential, if at all possible, to obtain the verbal assent of the subject. If a subject demonstrates or indicates an unwillingness to participate, regardless of the extent of loss of capacity, then the subject's participation in the research should be terminated.

Research that presents risks without benefits, or risks that exceed potential benefits will not be approved by the BRANY IRB for use of surrogate consent.

V.1.f.2. Assessment of Capacity

There should be an assessment of the subject's capacity to consent to participate. For all subjects in studies involving individuals for whom there is a question of capacity, the assessment should be undertaken by a physician not associated with the study and whose professional training and credentials are suitable given the nature of the subject's illness and the nature of the study. Factors to be considered in assessing the capacity include: the prospective subject's medical condition, the voluntariness of the subject's consent in light of the subject's hospitalization or relationship with the physicians conducting the study, as well as the subject's ability to assess the information provided to him/her and make informed and knowing decisions. The Principal Investigator will provide the IRB with a description of the plan for the assessment of the capacity to consent with the Research Application ([Appendix 11](#)). The Investigator's description must include the plan for obtaining assent of such participants, if appropriate, or an explanation of why assent will not be solicited. The IRB will evaluate whether the proposed plan is adequate. The IRB will also determine whether assent of such participants is required, and whether the plan for assent is adequate. The IRB's assessment will be documented in the Reviewer Checklist and the minutes of the IRB meeting at which the research was reviewed.

In the event the subject lacks capacity to consent to participate, consent must be given by a surrogate (an individual legally authorized to consent on behalf of the subject), but only in cases where the IRB has approved the research for surrogate consent by a legally authorized representative as defined above.

Where a patient is deemed incompetent or is incapacitated and unable to consent, the patient may be enrolled as a research subject by the patient's surrogate (*legally authorized representative*) as follows:

A **non-therapeutic** clinical trial (i.e., a trial in which there is no anticipated direct clinical benefit to the subject) should be conducted in subjects who personally give consent and who sign and date the written consent document.

For research that is **not subject to the requirements of the Department of Defense**, consent to participate in **non-therapeutic research** may be obtained from a **healthcare proxy authorized to consent for research** (or, if the proxy is silent with respect to research, it is acceptable for another legally authorized representative) if the following conditions are fulfilled:

- (a) The objectives of the trial cannot be met by means of a trial in subjects who can give consent personally.



IRB STANDARD OPERATING PROCEDURES

- (b) The foreseeable risks to the subject are low.
- (c) The negative impact on the subject's well-being is minimized and low.
- (d) The trial is not prohibited by law.
- (e) The opinion of the IRB is expressly sought on the inclusion of such subjects, and the written opinion covers this aspect.

Such trials (**non-therapeutic trials**), unless an exception is justified, should be conducted in patients having a disease or condition for which the investigational product is intended. Subjects in these trials should be particularly closely monitored and should be withdrawn if they appear to be unduly distressed.

Consent to participate in **therapeutic research** may be obtained from a **healthcare proxy authorized to consent for research**. If the proxy is silent with respect to research, it is acceptable for a health care proxy (or other legally authorized representative) to sign the consent if:

- (a) There is potential benefit over standard treatment; and
- (b) Standard treatment is not being withheld; and
- (c) There is no alternative standard treatment; and
- (d) Enrollment in the study is in the best interest of the patient; and
- (e) Participation in the research would not be contrary to the known wishes of the patient

THIS POLICY SHOULD ONLY BE FOLLOWED IF CONSISTENT WITH THE POLICY OF THE INVESTIGATOR'S INSTITUTION. In the event an Institution's policies are more stringent, the more stringent policies should be followed.

V.1.f.3. Assessment of Clinical Suitability

A qualified physician/investigator must assess the subject, and determine the subject's clinical suitability to participate in the study.

V.1.f.4. Enrollment

At the time of a subject's enrollment in a study, the informed consent process must take place and must be consistent with institutional guidelines for enrolling individuals in studies. Once a subject or surrogate signs the consent form, the subject is considered to be enrolled in the study. Any change in the subject's therapeutic regimen that may be necessary may only be made after the subject or surrogate has signed the consent form agreeing to participate in the study.



IRB STANDARD OPERATING PROCEDURES

V.1.f.5. Monitoring and Home Monitors

The mechanisms for monitoring the subject while on the protocol must be detailed in the research protocol (and the consent form) as described below. Those mechanisms must be appropriate given the subject's clinical condition and the nature of the study. In some circumstances the IRB may require that the subject must be seen and assessed by an independent physician with sufficient frequency to assure that the subject's health will not deteriorate while on the study:

- (a) In the event that the potential subject has a psychiatric illness affecting competency or capacity, an attending psychiatrist, or third party physician uninvolved in the research must assess capacity.
- (b) The name of this independent physician should not appear as an author on any published paper reporting on the study as that might lead to the appearance of a conflict.

For some protocols, particularly outpatient psychiatry protocols, the IRB might require an additional monitor, a "home monitor" who can evaluate the subject on a more frequent basis. The "home monitor" should be a reliable adult relative or friend who lives in close proximity to the subject and who is capable of reporting changes in the subject's status to the investigators.

V.1.g. Use of Waiting Periods

Subjects with diminished capacity may need more time to consider the information they are given about a research protocol. Information should be provided incrementally to facilitate understanding. Planning built-in waiting periods within the consent process also may be useful to allow potential participants time to consult with family members about whether or not to participate. When appropriate the IRB may recommend this method when consent is sought from a subject with diminished mental capacity.

V.1.h. Subject Advocate

In compliance with State and/or local law or at the discretion of the IRB, a Subject Advocate may be assigned to subjects who have fluctuating or limited decision making capacity or prospective incapacity.

V.1.i. Withdrawing Drugs from Subjects

The Biomedical Research Alliance of New York Institutional Review Board has developed the following guidelines for any research protocol involving the withdrawal of drugs from human subjects. For the purpose of these guidelines, withdrawal of medication includes a washout study, a withdrawal study, or a study that entails a washout or drug withdrawal that may be followed by administration of a drug or placebo.



IRB STANDARD OPERATING PROCEDURES

V.1.i.1. Content of the Consent Form for Withdrawal From Therapeutic Medication

The consent form and the consent process must comply with all the requirements for consent forms in human subject research. In addition, specifically with respect to studies in which a subject will be withdrawn from a therapeutic medication, it is critical that the consent form:

- (a) Identify
 - (i) The risks associated with the withdrawal from the subject's current medication;
 - (ii) The risks of being maintained on placebo (if applicable);
 - (iii) The risks of the experimental drug(s);
- (b) Describe the symptoms and assess the risks of the occurrence of those symptoms during the period of withdrawal, or while receiving placebo or experimental drug;
- (c) If the subject is expected to self-monitor for recurrence of the symptoms, the procedure for such self-monitoring should be clearly set forth. If there will be additional monitoring, the subject's must be told:
 - (iv) Who will do the monitoring;
 - (v) The frequency of the monitoring;
 - (vi) The place where monitoring will be done and;
 - (vii) The specific tests, lab data, and/or examinations that will be done for the purposes of monitoring. The actual purpose of monitoring (to assess possible relapse) should be stated and the specific symptoms that are to be evaluated should be listed;
- (d) The reversibility of any recurrence of symptoms as the result of medication withdrawal or placebo administration must be specifically described as well as the clinical steps that will be necessary to return the subject to the subject's former baseline;
- (e) The threshold of initiating treatment and removal from the study should be described as well as how the decision to return the subject to the subject's medication will be made and by whom

V.2. Requirements for HIV Testing/Consent Form

N.Y. State Public Health Law mandates that investigators conducting research in which HIV testing is planned or anticipated must comply with the following requirements:



IRB STANDARD OPERATING PROCEDURES

- (a) The N.Y. State Department of Health AIDS Institute Informed Consent to Perform an HIV Related Test form (HLT-21-91-00029-A; available online at <http://www.health.state.ny.us/diseases/aids/forms/index.htm>) must be signed in addition to the Informed Consent that has been approved by the Institutional Review Board. Alternatively, a separate “Research Participant Information Sheet and Consent for HIV Antibody Test” consent form (see [Appendix 28](#)) may be used with approval from the IRB.
- (b) The research consent form should include the following statements or some equivalent:
- “I have signed a separate consent form for HIV testing, and I have been counseled”
 - “HIV-related information may be shared with other members of the research team besides the principal investigator”

V.3. HIV Counseling

- (a) Pre- and Post-Test counseling must be conducted by a qualified individual certified in HIV counseling.
- (b) HIV testing related to procuring, distributing, or using a human body part, including organs, tissues, eyes, blood, semen or other bodily fluids for use in medical research or therapy or for transplantation to persons does not trigger the above requirements. Procedures listed in the consent form should state that subjects would be notified of positive results. In such a case, post-test counseling is required. The separate N.Y.S. consent form for HIV testing should not be used in these instances.

V.4. Release of HIV Information Form

The NY State HIV Release of HIV Information form should be signed, together with the research informed consent document when HIV information may be shared with researchers outside of the institution. The BRANY IRB will seek legal consult when HIV Research is reviewed for states other than New York.

V.5. Genetic Research and Tissue Banking

The BRANY Institutional Review Board is charged with the responsibility of assuring that subjects agreeing to participate in research are adequately informed of the issues related to their participation. In genetic research and research using stored tissue samples there are potential health, societal, emotional, and legal issues to consider.



IRB STANDARD OPERATING PROCEDURES

V.5.a. Definitions

“Human Genetic Research”

Genetic studies include but are not limited to a) pedigree studies (to learn the pattern of inheritance of a disease and to catalogue the range of symptoms of the disease); b) positional cloning studies (to identify and localize specific genes); c) DNA diagnostic studies (to develop techniques to determine specific DNA mutations); d) gene transfer research (to develop treatments for genetic diseases at the DNA level); e) longitudinal studies (to associate genetic conditions with health, health care, or social outcomes); and f) gene frequency studies. In contrast to the types of risks (often physical) that are presented by many biomedical research protocols that the IRB considers, the risks associated with genetic research may include social and psychological harm rather than physical injury.

In genetic research and research using stored tissue samples, there are potential health, societal, emotional and legal issues to consider. Many subjects may be naive to these issues and it is therefore necessary for the IRB to evaluate the protocols and consent forms for such studies with great care. As this new science develops and laws evolve, it is important to continuously rethink and refine the issues and the way in which they are presented to subjects.

It should be noted that “third parties” about whom identifiable and private information is collected in the course of research are human subjects. Under some circumstances informed consent must therefore be obtained from the “third party.” However, in accordance with 45 CFR 46.116, it is possible for the IRB to waive the requirement for informed consent. If the investigator requests a waiver of informed consent for the “third party,” the IRB will consider the request on a case-by-case basis. The outcome of the IRB deliberation will be documented in the IRB minutes.

“Genetic Tests”

The analysis of human DNA, RNA, chromosomes, proteins or other gene products to detect disease-related genotypes, mutations, phenotypes, or karyotypes for clinical purposes.

“Tissue Banking, Storehouse Research, and Databases”

All investigators who wish to develop tissue banks, repositories, and databases that utilize stored data or materials (cells, tissues, fluids, and body parts), whether the material is identifiable or not identifiable must submit their plans as projects for consideration by the IRB. Protocols must detail the policies and procedures for obtaining, storing, and sharing (with investigators on the faculty of Principal Investigator’s institution and/or other institutions) the material in the tissue bank, repository or database for future use in research, for assuring that the investigators who request the material have IRB approval (or exemption from IRB review) for the project that will utilize the material and verifying the informed consent provisions in those projects (when applicable), and for protecting the subject’s privacy and maintaining the confidentiality of the data.



IRB STANDARD OPERATING PROCEDURES

Projects in which the tissue banks, repositories and databases store only **non-identifiable or anonymous** material may be eligible for exemption from IRB review or may be reviewed by expedited review. This will be decided on a case-by-case basis.

Investigations involving the development of tissue banks, repositories, and databases that utilize stored data or material (cells, tissues, fluids, and body parts) from individually **identifiable** living persons qualify as human subject research and requires review at a convened meeting of the IRB.

V.5.b. Issues in Genetic Research

Genetic testing using proven methods for clinical purposes does not represent research. Genetic testing that is done for the acquisition of generalizable new knowledge constitutes research and all such studies that include genetic testing must conform to Federal, State and Local regulations for research in human subjects.

As described in the section on Genetic Testing in the OHRP Guide Book, the examination of biological samples (tissue, blood and other body fluids) in general represents no direct physical harm to subjects (inflicts no physical pain or suffering). However, genetic testing carries with it the very real possibility of psychosocial risks to the subjects (the risk of harm from learning genetic information about oneself, social stigmatization, discrimination, labeling, and potential loss of, or difficulty in, obtaining employment or insurance). Genetic studies that generate information about subjects' personal health risks can provoke anxiety and confusion and damage familial relationships. Information obtained through genetic research may also have repercussions for the subject's family members. Consequently, for these studies the IRB will consider these potential risks, and will take into account whether a biological sample can be linked back to a subject, directly or indirectly.

V.5.c. Disclosure of Results of Genetic Tests

The IRB requires that the consent document contain a statement included in the description of the study that indicates whether or not the information that derives from genetic studies will be given to that subject. NY law prevents disclosure of test results unless they are approved tests performed in a certified lab. If the study is being performed outside of New York State, the Investigator must comply with applicable law regarding genetic testing.

V.5.d. Family History Research

Family history research is used in bio-social and bio-behavioral research. Family history research typically involves obtaining information from one family member (the proband) about other family members (third parties). Third parties about whom identifiable and private information is collected in the course of research are human subjects. Confidentiality is a major concern in determining if minimal risk is involved. The IRB will consider on a case-by-case basis if informed consent from third parties can be waived and if so, document the decision in the IRB minutes.



IRB STANDARD OPERATING PROCEDURES

Please refer to [Appendix 21](#) (Genetic Research Consent Template) for consent guidelines for research involving genetic testing.

V.5.e. Types of Studies

- (a) **Prospective Studies** - the collection of new samples is part of the study design.
- (b) **Retrospective Studies** - utilize previously obtained samples collected for a purpose that is different from that of the current study.

V.5.f. Types of Samples

- (a) **Anonymous Biological** material that were originally collected without identifiers and are impossible to link to their sources.
- (b) **Anonymized** Biological materials that were initially identified, but have been irreversible stripped of all identifiers and are impossible to link to their sources. (This process does not preclude linkage with clinical, pathological, and demographic information before the subject identifiers are removed. Caution must be exercised so that the amount and type of linked information does not invalidate anonymity.)
- (c) **Identifiable** Biological materials that are unidentified for research purposes, but can be linked to their sources through the use of a code. Decoding can only be done by the investigator or another member of the research team.
- (d) **Identified** Biological material to which identifiers, such as name, patient number, or clear pedigree location, are attached and available to the researchers.

V.5.g. Research Using Properly Collected Samples

In **prospective** research, the investigators have the responsibility to communicate with the potential subject and obtain informed consent. Additionally the investigator has the obligation to maintain confidentiality to the extent permitted by law. (This is necessary unless the samples are collected anonymously or are anonymized).

The consent forms for such research should clearly indicate what information could result from the research, what the implications and limitations are, that unexpected findings may result, and what follow-up information they will receive (if any, as many studies are preliminary and results may not be meaningful or validated). They should be offered counseling, if appropriate, since results from such research could lead to adverse psychological outcomes, social stigmatization and discrimination. In certain cases they should be given the option to determine whether they want the results of their testing. The disposition of their samples should be included in the consent process and form; if samples are to be stored for future studies, they need to be informed of that as well as the expected length of time the samples may be stored and the possibility of storage failure.



IRB STANDARD OPERATING PROCEDURES

Note: In no case should results from a genetic test be given to subjects without proper validation of that test by a certified laboratory.

V.5.h. Retrospective Studies of Existing Samples

When **retrospective** research is done using anonymous or anonymized samples there is no need to obtain consent from the subjects. For research using samples that are identifiable, consent should be obtained. In certain cases the investigator may seek a waiver as detailed in 45 CFR 46.116.



IRB STANDARD OPERATING PROCEDURES

VI. CONFLICTS OF INTEREST

VI.1. Managing Conflicts of Interest

Conflict of Interest can be defined as any situation in which financial or personal obligations may compromise or present the appearance of compromising an individual's or group's professional judgment in conducting, reviewing, or reporting research. In research, this may refer to any interest that competes with the obligation to protect the rights and welfare of human subjects.

Research personnel, IRB members, IRB Chairpersons, the Institutional Official, BRANY staff and research sponsors may all have possible conflicts of interest. Such conflicts of interest may arise because of the intellectual property involved in many research discoveries or industry-academic partnerships, from financial incentives many pharmaceutical or biotech companies offer researchers for conducting trials or enrolling subjects, or due to particular role relationships within the governance structure of the institution.

In the event a conflict is identified and cannot be eliminated, the IRB, with guidance from the Conflict of Interest Committee (COIC), may impose such measures as deemed appropriate to manage the conflict. The IRB may seek input from the Institutional Official on an as needed basis.

VI.1.a. Definitions

“Financial Interest Related to the Research”

A financial interest in the sponsor, product, or service being tested, or anything of monetary value from a financially interested company, including but not limited to:

- Officer's/Director's fees
- Consulting fees
- Compensation for service on an Advisory Board (including scientific advisory boards)
- Honoraria for Lectures/Teaching;
- Gifts
- Other emoluments or "in kind" compensation such as travel and entertainment from a financially interested company (including those from a third party if the original source is a financially interested company), for any services not directly related to the reasonable costs of conducting the research as specified in the research agreement
- Compensation related to the research whose amount might be affected by the outcome of the research



IRB STANDARD OPERATING PROCEDURES

- Equity interest of any kind and in any amount in a non-publicly or publicly traded Financially Interested Company (e.g., stocks, stock options, convertible notes, other ownership interests), including those for which the value cannot be determined through reference to publicly available prices, those for which the value may be affected by the outcome of the research, and those which represent a 5% or more interest in any one single entity
- Intellectual property related to the proposed research
- License fees, technology transfers, and/or current and future royalties from patents and copyrights
- Board or executive relationships related to the research (regardless of compensation)
- Paid/reimbursed travel, meaning the occurrence and value of any paid/sponsored (i.e., sponsored travel is that which is paid on behalf of the Investigator and not reimbursed to the Investigator so that the exact monetary value may not be readily available), and/or reimbursed travel, whether in connection with an outside position or for consulting, lecturing, or service on a scientific advisory board, data safety monitoring board, steering committee for a clinical trial, executive committee for a clinical trial, or other committee for an outside entity, or for any other purpose including the purpose of the trip, the identity of the sponsor/organizer, the destination and the duration

The term “Financial Interest” does *not* include:

- (i) Salary or other remuneration received from the institution/organization
- (ii) Grant support for salaries from the institution/organization
- (iii) Holdings in mutual funds or 401K/403B retirement funds
- (iv) De minimus gifts whose aggregate value does not exceed \$100 per annum; or reasonable business expenses.

“Financially Interested Company”

An entity whose financial interests could reasonably appear to be affected by the conduct or outcome of a research project. The term “entity” means any corporation, limited liability company, partnership, limited partnership, limited liability partnership, joint venture, business trust, or other business organization, and any not-for-profit organization, charity or foundation.

“Related Party”

Spouse, domestic partner, and dependent children, siblings, parents, or equivalents by marriage, or other individuals residing in the household.



IRB STANDARD OPERATING PROCEDURES

“Significant Financial Interest”

A Financial Interest that is over \$5,000, or is less than \$5,000, and also involves a non-financial role in a Financially Interested Company, or is less than \$5,000, and the value cannot be determined through reference to publicly available prices, if the value will be affected by the outcome of the research, or the value represents 5% or more interest in any one single entity, and is determined by the COIC to be related to the research.

VI.1.b. Reporting of Financial Interests

The Research Application contains questions relating to an Investigator’s interest in any Financially Interested Company. All Principal Investigators and key study personnel (i.e. individuals involved in the design, conduct, or reporting of the research) must disclose financial interests that require disclosure under regulation, including financial interests related to the research as defined above, to the IRB with each research application. Disclosures must be made to BRANY IRB with each continuing review application for the research (at least annually), and any new Significant Financial Interests must be reported within 30 days of acquisition or discovery.

The responses to these questions shall be reviewed by the Director of the IRB or a designee. Any reported Financial Interest(s) shall be referred to the Conflict of Interest Committee of the Institution employing the Investigator. The Institution’s Conflict of Interest Committee then submits a report to the IRB outlining its determination as to whether the interest constitutes a significant financial interest and, if so, recommendations for eliminating, reducing or otherwise managing it.

In the event there is no Conflict of Interest Committee at the Investigator’s facility, the Financial Interest will be initially screened by the Director of the IRB or designee on behalf of the BRANY Conflict of Interest Committee (COIC). If the Financial Interest is less than \$5,000, unrelated to the research, and the Investigator has no other non-financial roles in any Financially Interested Company, the Director of the IRB or designee will inform the IRB and Investigator that the BRANY COIC has determined that there is no **Significant Financial Interest**, that a disclosure statement must be added to the informed consent document (when the study includes consent documents), and that the Committee has recommended no further action for the reported item. The Chairperson of the BRANY COIC will be notified of this determination. This recommendation and the resulting revised consent(s) shall be provided to the IRB for review.

If:

- the Financial Interest is over \$5,000, or,
- the Financial Interest is less than \$5,000, and also involves a non-financial role in a Financially Interested Company, or,
- the Financial Interest is less than \$5,000, and the value cannot be determined through reference to publicly available prices, if the value will be affected by the



IRB STANDARD OPERATING PROCEDURES

outcome of the research, or the value represents 5% or more interest in any one single entity, then,

it will be considered a potential **Significant Financial Interest** and will be reviewed by the BRANY COIC to determine whether it is related to the research, whether a conflict exists, and if so, how the conflict can be eliminated, reduced, or otherwise managed.

If the BRANY COIC determines the reported disclosure is not related to the research and/or that no Significant Financial Interest or other conflict exists and no management plan is required, the resulting determination shall be reported to the IRB at a subsequent meeting.

If it is determined that the reported disclosure is related to the research and/or a Significant Financial Interest or other conflict exists, and the resulting recommendation is to add a disclosure statement to the informed consent(s) (when the study includes consent documents), this recommendation and the resulting revised consent(s) shall be provided to the IRB for review.

If it is determined that the reported disclosure is related to the research and/or a Significant Financial Interest or other conflict exists, and the resulting recommendation is to require a management plan other than or in addition to adding a disclosure statement to the informed consent(s) (when the study includes consent documents), such recommendation will be provided to the IRB for review.

If the reviewed disclosure is from the Principal Investigator, the COIC's determination must be reviewed by the IRB before a final IRB approval can be granted. If the disclosure is from study personnel other than the Principal Investigator, BRANY IRB may grant approval for the research prior to receiving the outcome of the COIC review of the study personnel disclosure, only if the IRB's approval specifies that such personnel are not approved to participate in the research and that the personnel's participation will be reconsidered when the determination from the COIC is available for IRB review.

Wherever possible, conflicts should be eliminated. If a conflict cannot be eliminated, the conflict must be managed by distancing the investigator from aspects of the trial that may be influenced by the conflict, including trial design and monitoring, adverse event reporting, data analysis, and enrollment.

There may be special circumstances where the size or nature of the financial interest would, at the discretion of the IRB or the COIC, warrant a more detailed disclosure to the subjects or additional measures to manage the conflict. The IRB or the COIC, may draft additional disclosure language or prescribe additional appropriate action. These actions may include, among other things, limitations on particular investigator's participation in: study, design, subject recruitment, or data collection; monitoring of study conduct by the IRB or independent observers; or, prohibiting the research.



IRB STANDARD OPERATING PROCEDURES

The IRB or the COIC may mandate that the informed consent process for each subject be monitored by an independent party (someone who has no interest in the research being conducted).

The IRB has final authority to decide whether the interest and its management, if any, allows the research to be approved.

VI.1.c. IRB Meetings

OHRP regulations state: “No IRB may have a member participate in the IRB’s initial or continuing review of any project in which the member has a conflicting interest, except to provide information requested by the IRB” (45 CFR Part 46.107e). The International Conference on Harmonization Guideline states: “The investigator may provide information on any aspect of the trial, but should not participate in the deliberations of the IRB or in the vote/opinion of the IRB.”

Therefore:

- (1) Where an IRB member is an investigator for a study being reviewed by the board:
 - (a) The investigator will be asked to leave the meeting for discussion of his/her study and subsequent vote.
 - (b) The investigator may, however, be available to answer any specific questions raised by the IRB.
- (2) In the event an IRB member has any financial interest in connection with any study submitted for review, the member shall:
 - (c) Decline assignment as a primary or secondary reviewer of the protocol, and;
 - (d) Remove him/herself from the meeting during discussion and voting.

VI.1.d. Review of Conflicts

The following questions will be considered as appropriate:

- (3) Who is the sponsor?
- (4) Who designed the trial?
- (5) Who will analyze the safety and efficacy data?
- (6) What are the financial relationships between the Clinical Investigator and the commercial sponsor?
- (7) Is there any compensation that is affected by study outcome?



IRB STANDARD OPERATING PROCEDURES

- (8) Does the Investigator have any proprietary interests in the product including patents, trademarks, copyrights, and licensing arrangements?
- (9) Does the Investigator have an equity interest in the company? Is the company privately or publicly held?
- (10) Does the Investigator receive payments of other sorts from the sponsor (e.g., grants, equipment, retainers for consultation, honoraria)?
- (11) Does the Investigator have a board or executive relationship to the research (regardless of compensation)?

The IRB should carefully consider the specific mechanisms proposed to minimize the potential adverse consequences of the conflict in an effort to optimally protect the interests of the research subjects. If there are any financial conflict of interest issues on the part of the Investigator, he or she should not be directly engaged in aspects of the trial that could be influenced inappropriately by such conflict. These include, but are not limited to, the design of the trial, monitoring the trial, obtaining the informed consent, adverse event reporting, or data analysis.

When a conflict cannot be eliminated, the proposal regarding management/reduction of the conflict should be shared with the IRB for consideration.

In the event a conflict is identified and cannot be eliminated, the IRB and COI committee may impose such measures as deemed appropriate to manage the conflict. The IRB may seek input from the Institutional Official on an as needed basis.

In its discretion, the IRB may determine whether such proposal is acceptable, and if not, may either disapprove the research by the affected Investigator, or defer for further recommendations on management of the conflict.

This disclosure policy does not cover payments to physicians for referring patients into research protocols in which the physician does not participate as an investigator since these arrangements are prohibited.

VI.1.e. IRB Chairpersons, Members, and Consultants/Other Conflicts

IRB chairpersons, IRB members, and consultants may find themselves in any of the following conflicts of interest when reviewing research:

- (1) Where the IRB Chairperson, member, or consultant is listed as an investigator on the research
- (2) Where any investigator must report to or is under the supervision of an IRB Chairperson, member, or consultant.
- (3) Where the IRB Chairperson, member, or consultant (or their related party) is involved in the design, conduct, or reporting of the research.



IRB STANDARD OPERATING PROCEDURES

- (4) Where the IRB Chairperson, member, or consultant competes for research grants or contracts in the same or similar field as an investigator whose research is scheduled for review.
- (5) Where the IRB Chairperson, member, or consultant (or their related party) has an equity interest as described in the definition of Financial Interest in item VI.1.a. above.
- (6) Where the IRB Chairperson, member, or consultant (or their related party) receives salary, royalties or other payments as described in the definition of Financial Interest in section VI.1.a. above.

The Reviewer Checklist ([Appendix 6](#)) commences with a prompt for each reviewer to attest to the absence of a conflict of interest for the review at hand. In the event where the Chairperson or member identifies a potential conflict of interest, the individual must decline review and excuse him/herself from discussions and voting, except to provide information requested by the IRB. Chairpersons and/or members excused from discussions and voting will not be counted towards quorum. Consultants with a potential conflict of interest must decline review; instead BRANY IRB staff pursues another, non-conflicted consultant to conduct a needed consult review.

VI.1.f. Institutional Officials

To avoid possible conflict of interest, the institutional official will not serve as a voting member of the BRANY IRB.

VI.1.g. The Organization

BRANY does not and will not hold a license or patent on an investigational product, does not and will not participate in technology transfer agreements, does not permit the Organization to have any financial interests in companies sponsoring research reviewed by the BRANY IRB, and does not accept gifts from Financially Interested Companies. All members of BRANY staff are trained on this policy, and in the event that staff members are asked to accept a gift from a Financially Interested Company, BRANY staff must decline and report such offers to Senior Management.

VI.1.h. Organization Officials

In order to avoid a conflict of interest, or the appearance of a conflict, no administrative management of the organization (BRANY) may hold stock in any company sponsoring research reviewed by the BRANY IRB, unless such stock is held in a mutual fund or discretionary managed account in which no investment decisions may be made by the account holder. Individuals responsible for the IRB's business development are prohibited from serving as members on the IRB and from carrying out day-to-day operations of the review process.



IRB STANDARD OPERATING PROCEDURES

VI.1.i. IRB Conflict of Interest in Research Policy

Funding sources and financial interests that could affect or could be perceived as affecting the conduct of research should be routinely disclosed to research subjects. The following procedures should be followed:

The person or entity funding the research, and what their relationship is to the study (e.g., manufacturer of the drug or device) should be listed in one of the opening paragraphs of the consent form. This will give potential subjects the opportunity to question investigators regardless of whether a formal conflict exists.

In general, investigators should disclose to research subjects all financial interests of which they are aware. Specifically, financial interests should be disclosed in the following circumstances:

- (1) The study is sponsored by the manufacturer of the drug or device under investigation;
- (2) The Principal Investigator (PI) or other investigators or their related parties have a financial interest in the company that could benefit from the study findings;
- (3) Investigators or their related parties have a financial interest in the drug or device under investigation;
- (4) The Investigators are aware that the Principal Investigator's Department/Organization/Institution has a financial interest in the drug or device under investigation or in a company that could benefit from the study findings, or receives significant financial support from such a company. It is recommended that investigators contact appropriate administrative officials at their institution to ascertain whether such financial interests exist.

VI.1.j. Nature of Disclosure to Subjects

Financial arrangements between investigator, medical institutions and private industry and government are complex and diverse. Subjects have little knowledge of investigators' or medical institutions' financial interests in research that they conduct. This policy requires that subjects be informed in language that conveys the nature of the conflict and facilitates comprehension but does not alarm subjects or create a barrier to research. In general, specific information about the size of the financial holding is not necessary to make an informed decision about participating in research, but should be made available to the subject upon request.

Disclosure should be provided in a section of the informed consent form entitled, "Disclosure of Financial Interests." The disclosure may include:

- "Sometimes a research investigator owns a financial interest that could be affected by the results of a research study. The Biomedical Research Alliance of New York has policies in place to limit the possibility that financial interests will influence how studies are planned and conducted. This section will inform you if



IRB STANDARD OPERATING PROCEDURES

such a financial interest exists in this study that you are being asked to participate in.”

- “The *Sponsor* is providing funds to the *Investigator/or institution or both* on a per patient basis for conducting this clinical trial. If you would like further details regarding the funding of this trial, please contact the Biomedical Research Alliance Institutional Review Board at 516-470-6909.”
- For studies where an investigator holds a financial interest in the company that could benefit from the trial or in the drug/device under investigation, the consent form should additionally state that, “One or more investigators has a financial interest that could be affected by the outcome of this study.”

For studies where the PI’s Institution, Department or Division has a financial interest in the drug or device under investigation or in a company that could benefit from the study findings or receives significant support from the study sponsor, the consent form should additionally state that, “The Principal Investigator’s Institution, Department or Division has a financial interest or receives significant support from the study sponsor that could be affected by the outcome of this study.”

This disclosure provides basic information about the nature of the incentives, without disclosing details of the arrangements. It leaves open the possibility of a dialogue between the research subject and the investigators if the subject would like further information.

VI.1.k. Additional Measures

There may be special circumstances where the size or nature of the financial interest would, at the discretion of the IRB Administrative Staff, warrant a more detailed disclosure to the subjects or additional measures to manage the conflict. In those instances, the IRB Administrative Staff will pass this information on to the designated Conflict of Interest Committee and/or the BRANY IRB, which will have authority to draft additional disclosure language or prescribe additional appropriate action. These actions may include, among other things, limitations on particular investigator’s participation in: study, design, subject recruitment, or data collection; monitoring of study conduct by the IRB or independent observers; or, prohibiting the research.

VI.1.l. Required Education

Researchers and Research Staff must comply with requirements for initial training and retraining (at least every four years) about disclosures and responsibilities related to financial conflict of interest. Requirements can vary based on institution, funding source, or regulatory agency with oversight for the research, such as FDA or DHHS.

VI.1.m. Monitoring, Enforcement, and Reporting

Researchers and Research Staff must comply with requirements for monitoring and enforcement of management plans, and for external reporting of conflicts. BRANY IRB will collaborate with Institutional Conflict of Interest Committees by promptly providing



IRB STANDARD OPERATING PROCEDURES

any new or updated conflict of interest disclosures it receives, or any other requested documentation, to ensure researcher compliance. Requirements can vary based on institution, funding source, or regulatory agency with oversight for the research, such as FDA or DHHS. The Institution is responsible for ensuring reporting requirements to funding or regulatory agencies are met, and for reporting any non-compliance, enacted employee sanctions or other administrative actions to BRANY IRB. Reports of alleged non-compliance shall be processed in accordance with BRANY IRB SOP III.1.1.: “Reports of Non-Compliance” or III.1.i.: “Review of Reports of Unanticipated Problems Involving Risks to Subjects or Others” as appropriate.

VI.1.n. Providing for Protection of Privacy of Individual’s Financial Information Except as Needed to Manage Conflict of Interest

Information regarding Conflict of Interest is obtained from Investigators as part of the application process. IRB members report potential conflicts upon being accepted onto the IRB, and are reminded at each meeting to verify that no conflict exists concerning the protocols being reviewed. If a member has a conflict or a potential conflict, the member shall disclose it prior to discussion of the protocol in question. If the IRB agrees that a conflict exists, or if there is any disagreement or question as to whether a conflict exists, the member shall be excused from the meeting for voting on the protocol in question. Any new conflicts reported are noted by the IRB Director in order to aid in protocol review assignments and to ensure proper voting procedures, since no member may be present for voting on a protocol in which the member has a Financial Interest. Information collected regarding conflict interest including but not limited to conflict of interest disclosure forms shall be held in confidence and discussed only among those individuals involved in determining whether a conflict exists and those authorized to manage the conflict, if appropriate.

Conflict of interest information shall be collected from Investigators and all key study personnel in an addendum to the Research Application, and Application for Continuing Approval, if any information has changed. Such addenda shall be distributed to the IRB only in the event a conflict arises and the Conflict of Interest Committee has requested IRB input in review and management of the conflict. The financial information contained therein shall be held in confidence by the IRB. The IRB shall also hold in confidence any conflict of interest information received from or about fellow members. Conflict of Interest forms shall be maintained electronically in secure computer files. Conflict of Interest forms become part of the IRB’s records for the research in question. Access to IRB records shall be controlled in keeping with Section II.5.b of this policy.

VI.1.o. Violations of the Policy

In the event a violation of the conflict of interest policy is reported or suspected, such violation shall be immediately reported to the IRB Chairperson and Institutional Official. In the event of Investigator violation of the policy, the IRB Chairperson shall determine if any action is necessary to protect human subjects and may take such action, including suspension of IRB approval and reporting to the Investigator’s Conflict of Interest Committee (if applicable). The violation shall be reported to the IRB at its next convened meeting for further investigation and determination. Upon investigation and



IRB STANDARD OPERATING PROCEDURES

confirmation, the Institutional Official may also take any appropriate action, including removal of the Investigator from the affected research.

In the event of a report of IRB member violation of the policy, and upon investigation and confirmation, the Chairperson and/or Institutional Official may take such action as deemed appropriate and necessary to ensure the maintenance of the integrity of the IRB and the protection of human subjects, including but not limited to removal of the non-compliant member from the IRB.

In the event an Organization Official is found to be in violation of the Organization's Conflict of Interest Policy, the CEO and the Institutional Official shall determine appropriate action. Such action may include, but not be limited to: insistence on immediate elimination of the conflict, or modification of the official's duties to avoid conflict. In the event the violation involves the CEO, the matter shall be reported by the Institutional Official to the BRANY Management Committee, and the Committee shall take such action as it deems appropriate.



IRB STANDARD OPERATING PROCEDURES

VII. THE HIPAA PRIVACY RULE

The Biomedical Research Alliance is committed to conducting research in compliance with all applicable laws and regulations including the Health Insurance Portability and Accountability Act of 1996 (HIPAA), specifically the requirements of the HIPAA Privacy Rule ("Privacy Rule").

The Privacy Rule requires that those involved in research (Investigators, Research Staff, Institutions) adhere to specific requirements when using and/or disclosing a patient's protected health information.

VII.1. HIPAA Privacy Rule and the "Common Rule"

The Privacy Rule does not make any changes to the Common Rule. However, it does contain several provisions that resemble provisions of the Common Rule or that reference those provisions. For example, the Common Rule contains specific requirements for the composition of an institutional review board (IRB). Similarly, the Privacy Rule contains specific requirements for the composition of a Privacy Board, an alternative to the IRB that may be used exclusively for the review of privacy issues. The composition of a Privacy Board is similar to that of an IRB. The Privacy Rule does not require the development or use of a Privacy Board. Nor does it offer the Privacy Board as a replacement for the IRB. It merely sets up the mechanism for developing such a board as an alternative to using the IRB for reviewing privacy issues.

All researchers must continue to adhere to the mandates of the Common Rule while implementing the requirements of the HIPAA Privacy Rule.

VII.2. The Role of the BRANY IRB

The Privacy Rule does not regulate the work of IRBs as it relates to the protection of human subjects. However, in regard to research data, the Privacy Rule relies heavily on the IRBs as the key point of contact within a "covered entity" for researchers.

The Privacy Rule requires board approval of waivers or alterations of authorizations for release of PHI. The board can be either an IRB, established under the provisions of the Common Rule, or a Privacy Board, established according to the provisions of the Privacy rule. A Privacy Board is an alternative to an IRB for privacy issues.

The BRANY IRB will serve as the Privacy Board for HIPAA required determinations in BRANY IRB reviewed trials. The BRANY IRB shall ensure that consents to participate in BRANY IRB reviewed trials include HIPAA-compliant authorizations for release of research records.

VII.2.a. Definitions

Minimum Necessary - The Privacy Rule restricts use and disclosure of PHI. However, it does contain exceptions granting access in certain circumstances. Underlying all the exceptions, however, is the principle that any access should be limited to the minimum amount of information necessary to accomplish the intended purpose of the use or disclosure.



IRB STANDARD OPERATING PROCEDURES

For BRANY research purposes, this standard requires a BRANY researcher to evaluate the needs of his or her study and to request access only to those pieces of information that are necessary for the complete and accurate development of the research. This is advisable even if a research subject permits more information to be used or disclosed.

“Business Associate”

For the purpose of complying with the Privacy Rule the Biomedical Research Alliance of New York will be considered a Business Associate. A Business Associate performs a service on behalf of a Covered Entity that creates or requires access to a patient’s protected health information (PHI).

“Covered Entity”

May include: a health care provider that conducts certain transactions in electronic form (called here a "covered health care provider"); or a health care clearinghouse; or a health plan. An entity that is one or more of these types of entities is referred to as a "covered entity".

“Use and Disclosure of Information”

According to the definitions in the Privacy Rule, information is "used" when it remains within the entity holding the information and it is "disclosed" when it is released outside the entity that holds this information.

“PHI”

"Protected Health Information" (PHI) is individually identifiable health information transmitted or maintained electronically or in any other form or medium, except for education records or employment records, as excluded in the Privacy Rule.

“Representations”

In several sections, the Privacy Rule requires that a researcher give "representations" of certain facts to obtain access to PHI. The rule does not specify that such representations be made in writing; they could be oral or implied by actions. Where written representations are required under the Privacy Rule, they are specified. BRANY researchers are advised, however, that where the Privacy Rule requires that "representations" be made, the researcher should provide complete documentation.

VII.3. Access to Information

VII.3.a. Reviews Preparatory to Research

The HIPAA Privacy Rule and BRANY policy allow for the access to PHI without an authorization from the individual or a waiver from an IRB or Privacy Board when a BRANY researcher is preparing a protocol. However, the researcher must represent that access is only for the purpose of preparing a protocol. See discussion of representations, above. The representations necessary for preparatory access are 1) the



IRB STANDARD OPERATING PROCEDURES

access is only to prepare a protocol, 2) no protected health information will be removed from the Institution and 3) the protected health information accessed is necessary for the research proposed. This is the only instance of access allowed without authorization or IRB approval.

VII.3.b. Use and Disclosure of Information

The Privacy Rule identifies five distinct methods of using and disclosing information for research purposes. The researcher should be familiar with the five methods and should choose the method most suited to his or her study.

VII.3.c. Use and Disclosure With Authorization of the Subject

The most direct method of using and disclosing data is to ask the permission of the subject of that data. The permission is termed "authorization" in the Privacy Rule. A BRANY researcher may use or disclose PHI for research purposes after obtaining a privacy-related authorization from the individual who is the subject of the information. Such authorization is distinct from the informed consent for participation in a research study.

VII.3.d. Authorization

The Privacy Rule defines a valid authorization as having six "core elements" and three "required statements." These are detailed below. In addition to these items, the authorization must be written in plain language and a signed copy must be given to the individual. An authorization form does not have to be approved by an IRB or Privacy Board to be valid for purposes of the Privacy Rule. However, because it will generally be part of the informed consent process, an IRB or Privacy Board may review the authorization as part of its review of the informed consent process proposed by the researcher. The authorization language may be included either as a separate form or within the text of informed consent document.

VII.3.d.1. Core Elements of an Authorization

- (1) Description of the PHI to be used and disclosed "in a specific and meaningful fashion." To meet this definition, the description should be understandable to the individual; not a mere recitation of data elements understandable only to the research team. The description should be specific and the request should be limited to that information necessary to the research protocol. Examples of specific and meaningful descriptions include "Lab tests" "clinic visit data" "X-ray readings." Do not use medical jargon or test codes ("Chem7").
- (2) Name or specific identification of the person or class of persons authorized to make the disclosure. This refers to the "covered entity" that holds the information. Because the BRANY is a single covered entity, use of "BRANY" as the releasing entity is acceptable.
- (3) Name or specific identification of the person or class of persons authorized to receive the information. It is advisable to identify the principal investigator as



IRB STANDARD OPERATING PROCEDURES

receiving this information. An authorization also should refer to the "research team" that will work with the PI in conducting the research.

- (4) Description of each purpose of the requested use or disclosure. The authorization should include a clear, concise and understandable description of the purpose of the research. This description may be drawn from the explanation of the research contained in the informed consent form.
- (5) Expiration date or event. This is the date that the authorization to use or disclose the information will expire. For research purposes, this may be the end of the study. It is acceptable, for studies that will include development of a database, for the authorization to indicate "no expiration date." If a study has a specific end date or event that will occur at the end, this should be used. However, the authorization must include this information in some form.

VII.3.d.2. Required Statements in an Authorization

- A statement that the individual has a right to revoke the authorization in writing *and*
 - ***EITHER***
 - The exceptions to this right and description of how the individual may revoke
 - ***OR***
 - A reference to the covered entity's notice of privacy practices, if the exception information is contained there.
- Ability or inability to condition treatment, etc., on signing the authorization. Because research may be dependent on the use and disclosure of PHI, participation in the study may be conditioned on the subject signing the authorization.
- The potential for information to be redisclosed and no longer protected under HIPAA.

[Appendix 18](#) contains template language to be incorporated into a separate authorization form. [Appendix 19](#) contains a sample informed consent form with integrated HIPAA authorization language. All indicated information must be inserted at the appropriate places in the document. Once the form has been signed, a copy must be given to the subject. In addition, [Appendix 36](#) contains a template form for a revocation of authorization that can be given to a subject who expresses a desire to revoke a previously granted authorization.



IRB STANDARD OPERATING PROCEDURES

VII.3.e. Waiver of Authorization

An alternative to asking each research subject for an authorization is to ask an IRB or Privacy Board for a waiver of authorization or an alteration of the standard elements of an authorization. The Privacy Rule includes specific guidelines for the IRB or Privacy Board to follow in granting the request for a waiver of authorization.

The IRB or Privacy Board must obtain from the researcher a statement that is sufficient for the IRB or Privacy Board to determine the following:

- (1) The use or disclosure of PHI for the study involves no more than minimal risk to the privacy of the subject individual(s) based on the presence of:
 - An adequate plan by the researcher to protect the identifiers from improper use or disclosure. A full explanation of the plan is required.
 - An adequate plan to destroy the identifiers at the earliest opportunity UNLESS there is a health or research justification for retaining the identifiers is required by law
 - Adequate written assurances by the researcher that all efforts will be made to protect the information
- (2) The research could not practicably be done without the requested waiver or alteration
- (3) The research could not practicably be done without access to and use of the PHI

Once the BRANY IRB has granted a waiver, the researcher must have in his or her file, documentation of the action taken by the IRB or Privacy Board to grant the waiver. The documentation must include the following:

- (1) Identification of the IRB and the date of the action
- (2) The waiver criteria used by the IRB in reaching its decision
- (3) A description of the PHI being requested
- (4) Review and approval procedures used by the IRB in reaching its decision
- (5) Signature of the IRB Chairman or authorized member (available via the completed Reviewer Checklist).

VII.3.f. De-Identification (Safe Harbor)

The HIPAA Privacy Rule applies only to identifiable information. If information is de-identified, it no longer is subject to the Privacy Rule. CAUTION: de-identification for HIPAA purposes may not be the same as "anonymizing" data as commonly understood by researchers.



IRB STANDARD OPERATING PROCEDURES

To meet the standard for de-identified data under the Privacy Rule, a data set cannot include any of the following 18 elements:

- (1) Names
- (2) All geographical subdivisions smaller than a State, including street address, city, county, precinct, zip code, and their equivalent geo-codes, except for the initial three digits of the zip code if according to the current publicly available data from the Bureau of the census: a) the geographic unit formed by combining all zip codes with the same three initial digits contains more than 20,000 people; and b) the initial three digits of a zip code for all such geographic units containing 20,000 or fewer people is changed to 000.
- (3) All elements of dates (except year) for dates directly related to an individual, including birth date, admission date, discharge date, date of death; and all ages over 89 and all elements of dates (including year) indicative of such age, except that such ages and elements may be aggregated into a single category of age 90 or older.
- (4) Telephone numbers
- (5) Fax numbers
- (6) Electronic mail addresses
- (7) Social security numbers
- (8) Medical record numbers
- (9) Health plan beneficiary numbers
- (10) Account numbers
- (11) Certificate/license numbers
- (12) Vehicle identifiers and serial numbers, including license plate numbers
- (13) Device identifiers and serial numbers
- (14) Web Universal Resource Locators (URLs)
- (15) Internet Protocol (IP) address numbers
- (16) Biometric identifiers, including finger and voice prints
- (17) Full face photographic images and any comparable images
- (18) Any other unique identifying number, characteristic, or code.



IRB STANDARD OPERATING PROCEDURES

VII.3.g. Statistical Method of De-identification

An alternative to the "safe harbor method" is the statistical method. This standard is met if a person with appropriate knowledge and experience applying generally acceptable statistical and scientific principles and methods for rendering information not individually identifiable makes and documents a determination that there is only a small risk that the information could be used by others to identify a subject of the information. These techniques include removing all direct identifiers, reducing the number of variables on which a match might be made, and limiting the distribution of records through a "data use agreement" or "restricted access agreement" in which the recipient agrees to limits on who can use or receive the data.

VII.3.h. Limited Data Set

The limited data set option is less restrictive than complete de-identification but does not allow unfettered access to identifiable information but requires certain safeguards. A limited data set is one that has been stripped of the following elements:

- (1) Name
- (2) Street address (specifically, a postal address other than city, State and Zip code)
- (3) Telephone and fax numbers
- (4) E-mail address
- (5) Social security number
- (6) Certificate/license number
- (7) Vehicle identifiers and serial numbers
- (8) URLs and IP addresses
- (9) Full face photos and any other comparable images
- (10) Medical record numbers, health plan beneficiary numbers, and other account numbers
- (11) Device identifiers and serial numbers
- (12) Biometric identifiers, including finger and voice prints

The key differences between a de-identified data set and a limited data set would be the inclusion, in the latter, of dates and some geographic codes.

The use of a limited data set requires a data use agreement. This document is intended to provide assurance of the limited use or disclosure of the information in the limited data set. Under the Privacy Rule, a valid data use agreement must specify 1) the permitted



IRB STANDARD OPERATING PROCEDURES

uses and disclosures of information by the recipient, consistent with the purposes of the research, 2) the limits on who can use or receive the data, 3) that the recipient will not re-identify the data or contact the individuals, and 4) that the recipient will use appropriate safeguards to prevent use or disclosure of the limited data set other than as permitted by the Privacy Rule and data use agreement or as required by law.

Disclosure of the information in a limited data set does not require review by an IRB or Privacy Board.

VII.3.i. Research on Decedents' Information

Research on decedent's information is permitted if the covered entity (BRANY) obtains from the researcher, either orally or writing: 1) representation that the use or disclosure is sought solely for research on the PHI of decedents; 2) documentation, at the request of the covered entity, of the death of such individuals; and 3) representation that the PHI for which use or disclosure is sought is necessary for the research purposes.

It is suggested that the researcher have written documentation in his/her files covering these issues.

VII.4. Safeguarding Confidentiality

When information linked to individuals will be recorded as part of the research design, the IRB will ensure that adequate precautions will be taken to safeguard the confidentiality of the information. The more sensitive the data being collected, the more important it is for the researcher and the IRB to be familiar with techniques for protecting confidentiality.

- (a) In reviewing survey and interview research the IRB will consider the regulatory provision (45 CFR 46.117 (c)(1) for waiving documentation of consent when a signed consent form constitutes the only link between the research and the subjects and would itself be a risk to the subjects.
- (b) Among the available methods for ensuring confidentiality that may be used are coding of records, statistical techniques, and physical or computerized methods form maintaining the security of stored data.
- (c) Federal regulations (45 CFR 46.116(a)(5), and 21 CFR 56.116(a)(5) require that subjects be informed of the extent to which confidentiality of research records will be maintained. All consent documents must include the appropriate confidentiality language as noted in the Sample Informed Consent Form in [Appendix 19](#).
- (d) As indicated above subjects must be advised that Federal officials have the right to inspect and copy research records, including consent forms and individual medical records, to ensure compliance with the rules and standards of their programs. As required by FDA, information regarding this authority will be included in the consent information for all research that it regulates. Identifiable information obtained by Federal officials during such inspections is protected by the provisions of the Privacy Act of 1974.



IRB STANDARD OPERATING PROCEDURES

- (e) The IRB may require that an investigator obtain a Department of Health and Human Services (DHHS) Certificate of Confidentiality (see Section III.4.). The Certificate of Confidentiality protects against the involuntary release of sensitive information about individual subjects for use in Federal, state, or local civil, criminal, administrative, legislative, or other legal proceedings.

For more detailed information regarding the IRB's review of this information see Section IV.4.



IRB STANDARD OPERATING PROCEDURES

VIII. INVESTIGATIONAL DRUGS, DEVICES, AND BIOLOGICS

VIII.1. Investigational Drugs, Devices, and Biologics

The Food and Drug Administration (FDA) is a component of the U.S. Department of Health and Human Services (DHHS). The FDA's mission is to promote and protect the public health by helping safe and effective products reach the market, and then monitoring these products for continued safety after they are in use.

The FDA regulates clinical investigations (research) conducted on drugs, biologics, devices, diagnostics, and in some cases, dietary supplements and food additives, referred to as FDA regulated "test articles". All such investigations must be conducted in accordance with FDA requirements for informed consent and IRB review, regardless of funding source or sponsor.

When an FDA regulated test article is used in research more than one set of regulations may apply. For example, clinical trials involving FDA regulated test articles that are supported by DHHS human (e.g., the National Institutes of Health) fall under the jurisdiction of both the FDA and the DHHS OHRP. Such trials must comply with the FDA and the DHHS human subject regulations as well as other applicable Federal regulations. Where regulations differ between FDA and OHRP, the stricter regulation will apply.

VIII.1.a. FDA Requirements in Relation to 45 CFR 46

The human subject protection requirements found in FDA regulations are substantially the same as those in 45 CFR 46; however there are the following important differences:

- (1) The FDA has different definitions for "human subject" and "clinical investigation (research)."
- (2) FDA regulations contain no Assurance requirement.
- (3) Conditions for exemption, exception, and waiver of IRB review and informed consent requirements differ.
- (4) FDA regulations require specific determinations for the IRB review of device studies (see below).
- (5) FDA regulations include specific requirements for reporting adverse events that are not found in 45 CFR 46.
- (6) DHHS regulations include specific additional protections for pregnant women, fetuses, and human in vitro fertilization (Subpart B); prisoners (Subpart C); and Children (Subpart D). In April 2001 FDA issued regulations to protect children in research (20 CFR 50 Subpart D).

In addition to regulations governing human subject protection, the FDA also has regulations governing the use of investigational drugs and biological drugs (21 CFR 312) and devices (21 CFR 812).



IRB STANDARD OPERATING PROCEDURES

VIII.1.b. Research Involving Investigational FDA Regulated Test Articles

Medical products, such as drugs, biologics, and medical devices need to be proven safe and effective before the FDA can approve them for sale to and use by patients. FDA reviews the results of laboratory, animal and human clinical testing to determine if the product to be put on the market is safe and effective. New medical products that have not yet been approved for marketing by the FDA require a special status so they can be legally shipped for the purpose of conducting clinical investigations to establish safety and efficacy.

- (1) The IND is an investigational new drug application and is synonymous with “Notice of Claimed Investigational Exemption for a New Drug”. Investigational new drug (or investigational drug) means a new drug or biological drug used in a clinical investigation. An investigational drug must have an IND before it can be shipped. The IND goes into effect 30 days after the FDA receives the IND, unless the sponsor receives earlier notice from the FDA
- (2) An approved investigational device exemption (IDE) permits a device not approved by FDA to be shipped to conduct clinical investigations of that device. Not all investigational devices need an IDE.

When research involves the use of a drug other than the use of a marketed drug in the course of medical practice:

- (1) An Investigational New Drug (IND) must be on file with the FDA and an IND number granted, or
- (2) The protocol meets one of the FDA exemptions for the requirement to have an IND:
 - Exemption 1 (all of the following must be true):
 - (a) The drug product is lawfully marketed in the United States.
 - (b) The investigation is not intended to be reported to FDA as a well-controlled study in support of a new indication for use nor intended to be used to support any other significant change in the labeling for the drug.
 - (c) If the drug that is undergoing investigation is lawfully marketed as a prescription drug product, the investigation is not intended to support a significant change in the advertising for the product.
 - (d) The investigation does not involve a route of administration or dosage level or use in a patient population or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product.
 - (e) The investigation is conducted in compliance with 21 CFR 50 and 56.



IRB STANDARD OPERATING PROCEDURES

- (f) The investigation is conducted in compliance with the requirements of 21 CFR 312.7.
- Exemption 2 (all of the following must be true):
 - (a) A clinical investigation is for an in vitro diagnostic biological product that involves one or more of the following:
 - (b) Blood grouping serum.
 - (c) Reagent red blood cells.
 - (d) Anti-human globulin.
 - (e) The diagnostic test is intended to be used in a diagnostic procedure that confirms the diagnosis made by another, medically established, diagnostic product or procedure.
 - (f) The diagnostic test is shipped in compliance with 21 CFR 312.160.
- Exemption 3 (all of the following must be true):
 - (a) A clinical investigation involving use of a placebo if the investigation does not otherwise require submission of an IND.

The research can also be submitted to the FDA who may determine that an IND is not required. This determination must be documented in writing by the FDA. Copies of such documentation must be included with the Research Application.

Note: There is one exemption criterion not listed above that refers to *in vitro* animal use.

With only a few exceptions, most clinical research being done on FDA regulated test articles with either an IND or IDE will need initial review at a convened IRB meeting.

When applicable, FDA or sponsor correspondence confirming the IND NUMBER for the research must be included with the application for IRB review. This requirement may be waived if the IND number is referenced within the protocol. At the time of initial review the Primary Reviewer will be asked to determine and document that a valid IND is present before approving the research (See [Appendix 45 – IND Determination Form - Determining Whether a Proposed Activity is Exempt from the Requirement to Submit an IND Application to the FDA](#)). BRANY IRB will not release a final IRB approval determination without confirmation that a valid IND is in effect, when applicable. Thus, no recruiting, obtaining consent, or screening of participants for a study that is subject to an IND can occur until a valid IND has been confirmed.



IRB STANDARD OPERATING PROCEDURES

VIII.2. Protocols Involving the Investigational Use of Marketed Products

When a physician uses a product for an indication not in the approved labeling, he/she has the responsibility to be well-informed about this product and to base its use on a firm, scientific rationale and on sound medical evidence and to maintain records on the product's use and effects. When used in the practice of medicine, this is a matter between the physician and his/her patient and does not require submission to or approval by the BRANY IRB.

The investigational use of a marketed product, however, suggests the use of the product in context of a study protocol. The intent is to develop information about the safety and efficacy of the product. In this case, the PI shall prepare and submit a protocol in accordance with Section III.1.n.1-18., III.2.-III.9. (see also the Research Application – [Appendix 11](#) – which includes submission guidelines).

VIII.3. Investigators also Serving as Sponsors

In cases where an Investigator is also serving as the Sponsor (Investigator-Sponsor) to conduct a clinical study, the Investigator must assume the responsibilities of the Sponsor, including reporting requirements to the FDA, in addition to the responsibilities of the Investigator.

An Investigator-sponsor for a project with an IND must follow the FDA regulations in 21 CFR 312 applicable to sponsor responsibilities, including the record keeping requirements and prompt reporting to the FDA and all participating investigators of significant new adverse effects or risks with respect to the drug or biologic.

An Investigator-sponsor for an IDE protocol must follow the FDA regulations in 21 CFR 812 applicable to sponsor responsibilities, including the record keeping requirements and the required notification to the FDA and all participating investigators of any evaluation of unanticipated device effects within ten (10) working days of first receiving notice of the effect.

Included with the application for IRB review, the investigator must include evidence of experience and/or training regarding the regulatory requirements of sponsors. The IRB will evaluate the investigator's credentials and make a determination as to whether the investigator's knowledge is sufficient to adequately fill the role of Sponsor for the research. Investigators applying for review of such research projects will be informed to contact the BRANY IRB to obtain additional information.

The FDA regulatory requirements for sponsors can be found in the Code of Federal Regulations. The following is a list that a sponsor-investigator may need to comply with:

Drugs or devices:

- 21 CFR 11 (Electronic records and electronic signature)



IRB STANDARD OPERATING PROCEDURES

- 21 CFR 54 (Financial Disclosure by Clinical Investigators)

Drugs and Biologics:

- 21 CFR 210 (Current Good Manufacturing Practice In Manufacturing, Processing, Packing, Or Holding of Drugs; General)
- 21 CFR 211 (Current Good Manufacturing Practice for Finished Pharmaceuticals)
- 21 CFR 312 (Investigational New Drug Application)
- 21 CFR 314 (Drugs for Human Use)
- 21 CFR 320 (Bioavailability and Bioequivalence Requirements)
- 21 CFR 330 (Over-The-Counter (OTC) Human Drugs Which are Generally Recognized as Safe and Effective and Not Misbranded)
- 21 CFR 601 (Biologics Licensing)

Devices:

- 21 CFR 807 (Establishment Registration and Device Listing for Manufacturers and Initial Importers Of Devices)
- 21 CFR 812 (Investigational Device Exemptions)
- 21 CFR 814 (Premarket Approval of Medical Devices)
- 21 CFR 820 (Quality System Regulation)
- 21 CFR 860 (Medical Device Classification Procedures)

VIII.4. Gene Transfer Research:

Gene transfer involves the administration of genetic material to alter the biological properties of living cells for therapeutic use. Gene transfer activities in humans are investigational and are regulated by both FDA and the National Institutes of Health (NIH) Office of Biotechnology Activities (OBA).

- (a) FDA regulations require the submission of an IND for human gene transfer research through the FDA Center for Biologics.
- (b) DHHS regulations specify state that no individual may be enrolled in human gene transfer research until review has been completed by the NIH Recombinant DNA Advisory Committee (RAC), local Institutional BioSafety Committee (IBC) approval has been obtained, local IRB approval has been obtained, and the investigator has obtained all other regulatory authorizations from the subject.



IRB STANDARD OPERATING PROCEDURES

- (c) While the RAC is advisory to the Director of the NIH, compliance with its guidelines is mandatory for all investigators at institutions that receive NIH funds for research involving recombinant DNA.

VIII.5. IRB Review of Medical Devices

FDA device regulations differentiate between significant risk (SR) and non-significant risk (NSR) devices. A significant risk device must have an IDE, while a non-significant risk device requires an Abbreviated IDE issued by the IRB (21 CFR 812.2(b)). Thus, if a clinical investigation is submitted to an IRB for a device that has an IDE, the device is considered a SR device. The initial risk assessment may be determined by the sponsor, but the IRB must make a formal determination during a convened meeting regarding the appropriate SR/NSR category (see [Appendix 46](#) – IDE Determination Form). When applicable, a copy of the FDA correspondence that includes the IDE information must be submitted to the BRANY IRB with the Research application. Devices may also be determined to be exempt from the IDE requirements under 21 CFR 812.2(c) and 812.2(d).

VIII.5.a. Definitions and IRB Determinations

VIII.5.a.1. Significant Risk Device

A SR device study presents a potential for serious risk to the health, safety, or welfare of a subject and (a) is intended as an implant, or (b) is used in supporting or sustaining human life, or (c) is of substantial importance in diagnosing, curing, mitigating or treating disease, or otherwise prevents impairment of human health (21CFR812.3(m)). The IRB must consider the proposed use of the device and not the device alone in determining risk.

VIII.5.a.2. Non-Significant Risk Device

A NSR device study is one that does not meet the definition of a SR study. This determination is independent of the designations of the study as minimal risk.

VIII.5.a.3. IRB's Role in Classification of Devices

Under some circumstances, the IRB will have to determine whether a device involves significant risk (SR) or non-significant (NSR) to subjects. Because NSR studies require an Abbreviated IDE issued by the IRB, a clinical investigation involving an investigational device classified by the sponsor as NSR may be submitted to an IRB for review without an IDE. The sponsor should provide the IRB with a risk assessment and the rationale used in making its NSR risk determination in keeping with 21 CFR 812.2(b).

For studies of devices classified by Sponsors as NSR, the IRB will review the information and make its own independent determination regarding whether the device is SR or NSR. If the IRB determines that an investigation presented for approval as NSR involves a SR device, it shall so notify the investigator, and where appropriate the sponsor, in keeping with 21 CFR 812.66.



IRB STANDARD OPERATING PROCEDURES

The BRANY IRB will use the list of NSR and SR devices as detailed by the FDA (see [Appendix 16](#)) for comparison with the device that requires classification, as well as the information obtained by the sponsor and investigator in making the NSR/SR determination. The IRB shall make an independent determination, notwithstanding any designation by the sponsor or Investigator of the device as SR or NSR.

The IRB must determine whether it is in agreement with the rendering of the decision by the sponsor of the device being a non-significant risk or a significant risk device. If the IRB is in agreement with the sponsor's determination of NSR, no report to the FDA is required until the data are submitted. However, the sponsor must be notified if the IRB disagrees with the sponsor's NSR determination. The IRB will consider all of the following when classifying a device study with regard to significant or non-significant risk:

- Risks from the investigational form of the device;
- Risk of the entire device;
- Risks from tests done to evaluate research results;
- Risks of the treatment of the patient; and
- Underlying condition.

Note: Protocols Involving SR devices DO NOT qualify for expedited review.

VIII.5.a.4. IRB Determinations

The initial risk assessment may be determined by the sponsor, but the IRB must make a formal determination during a convened meeting regarding the appropriate SR/NSR category (see [Appendix 46](#) – IDE Determination Form).

When research is conducted to determine the safety or effectiveness of a device, the IRB will determine:

- The device has an IDE issued by the FDA.
- The device fulfills the requirements for an abbreviated IDE.
 - The device is not a banned device.
 - The sponsor labels the device in accordance with 21 CFR 812.5.
 - The sponsor obtains IRB approval of the investigation after presenting the reviewing IRB with a brief explanation of why the device is not a significant risk device, and maintains such approval.



IRB STANDARD OPERATING PROCEDURES

- The sponsor ensures that each investigator participating in an investigation of the device obtains from each subject under the investigator's care, consent under 21 CFR 50 and documents it, unless documentation is waived.
- The sponsor complies with the requirements of 21 CFR 812.46 with respect to monitoring investigations;
- The sponsor maintains the records required under 21 CFR 812.140(b) (4) and (5) and makes the reports required under 21 CFR 812.150(b) (1) through (3) and (5) through (10);
- The sponsor ensures that participating investigators maintain the records required by 21 CFR 812.140(a)(3)(i) and make the reports required under 812.150(a) (1), (2), (5), and (7); and
- The sponsor complies with the prohibitions in 21 CFR 812.7 against promotion and other practices.
- The device fulfills one of the IDE exemption categories:
 - A device, other than a transitional device, in commercial distribution immediately before May 28, 1976, when used or investigated in accordance with the indications in labeling in effect at that time.
 - A device, other than a transitional device, introduced into commercial distribution on or after May 28, 1976, that FDA has determined to be substantially equivalent to a device in commercial distribution immediately before May 28, 1976, and that is used or investigated in accordance with the indications in the labeling FDA reviewed under subpart E of part 807 in determining substantial equivalence.
 - A diagnostic device, if the sponsor complies with applicable requirements in 21 CFR 809.10(c) and if the testing:
 - Is noninvasive.
 - Does not require an invasive sampling procedure that presents significant risk.
 - Does not by design or intention introduce energy into a participant.
 - Is not used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure.
 - A device undergoing consumer preference testing, testing of a modification, or testing of a combination of two or more devices in



IRB STANDARD OPERATING PROCEDURES

commercial distribution, if the testing is not for the purpose of determining safety or effectiveness and does not put participants at risk.

- A custom device as defined in 21 CFR 812.3(b), unless the device is being used to determine safety or effectiveness for commercial distribution.

VIII.5.a.4.1. Study Involves a SR Device

If the IRB determines that the study involves a SR device, then the IRB will be governed by the IDE regulations at 21 CFR 812. The IRB will notify both the investigator and the sponsor in writing of its determination, and the sponsor will need to submit an IDE application to the FDA. The study may not be approved without submission of proof of IDE approval. The study may not begin until the FDA approves the IDE and the IRB approves the study. If an IDE has already been obtained, then the IRB may proceed with its review. Sponsor and PI notification is not required if device is submitted as SR and IRB verifies that IDE approval has been obtained.

VIII.5.a.4.2. Study Involves a NSR Device

If the IRB determines that the device is classified as NSR, the clinical investigation may begin once IRB approval is obtained since the submission of an IDE application to the FDA is not required. (Note: The terms “non-significant risk” and minimal risks are defined separately, and are not synonymous).

VIII.5.a.4.3. Study Involves Device Equivalent to Marketed Device

If FDA agrees that a new device is substantially equivalent to a device already on the market, it can be marketed without clinical testing. However, if clinical data are necessary to demonstrate equivalence, any clinical studies must be conducted in compliance with the requirements of the IDE regulations, IRB review, and informed consent.



IRB STANDARD OPERATING PROCEDURES

Appendix

1	The Belmont Report	212
2	Declaration of Helsinki.....	223
3	Nuremberg Code.....	228
4	Glossary	229
5	Glossary of Lay Terms for Use in Preparing Informed Consent Documents	246
6	Reviewer Checklist.....	259
7	Addendum Checklist – Consultant Review	316
8	Application for Continuing Approval.....	317
9	Checklist – Human Research	338
10	Sample IRB Approval Letter	340
11	Research Application	345
12	CIRB Sponsor Request for IRB Review Form	394
13	Reportable Event Form	395
14	ARCHIVED – IND Safety Report Submission Form.....	405
15	Request for IRB Review of Modifications Form	406
16	FDA List of NSR and SR Devices.....	424
17	Risks and Procedures – Lay Terminology	428
18	HIPAA Authorization Template Language	439
19	Sample Informed Consent Form.....	441
20	Sample Assent Form and Preparation Guidelines	452
21	Genetic Research Consent Template.....	455
22	Sample QA Review Report.....	459
23	Termination and Enrollment Closure Form	465
24	Confidentiality Agreement	470
25	Informed Consent Feedback Tool	471
26	Continuing Review Multi-center Sponsor Supplement	472
27	Application for Determination of Exempt Status.....	474
28	Research Participant Information Sheet and Consent for HIV Antibody Test.....	477
29	Request for Waiver or Alteration of Informed Consent	479
30	ARCHIVED – Access to PHI in Preparation of Research Form	481
31	Guidelines for Drafting Protocols.....	482
32	Binder Organization List	486



IRB STANDARD OPERATING PROCEDURES

33	ARCHIVED – Document Retention Schedule.....	488
34	Sample Subject Enrollment Note.....	489
35	Investigator Database Information Form.....	490
36	Revocation of Authorization to Release PHI for Research Purposes.....	495
37	Chairperson Evaluation	496
38	IRB Checklist – Emergency Use.....	497
39	Emergency Use Notification Form	499
40	ARCHIVED – CIRB IND Safety Report Submission Form	501
41	Site Research Application (CIRB).....	502
42	Sponsor/CRO Research Application (CIRB).....	516
43	Request for Waiver of Authorization to Release PHI for Research Purposes	521
44	Data Use Agreement.....	524
45	IND Determination Form.....	526
46	IDE Determination Form.....	527
47	Change of Principal Investigator Form.....	529
48	Conflict of Interest in Research Disclosure Forms	533
49	Change of Study Site/Institution Form	537
50	Application for Transfer of IRB Oversight to BRANY IRB.....	540
51	IRB SOP Document Control Checklist.....	543
52	Additional Research Site Location(s) Form.....	544
53	IRB Member Evaluation Questionnaire.....	547
54	Minor Protocol Deviation Log.....	550
55-199	Reserved	551
200	Jun 2011 IRB SOP Change Summary.....	552
201	Dec 2011 IRB SOP Change Summary	557
202	Aug 2012 IRB SOP Change Summary	560
203	Dec 2012 IRB SOP Change Summary	561
204	Jun 2013 IRB SOP Change Summary	563
205	Dec 2013 IRB SOP Change Summary	575
206	Mar 2014 IRB SOP Change Summary	580
207	Sept 2014 IRB SOP Change Summary	586
208	Apr 2015 IRB SOP Change Summary	592



IRB STANDARD OPERATING PROCEDURES

Appendix 1 - BRANY IRB Standard Operating Procedures

Department of Health, Education, and Welfare
Office of the Secretary
PROTECTION OF HUMAN SUBJECTS

**BELMONT REPORT:
ETHICAL PRINCIPLES AND GUIDELINES
FOR THE PROTECTION OF
HUMAN SUBJECTS OF RESEARCH**

Report of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research

Table of Contents

- I. Summary
- II. Members of the Commission
- III. The Belmont Report: An Introduction
 - A. Boundaries Between Practice and Research
 - B. Basic Ethical Principles
 - 1. Respect for Persons
 - 2. Beneficence
 - 3. Justice
 - C. Applications
 - 1. Informed Consent
 - 2. Assessment of Risk and Benefits
 - 3. Selection of Subjects

I. Summary

On July 12, 1974, the National Research Act (Public Law 93348) was signed into law, thereby creating the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. One of the charges to the Commission was to identify the basic ethical principles that should underlie the conduct of biomedical and behavioral research involving human subjects, and to develop guidelines, which should be followed to assure that such research is conducted in accordance with those principles. In carrying out the above, the Commission was directed to consider: (i) the boundaries between biomedical and behavioral research and the accepted and routine practice of medicine, (ii) the role of assessment of risk-benefit criteria in the determination of the appropriateness of research involving human subjects, (iii) appropriate guidelines for the selection of human subjects for participation in such research, and (iv) the nature and definition of informed consent in various research settings.



IRB STANDARD OPERATING PROCEDURES

The *Belmont Report* attempts to summarize the basic ethical principles identified by the Commission in the course of its deliberations. It is the outgrowth of an intensive four-day period of discussions that were held in February 1976 at the Smithsonian Institution's Belmont Conference Center, supplemented by the monthly deliberations of the Commission that were held over a period of nearly four years. It is a statement of basic ethical principles and guidelines that should assist in resolving the ethical problems that surround the conduct of research with human subjects.

By publishing the Report in the **Federal Register**, and providing reprints upon request, the Secretary intends that it may be made readily available to scientists, members of institutional review boards, and Federal employees. The two-volume Appendix, containing the lengthy reports of experts and specialists, who assisted the Commission in fulfilling this part of its charge, is available as DHEW Publication No. (OS) 780013 and No. (OS) 78-0014, for sale by the Superintendent of Documents, U.S. Government Printing Office, Washington, D.C. 20402.

Unlike most other reports of the Commission, the *Belmont Report* does not make specific recommendations for administrative action by the Secretary of Health, Education, and Welfare. Rather, the Commission recommended that the *Belmont Report* be adopted in its entirety, as a statement of the Department's policy. The Department requests public comment on this recommendation.

II. Members of the Commission

Kenneth John Ryan, M.D., Chairman, Chief of Staff, Boston Hospital for Women.
Joseph V. Brady, Ph.D., Professor of Behavioral Biology, Johns Hopkins University.
Robert E. Cooke, M.D., President, Medical College of Pennsylvania.
Dorothy I. Height, President, National Council of Negro Women, Inc.
Albert R. Jonsen, Ph.D., Associate Professor of Bioethics, University of California at San Francisco.
Patricia King, J.D., Associate Professor of Law, Georgetown University Law Center.
Karen Lebacqz, Ph.D., Associate Professor of Christian Ethics, Pacific School of Religion.
*David W. Louisell, J. D., Professor of Law, University of California at Berkeley.
Donald W. Seldin, M.D., Professor and Chairman, Department of Internal Medicine, University of Texas at Dallas.
Eliot Stellar, Ph.D., Provost of the University and Professor of Physiological Psychology, University of Pennsylvania.
*Robert H. Turtle, LL.B., Attorney, VomBaur, Coburn, Simmons & Turtle, Washington, D.C.
* *Deceased.*

III. THE BELMONT REPORT

Scientific research has produced substantial social benefits. It has also posed some troubling ethical questions. Public attention was drawn to these questions by reported abuses of human subjects in biomedical experiments, especially during the Second World War. During the Nuremberg War Crime Trials, the *Nuremberg Code* was drafted as a set of standards for judging physicians and scientists who had conducted biomedical experiments on concentration camp prisoners. This Code became the prototype of many later [codes](#) intended to assure that research involving human subjects would be carried out in an ethical manner.

The codes consist of rules, some general, others specific, that guide the investigators or the reviewers of research in their work. Such rules often are inadequate to cover complex situations; at times they come into conflict, and they are frequently difficult to interpret or apply.



IRB STANDARD OPERATING PROCEDURES

Broader ethical principles will provide a basis on which specific rules may be formulated, criticized and interpreted.

Three principles, or general prescriptive judgments, that are relevant to research involving human subjects are identified in this statement. Other principles may also be relevant. These three are comprehensive, however, and are stated at a level of generalization that should assist scientists, subjects, reviewers and interested citizens to understand the ethical issues inherent in research involving human subjects. These principles cannot always be applied, so as to resolve beyond dispute particular ethical problems. The objective is to provide an analytical framework that will guide the resolution of ethical problems arising from research involving human subjects.

This statement consists of a distinction between research and practice, a discussion of the three basic ethical principles, and remarks about the application of these principles.

A. Boundaries Between Practice and Research

It is important to distinguish between biomedical and behavioral research, on the one hand, and the practice of accepted therapy on the other, in order to know what activities ought to undergo review for the protection of human subjects of research. The distinction between research and practice is blurred, partly because both often occur together (as in research designed to evaluate a therapy), and partly because notable departures from standard practice are often called "experimental", when the terms "experimental" and "research" are not carefully defined.

For the most part, the term "practice" refers to interventions that are designed solely to enhance the well-being of an individual patient or client and that have a reasonable expectation of success. The purpose of medical or behavioral practice is to provide diagnosis, preventive treatment or therapy to particular individuals. By contrast, the term "research" designates an activity designed to test an hypothesis, permit conclusions to be drawn, and thereby to develop or contribute to generalizable knowledge (expressed, for example, in theories, principles, and statements of relationships). Research is usually described in a formal protocol that sets forth an objective and a set of procedures designed to reach that objective.

When a clinician departs in a significant way from standard or accepted practice, the innovation does not, in and of itself, constitute research. The fact that a procedure is "experimental" in the sense of new, untested or different, does not automatically place it in the category of research. Radically new procedures of this description should, however, be made the object of formal research at an early stage, in order to determine whether they are safe and effective. Thus, it is the responsibility of medical practice committees, for example, to insist that a major innovation be incorporated into a formal research project.

Research and practice may be carried on together, when research is designed to evaluate the safety and efficacy of a therapy. This need not cause any confusion regarding whether or not the activity requires review; the general rule is, that if there is any element of research in an activity, that activity should undergo review for the protection of human subjects.

B. Basic Ethical Principles

The expression "basic ethical principles" refers to those general judgments that serve as a basic justification for the many particular ethical prescriptions and evaluations of human actions.



IRB STANDARD OPERATING PROCEDURES

Three basic principles, among those generally accepted in our cultural tradition, are particularly relevant to the ethics of research involving human subjects: the principles of respect for persons, beneficence and justice.

1. Respect for Persons

Respect for persons incorporates at least two ethical convictions: first, that individuals should be treated as autonomous agents, and second, that persons with diminished autonomy are entitled to protection. The principle of respect for persons thus divides into two separate moral requirements: the requirement to acknowledge autonomy, and the requirement to protect those with diminished autonomy.

An autonomous person is an individual capable of deliberation about personal goals, and of acting under the direction of such deliberation. To respect autonomy is to give weight to autonomous persons' considered opinions and choices, while refraining from obstructing their actions, unless they are clearly detrimental to others. To show lack of respect for an autonomous agent is to repudiate that person's considered judgments, to deny an individual the freedom to act on those considered judgments, or to withhold information necessary to make a considered judgment, when there are no compelling reasons to do so.

However, not every human being is capable of self-determination. The capacity for self-determination matures during an individual's life, and some individuals lose this capacity wholly or in part, because of illness, mental disability, or circumstances that severely restrict liberty. Respect for the immature and the incapacitated may require protecting them as they mature or while they are incapacitated.

Some persons are in need of extensive protection, even to the point of excluding them from activities which may harm them; other persons require little protection beyond making sure they undertake activities freely and with awareness of possible adverse consequences. The extent of protection afforded should depend upon the risk of harm, and the likelihood of benefit. The judgment that any individual lacks autonomy should be periodically reevaluated, and will vary in different situations.

In most cases of research involving human subjects, respect for persons demands that subjects enter into the research voluntarily and with adequate information. In some situations, however, application of the principle is not obvious. The involvement of prisoners as subjects of research provides an instructive example. On the one hand, it would seem that the principle of respect for persons requires that prisoners not be deprived of the opportunity to volunteer for research. On the other hand, under prison conditions they may be subtly coerced or unduly influenced to engage in research activities, for which they would not otherwise volunteer. Respect for persons would then dictate that prisoners be protected. Whether to allow prisoners to "volunteer" or to "protect" them presents a dilemma. Respecting persons, in most hard cases, is often a matter of balancing competing claims urged by the principle of respect itself.

2. Beneficence

Persons are treated in an ethical manner, not only by respecting their decisions and protecting them from harm, but also by making efforts to secure their well-being. Such



IRB STANDARD OPERATING PROCEDURES

treatment falls under the principle of beneficence. The term "beneficence" is often understood to cover acts of kindness or charity that go beyond strict obligation. In this document, beneficence is understood in a stronger sense, as an obligation. Two general rules have been formulated as complementary expressions of beneficent actions in this sense: (1) do not harm; and (2) maximize possible benefits, and minimize possible harms.

The Hippocratic maxim "do no harm" has long been a fundamental principle of medical ethics. Claude Bernard extended it to the realm of research, saying that one should not injure one person, regardless of the benefits that might come to others. However, even avoiding harm requires learning what is harmful; and, in the process of obtaining this information, persons may be exposed to risk of harm. Further, the Hippocratic Oath requires physicians to benefit their patients "according to their best judgment". Learning what will in fact benefit may require exposing persons to risk. The problem posed by these imperatives is to decide when it is justifiable to seek certain benefits despite the risks involved, and when the benefits should be foregone because of the risks.

The obligations of beneficence affect both individual investigators and society at large, because they extend both to particular research projects and to the entire enterprise of research. In the case of particular projects, investigators and members of their institutions are obliged to give forethought to the maximization of benefits and the reduction of risk that might occur from the research investigation. In the case of scientific research in general, members of the larger society are obliged to recognize the longer term benefits and risks that may result from the improvement of knowledge, and from the development of novel medical, psychotherapeutic, and social procedures.

The principle of beneficence often occupies a well-defined, justifying role in many areas of research involving human subjects. An example is found in research involving children. Effective ways of treating childhood diseases and fostering healthy development are benefits that serve to justify research involving children --even when individual research subjects are not direct beneficiaries. Research also makes it possible to avoid the harm that may result from the application of previously accepted routine practices that, on closer investigation, turn out to be dangerous. But the role of the principle of beneficence is not always so unambiguous. A difficult ethical problem remains, for example, about research that presents more than minimal risk, without immediate prospect of direct benefit to the children involved. Some have argued that such research is inadmissible, while others have pointed out, that this limit would rule out much research promising great benefit to children in the future. Here again, as with all hard cases, the different claims covered by the principle of beneficence may come into conflict and force difficult choices.

3. Justice

Who ought to receive the benefits of research and bear its burdens? This is a question of justice, in the sense of "fairness in distribution" or "what is deserved". An injustice occurs, when some benefit to which a person is entitled is denied without good reason, or when some burden is imposed unduly. Another way of conceiving the principle of justice is that, equals ought to be treated equally. However, this statement requires explication. Who is equal and who is unequal? What considerations justify

IRB STANDARD OPERATING PROCEDURES

departure from equal distribution? Almost all commentators allow that distinctions based on experience, age, deprivation, competence, merit and position do sometimes constitute criteria justifying differential treatment for certain purposes. It is necessary, then, to explain in what respects people should be treated equally. There are several widely accepted formulations of just ways to distribute burdens and benefits. Each formulation mentions some relevant property, on the basis of which burdens and benefits should be distributed. These formulations are (1) to each person an equal share, (2) to each person according to individual need, (3) to each person according to individual effort, (4) to each person according to societal contribution, and (5) to each person according to merit.

Questions of justice have long been associated with social practices, such as punishment, taxation and political representation. Until recently, these questions have not generally been associated with scientific research. However, they are foreshadowed, even in the earliest reflections on the ethics of research involving human subjects. For example, during the 19th and early 20th centuries, the burdens of serving as research subjects fell largely upon poor ward patients, while the benefits of improved medical care flowed primarily to private patients. Subsequently, the exploitation of unwilling prisoners as research subjects in Nazi concentration camps was condemned as a particularly vagrant injustice. In this country, in the 1940's, the Tuskegee syphilis study used disadvantaged, rural black men to study the untreated course of a disease that is by no means confined to that population. These subjects were deprived of demonstrably effective treatment in order not to interrupt the project, long after such treatment became generally available.

Against this historical background, it can be seen how conceptions of justice are relevant to research involving human subjects. For example, the selection of research subjects needs to be scrutinized in order to determine whether some classes (e.g., welfare patients, particular racial and ethnic minorities, or persons confined to institutions) are being systematically selected, simply because of their easy availability, their compromised position, or their manipulability, rather than for reasons directly related to the problem being studied. Finally, whenever research supported by public funds leads to the development of therapeutic devices and procedures, justice demands both that these not provide advantages only to those who can afford them, and that such research should not unduly involve persons from groups unlikely to be among the beneficiaries of subsequent applications of the research.

C. Applications

Applications of the general principles to the conduct of research leads to consideration of the following requirements: informed consent, risk / benefit assessment, and the selection of subjects of research.

1. Informed Consent

Respect for persons requires that subjects, to the degree that they are capable, be given the opportunity to choose what shall or shall not happen to them. This opportunity is provided, when adequate standards for informed consent are satisfied.



IRB STANDARD OPERATING PROCEDURES

While the importance of informed consent is unquestioned, controversy prevails over the nature and possibility of an informed consent. Nonetheless, there is widespread agreement that the consent process can be analyzed as containing three elements: information, comprehension and voluntariness.

- **Information**

Most codes of research establish specific items for disclosure, intended to assure that subjects are given sufficient information. These items generally include: the research procedure, their purposes, risks and anticipated benefits, alternative procedures (where therapy is involved), and a statement offering the subject the opportunity to ask questions and to withdraw at any time from the research. Additional items have been proposed, including how subjects are selected, the person responsible for the research, *etc.*

However, a simple listing of items does not answer the question of what the standard should be for judging how much and what sort of information should be provided. One standard frequently invoked in medical practice, namely the information commonly provided by practitioners in the field or in the locale, is inadequate, since research takes place precisely when a common understanding does not exist. Another standard, currently popular in malpractice law, requires the practitioner to reveal the information that reasonable persons would wish to know in order to make a decision regarding their care. This, too, seems insufficient, since the research subject, being in essence a volunteer, may wish to know considerably more about risks gratuitously undertaken than do patients who deliver themselves into the hand of a clinician for needed care. It may be, that a standard of "the reasonable volunteer" should be proposed: the extent and nature of information should be such that persons, knowing that the procedure is neither necessary for their care nor perhaps fully understood, can decide whether they wish to participate in the furthering of knowledge. Even when some direct benefit to them is anticipated, the subjects should understand clearly the range of risk, and the voluntary nature of participation.

A special problem of consent arises, where informing subjects of some pertinent aspect of the research is likely to impair the validity of the research. In many cases, it is sufficient to indicate to subjects that they are being invited to participate in research, of which some features will not be revealed until the research is concluded. In all cases of research involving incomplete disclosure, such research is justified, only if it is clear that (1) incomplete disclosure is truly necessary to accomplish the goals of the research, (2) there are no undisclosed risks to subjects that are more than minimal, and (3) there is an adequate plan for debriefing subjects, when appropriate, and for dissemination of research results to them. Information about risks should never be withheld for the purpose of eliciting the cooperation of subjects, and truthful answers should always be given to direct questions about the research. Care should be taken to distinguish cases, in which disclosure would destroy or invalidate the research, from cases in which disclosure would simply inconvenience the investigator.

- **Comprehension**



IRB STANDARD OPERATING PROCEDURES

The manner and context, in which information is conveyed is as important as the information itself. For example, presenting information in a disorganized and rapid fashion, allowing too little time for consideration, or curtailing opportunities for questioning, all may adversely affect a subject's ability to make an informed choice.

Because the subject's ability to understand is a function of intelligence, rationality, maturity and language, it is necessary to adapt the presentation of the information to the subject's capacities. Investigators are responsible for ascertaining that the subject has comprehended the information. While there is always an obligation to ascertain that the information about risk to subjects is complete and adequately comprehended, when the risks are more serious, that obligation increases. On occasion, it may be suitable to give some oral or written tests of comprehension.

Special provision may need to be made, when comprehension is severely limited --for example, by conditions of immaturity or mental disability. Each class of subjects that one might consider as incompetent (e.g., infants and young children, mentally disabled patients, the terminally ill, and the comatose) should be considered on its own terms. Even for these persons, however, respect requires giving them the opportunity to choose, to the extent they are able, whether or not to participate in research. The objections of these subjects to involvement should be honored, unless the research entails providing them a therapy unavailable elsewhere. Respect for persons also requires seeking the permission of other parties in order to protect the subjects from harm. Such persons are thus respected, both by acknowledging their own wishes, and by the use of third parties to protect them from harm.

The third parties chosen should be those, who are most likely to understand the incompetent subject's situation, and to act in that person's best interest. The person authorized to act on behalf of the subject should be given an opportunity to observe the research, as it proceeds, in order to be able to withdraw the subject from the research, if such action appears in the subject's best interest.

- **Voluntariness**

An agreement to participate in research constitutes a valid consent, only if voluntarily given. This element of informed consent requires conditions free of coercion and undue influence. Coercion occurs when an overt threat of harm is intentionally presented by one person to another, in order to obtain compliance. Undue influence, by contrast, occurs through an offer of an excessive, unwarranted, inappropriate or improper reward or other overture, in order to obtain compliance. Also, inducements that would ordinarily be acceptable may become undue influences, if the subject is especially vulnerable.

Unjustifiable pressures usually occur, when persons in positions of authority or commanding influence --especially where possible sanctions are involved-- urge a course of action for a subject. A continuum of such influencing factors exists, however, and it is impossible to state precisely, where justifiable persuasion ends and undue influence begins. But undue influence would include actions, such as manipulating a person's choice through the controlling influence



IRB STANDARD OPERATING PROCEDURES

of a close relative, and threatening to withdraw health services to which an individual would otherwise be entitled.

2. Assessment of Risks and Benefits

The assessment of risks and benefits requires a careful arrayal of relevant data, including, in some cases, alternative ways of obtaining the benefits sought in the research. Thus, the assessment presents both an opportunity and a responsibility to gather systematic and comprehensive information about proposed research. For the investigator, it is a means to examine whether the proposed research is properly designed. For a review committee, it is a method for determining whether the risks that will be presented to subjects are justified. For prospective subjects, the assessment will assist the determination whether or not to participate.

- **The Nature and Scope of Risks and Benefits**

The requirement that research be justified on the basis of a favorable risk / benefit assessment, bears a close relation to the principle of beneficence, just as the moral requirement that informed consent be obtained is derived primarily from the principle of respect for persons.

The term "risk" refers to a possibility that harm may occur. However, when expressions such as "small risk" or "high risk" are used, they usually refer (often ambiguously) both to the chance (probability) of experiencing a harm, and the severity (magnitude) of the envisioned harm.

The term "benefit" is used in the research context to refer to something of positive value related to health or welfare. Unlike "risk", "benefit" is not a term that expresses probabilities. Risk is properly contrasted to probability of benefits, and benefits are properly contrasted with harms rather than risks of harm. Accordingly, so-called risk / benefit assessments are concerned with the probabilities and magnitudes of possible harms, and anticipated benefits. Many kinds of possible harms and benefits need to be taken into account. There are, for example, risks of psychological harm, physical harm, legal harm, social harm and economic harm, and the corresponding benefits. While the most likely types of harms to research subjects are those of psychological or physical pain or injury, other possible kinds should not be overlooked.

Risks and benefits of research may affect the individual subjects, the families of the individual subjects, and society at large (or special groups of subjects in society). Previous codes and Federal regulations have required that risks to subjects be outweighed by the sum of both the anticipated benefit to the subject, if any, and the anticipated benefit to society in the form of knowledge to be gained from the research. In balancing these different elements, the risks and benefits affecting the immediate research subject will normally carry special weight. On the other hand, interests, other than those of the subject, may on some occasions be sufficient by themselves to justify the risks involved in the research, so long as the subjects' rights have been protected. Beneficence thus

IRB STANDARD OPERATING PROCEDURES

requires that we protect against risk of harm to subjects, and also that we be concerned about the loss of the substantial benefits that might be gained from research.

- **The Systematic Assessment of Risks and Benefits**

It is commonly said that benefits and risks must be "balanced", and shown to be "in a favorable ratio". The metaphorical character of these terms draws attention to the difficulty of making precise judgments. Only on rare occasions will quantitative techniques be available for the scrutiny of research protocols. However, the idea of systematic, non-arbitrary analysis of risks and benefits should be emulated insofar as possible. This ideal requires those making decisions about the justifiability of research to be thorough in the accumulation and assessment of information about all aspects of the research, and to consider alternatives systematically. This procedure renders the assessment of research more rigorous and precise, while making communication between review board members and investigators less subject to misinterpretation, misinformation and conflicting judgments. Thus, there should first be a determination of the validity of the presuppositions of the research; then the nature, probability and magnitude of risk should be distinguished, with as much clarity as possible. The method of ascertaining risks should be explicit, especially where there is no alternative to the use of such vague categories as small or slight risk. It should also be determined whether an investigator's estimates of the probability of harm or benefits are reasonable, as judged by known facts or other available studies.

Finally, assessment of the justifiability of research should reflect at least the following considerations: (i) Brutal or inhumane treatment of human subjects is never morally justified. (ii) Risks should be reduced to those necessary to achieve the research objective. It should be determined whether it is in fact necessary to use human subjects at all. Risk can perhaps never be entirely eliminated, but it can often be reduced by careful attention to alternative procedures. (iii) When research involves significant risk of serious impairment, review committees should be extraordinarily insistent on the justification of the risk (looking usually to the likelihood of benefit to the subject --or, in some rare cases, to the manifest voluntariness of the participation). (iv) When vulnerable populations are involved in research, the appropriateness of involving them should itself be demonstrated. A number of variables go into such judgments, including the nature and degree of risk, the condition of the particular population involved, and the nature and level of the anticipated benefits. (v) Relevant risks and benefits must be thoroughly arrayed in documents and procedures used in the informed consent process.

3. Selection of Subjects

Just as the principle of respect for persons finds expression in the requirements for consent, and the principle of beneficence in risk / benefit assessment, the principle of



IRB STANDARD OPERATING PROCEDURES

justice gives rise to moral requirements that there be fair procedures and outcomes in the selection of research subjects.

Justice is relevant to the selection of subjects of research at two levels: the social and the individual. Individual justice in the selection of subjects would require that researchers exhibit fairness: thus, they should not offer potentially beneficial research only to some patients, who are in their favor, or select only "undesirable" persons for risky research. Social justice requires that distinction be drawn between classes of subjects that ought, and ought not, to participate in any particular kind of research, based on the ability of members of that class to bear burdens, and on the appropriateness of placing further burdens on already burdened persons. Thus, it can be considered a matter of social justice, that there is an order of preference in the selection of classes of subjects (*e.g.*, adults before children), and that some classes of potential subjects (*e.g.*, the institutionalized mentally infirm or prisoners) may be involved as research subjects, if at all, only on certain conditions.

Injustice may appear in the selection of subjects, even if individual subjects are selected fairly by investigators, and treated fairly in the course of research. Thus, injustice arises from social, racial, sexual and cultural biases institutionalized in society. Thus, even if individual researchers are treating their research subjects fairly, and even if institutional review boards are taking care to assure that subjects are selected fairly within a particular institution, unjust social patterns may nevertheless appear in the overall distribution of the burdens and benefits of research. Although individual institutions or investigators may not be able to resolve a problem that is pervasive in their social setting, they can consider distributive justice in selecting research subjects.

Some populations, especially institutionalized ones, are already burdened in many ways by their infirmities and environments. When research is proposed that involves risks and does not include a therapeutic component, other less burdened classes of persons should be called upon first to accept these risks of research, except where the research is directly related to the specific conditions of the class involved. Also, even though public funds for research may often flow in the same directions as public funds for health care, it seems unfair that populations dependent on public health care constitute a pool of preferred research subjects, if more advantaged populations are likely to be the recipients of the benefits. One special instance of injustice results from the involvement of vulnerable subjects. Certain groups, such as racial minorities, the economically disadvantaged, the very sick, and the institutionalized, may continually be sought as research subjects, owing to their ready availability in settings, where research is conducted. Given their dependent status and their frequently compromised capacity for free consent, they should be protected against the danger of being involved in research solely for administrative convenience, or because they are easy to manipulate as a result of their illness or socioeconomic condition.



IRB STANDARD OPERATING PROCEDURES

Appendix 2 - BRANY IRB Standard Operating Procedures

WMA Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects

Adopted by the 18th WMA General Assembly, Helsinki, Finland, June 1964

and amended by the:

29th WMA General Assembly, Tokyo, Japan, October 1975

35th WMA General Assembly, Venice, Italy, October 1983

41st WMA General Assembly, Hong Kong, September 1989

48th WMA General Assembly, Somerset West, South Africa, October 1996

52nd WMA General Assembly, Edinburgh, Scotland, October 2000

53rd WMA General Assembly, Washington, DC, USA, October 2002

(Note of Clarification on paragraph 29 added)

55th WMA General Assembly, Tokyo, Japan, October 2004

(Note of Clarification on Paragraph 30 added)

59th WMA General Assembly, Seoul, Korea, October 2008

A. INTRODUCTION

1. The World Medical Association (WMA) has developed the Declaration of Helsinki as a statement of ethical principles for medical research involving human subjects, including research on identifiable human material and data.

The Declaration is intended to be read as a whole and each of its constituent paragraphs should not be applied without consideration of all other relevant paragraphs.

2. Although the Declaration is addressed primarily to physicians, the WMA encourages other participants in medical research involving human subjects to adopt these principles.

3. It is the duty of the physician to promote and safeguard the health of patients, including those who are involved in medical research. The physician's knowledge and conscience are dedicated to the fulfilment of this duty.

4. The Declaration of Geneva of the WMA binds the physician with the words, "The health of my patient will be my first consideration," and the International Code of Medical Ethics declares that, "A physician shall act in the patient's best interest when providing medical care."



IRB STANDARD OPERATING PROCEDURES

5. Medical progress is based on research that ultimately must include studies involving human subjects. Populations that are underrepresented in medical research should be provided appropriate access to participation in research.
6. In medical research involving human subjects, the well-being of the individual research subject must take precedence over all other interests.
7. The primary purpose of medical research involving human subjects is to understand the causes, development and effects of diseases and improve preventive, diagnostic and therapeutic interventions (methods, procedures and treatments). Even the best current interventions must be evaluated continually through research for their safety, effectiveness, efficiency, accessibility and quality.
8. In medical practice and in medical research, most interventions involve risks and burdens.
9. Medical research is subject to ethical standards that promote respect for all human subjects and protect their health and rights. Some research populations are particularly vulnerable and need special protection. These include those who cannot give or refuse consent for themselves and those who may be vulnerable to coercion or undue influence.
10. Physicians should consider the ethical, legal and regulatory norms and standards for research involving human subjects in their own countries as well as applicable international norms and standards. No national or international ethical, legal or regulatory requirement should reduce or eliminate any of the protections for research subjects set forth in this Declaration.

B. PRINCIPLES FOR ALL MEDICAL RESEARCH

11. It is the duty of physicians who participate in medical research to protect the life, health, dignity, integrity, right to self-determination, privacy, and confidentiality of personal information of research subjects.
12. Medical research involving human subjects must conform to generally accepted scientific principles, be based on a thorough knowledge of the scientific literature, other relevant sources of information, and adequate laboratory and, as appropriate, animal experimentation. The welfare of animals used for research must be respected.
13. Appropriate caution must be exercised in the conduct of medical research that may harm the environment.
14. The design and performance of each research study involving human subjects must be clearly described in a research protocol. The protocol should contain a statement of the ethical considerations involved and should indicate how the principles in this Declaration have been addressed. The protocol should include information regarding funding, sponsors, institutional affiliations, other potential conflicts of interest, incentives for subjects and provisions for treating and/or compensating subjects who are harmed as a consequence of participation in the research study. The protocol should describe arrangements for post-study access by study subjects to interventions identified as beneficial in the study or access to other appropriate care or benefits.



IRB STANDARD OPERATING PROCEDURES

15. The research protocol must be submitted for consideration, comment, guidance and approval to a research ethics committee before the study begins. This committee must be independent of the researcher, the sponsor and any other undue influence. It must take into consideration the laws and regulations of the country or countries in which the research is to be performed as well as applicable international norms and standards but these must not be allowed to reduce or eliminate any of the protections for research subjects set forth in this Declaration. The committee must have the right to monitor ongoing studies. The researcher must provide monitoring information to the committee, especially information about any serious adverse events. No change to the protocol may be made without consideration and approval by the committee.

16. Medical research involving human subjects must be conducted only by individuals with the appropriate scientific training and qualifications. Research on patients or healthy volunteers requires the supervision of a competent and appropriately qualified physician or other health care professional. The responsibility for the protection of research subjects must always rest with the physician or other health care professional and never the research subjects, even though they have given consent.

17. Medical research involving a disadvantaged or vulnerable population or community is only justified if the research is responsive to the health needs and priorities of this population or community and if there is a reasonable likelihood that this population or community stands to benefit from the results of the research.

18. Every medical research study involving human subjects must be preceded by careful assessment of predictable risks and burdens to the individuals and communities involved in the research in comparison with foreseeable benefits to them and to other individuals or communities affected by the condition under investigation.

19. Every clinical trial must be registered in a publicly accessible database before recruitment of the first subject.

20. Physicians may not participate in a research study involving human subjects unless they are confident that the risks involved have been adequately assessed and can be satisfactorily managed. Physicians must immediately stop a study when the risks are found to outweigh the potential benefits or when there is conclusive proof of positive and beneficial results.

21. Medical research involving human subjects may only be conducted if the importance of the objective outweighs the inherent risks and burdens to the research subjects.

22. Participation by competent individuals as subjects in medical research must be voluntary. Although it may be appropriate to consult family members or community leaders, no competent individual may be enrolled in a research study unless he or she freely agrees.

23. Every precaution must be taken to protect the privacy of research subjects and the confidentiality of their personal information and to minimize the impact of the study on their physical, mental and social integrity.



IRB STANDARD OPERATING PROCEDURES

24. In medical research involving competent human subjects, each potential subject must be adequately informed of the aims, methods, sources of funding, any possible conflicts of interest, institutional affiliations of the researcher, the anticipated benefits and potential risks of the study and the discomfort it may entail, and any other relevant aspects of the study. The potential subject must be informed of the right to refuse to participate in the study or to withdraw consent to participate at any time without reprisal. Special attention should be given to the specific information needs of individual potential subjects as well as to the methods used to deliver the information. After ensuring that the potential subject has understood the information, the physician or another appropriately qualified individual must then seek the potential subject's freely-given informed consent, preferably in writing. If the consent cannot be expressed in writing, the non-written consent must be formally documented and witnessed.

25. For medical research using identifiable human material or data, physicians must normally seek consent for the collection, analysis, storage and/or reuse. There may be situations where consent would be impossible or impractical to obtain for such research or would pose a threat to the validity of the research. In such situations the research may be done only after consideration and approval of a research ethics committee.

26. When seeking informed consent for participation in a research study the physician should be particularly cautious if the potential subject is in a dependent relationship with the physician or may consent under duress. In such situations the informed consent should be sought by an appropriately qualified individual who is completely independent of this relationship.

27. For a potential research subject who is incompetent, the physician must seek informed consent from the legally authorized representative. These individuals must not be included in a research study that has no likelihood of benefit for them unless it is intended to promote the health of the population represented by the potential subject, the research cannot instead be performed with competent persons, and the research entails only minimal risk and minimal burden.

28. When a potential research subject who is deemed incompetent is able to give assent to decisions about participation in research, the physician must seek that assent in addition to the consent of the legally authorized representative. The potential subject's dissent should be respected.

29. Research involving subjects who are physically or mentally incapable of giving consent, for example, unconscious patients, may be done only if the physical or mental condition that prevents giving informed consent is a necessary characteristic of the research population. In such circumstances the physician should seek informed consent from the legally authorized representative. If no such representative is available and if the research cannot be delayed, the study may proceed without informed consent provided that the specific reasons for involving subjects with a condition that renders them unable to give informed consent have been stated in the research protocol and the study has been approved by a research ethics committee. Consent to remain in the research should be obtained as soon as possible from the subject or a legally authorized representative.

30. Authors, editors and publishers all have ethical obligations with regard to the publication of the results of research. Authors have a duty to make publicly available the results of their

IRB STANDARD OPERATING PROCEDURES

research on human subjects and are accountable for the completeness and accuracy of their reports. They should adhere to accepted guidelines for ethical reporting. Negative and inconclusive as well as positive results should be published or otherwise made publicly available. Sources of funding, institutional affiliations and conflicts of interest should be declared in the publication. Reports of research not in accordance with the principles of this Declaration should not be accepted for publication.

C. ADDITIONAL PRINCIPLES FOR MEDICAL RESEARCH COMBINED WITH MEDICAL CARE

31. The physician may combine medical research with medical care only to the extent that the research is justified by its potential preventive, diagnostic or therapeutic value and if the physician has good reason to believe that participation in the research study will not adversely affect the health of the patients who serve as research subjects.

32. The benefits, risks, burdens and effectiveness of a new intervention must be tested against those of the best current proven intervention, except in the following circumstances:

- The use of placebo, or no treatment, is acceptable in studies where no current proven intervention exists; or
- Where for compelling and scientifically sound methodological reasons the use of placebo is necessary to determine the efficacy or safety of an intervention and the patients who receive placebo or no treatment will not be subject to any risk of serious or irreversible harm. Extreme care must be taken to avoid abuse of this option.

33. At the conclusion of the study, patients entered into the study are entitled to be informed about the outcome of the study and to share any benefits that result from it, for example, access to interventions identified as beneficial in the study or to other appropriate care or benefits.

34. The physician must fully inform the patient which aspects of the care are related to the research. The refusal of a patient to participate in a study or the patient's decision to withdraw from the study must never interfere with the patient-physician relationship.

35. In the treatment of a patient, where proven interventions do not exist or have been ineffective, the physician, after seeking expert advice, with informed consent from the patient or a legally authorized representative, may use an unproven intervention if in the physician's judgement it offers hope of saving life, re-establishing health or alleviating suffering. Where possible, this intervention should be made the object of research, designed to evaluate its safety and efficacy. In all cases, new information should be recorded and, where appropriate, made publicly available.

Retrieved 07.30.2013 from <http://www.wma.net/en/30publications/10policies/b3/>

IRB STANDARD OPERATING PROCEDURES**Appendix 3 – BRANY IRB Standard Operating Procedures**

Nuremberg Code

1. The voluntary consent of the human subject is absolutely essential. This means that the person involved should have legal capacity to give consent; should be so situated as to be able to exercise free power of choice, without the intervention of any element of force, fraud, deceit, duress, over-reaching, or other ulterior form of constraint or coercion; and should have sufficient knowledge and comprehension of the elements of the subject matter involved as to enable him to make an understanding and enlightened decision. This latter element requires that before the acceptance of an affirmative decision by the experimental subject there should be made known to him the nature, duration, and purpose of the experiment; the method and means by which it is to be conducted; all inconveniences and hazards reasonable to be expected; and the effects upon his health or person which may possibly come from his participation in the experiment.

The duty and responsibility for ascertaining the quality of the consent rests upon each individual who initiates, directs or engages in the experiment. It is a personal duty and responsibility which may not be delegated to another with impunity.

2. The experiment should be such as to yield fruitful results for the good of society, unprocurable by other methods or means of study, and not random and unnecessary in nature.
3. The experiment should be so designed and based on the results of animal experimentation and a knowledge of the natural history of the disease or other problem under study that the anticipated results will justify the performance of the experiment.
4. The experiment should be so conducted as to avoid all unnecessary physical and mental suffering and injury.
5. No experiment should be conducted where there is an *a priori* reason to believe that death or disabling injury will occur; except, perhaps, in those experiments where the experimental physicians also serve as subjects.
6. The degree of risk to be taken should never exceed that determined by the humanitarian importance of the problem to be solved by the experiment.
7. Proper preparations should be made and adequate facilities provided to protect the experimental subject against even remote possibilities of injury, disability, or death.
8. The experiment should be conducted only by scientifically qualified persons. The highest degree of skill and care should be required through all stages of the experiment of those who conduct or engage in the experiment.
9. During the course of the experiment the human subject should be at liberty to bring the experiment to an end if he has reached the physical or mental state where continuation of the experiment seems to him to be impossible.
10. During the course of the experiment the scientist in charge must be prepared to terminate the experiment at any stage, if he has probable cause to believe, in the exercise of the good faith, superior skill and careful judgment required of him that a continuation of the experiment is likely to result in injury, disability, or death to the experimental subject.

Reprinted from *Trials of War Criminals before the Nuremberg Military Tribunals under Control Council Law No. 10, Vol. 2, pp. 181-182.* Washington, D.C.: U.S. Government Printing Office, 1949



IRB STANDARD OPERATING PROCEDURES

Appendix 4 – BRANY IRB Standard Operating Procedures

Glossary

ABUSE-LIABLE Pharmacological substances that have the potential for creating abusive dependency. Abuse-labile substances can include both illicit drugs (e.g., heroine) and licit drugs (e.g., methamphetamines).

ADAMHA Alcohol, Drug Abuse, and Mental Health Administration; reorganized in October 1992 as the Substance Abuse and Mental Health Services Administration (SAMHSA). ADAMHA included the National Institute of Mental Health (NIMH), the National Institute on Alcohol Abuse and Alcoholism (NIAAA), the National Institute on Drug Abuse (NIDA), the Office for Substance Abuse Prevention (OSAP), and the Office for Treatment Intervention (OTI). NIMH, NIAAA, and NIDA are now part of the National Institutes of Health (NIH). (See also: SAMHSA.)

ADJUVANT THERAPY Therapy provided to enhance the effect of a primary therapy; auxiliary therapy.

ADVERSE EFFECT An undesirable and unintended, although not necessarily unexpected, result of therapy or other intervention (e.g., headache following spinal tap or intestinal bleeding associated with aspirin therapy).

ASSENT Agreement by an individual not competent to give legally valid informed consent (e.g., a child or cognitively impaired person) to participate in research.

ASSURANCE A formal written, binding commitment that is submitted to a federal agency in which an institution promises to comply with applicable regulations governing research with human subjects and stipulates the procedures through which compliance will be achieved [Federal Policy §____.103].

AUTHORIZED INSTITUTIONAL OFFICIAL An officer of an institution with the authority to speak for and legally commit the institution to adherence to the requirements of the federal regulations regarding the involvement of human subjects in biomedical and behavioral research.

AUTONOMY Personal capacity to consider alternatives, make choices, and act without undue influence or interference of others.

AUTOPSY Examination by dissection of the body of an individual to determine cause of death and other medically relevant facts.

BELMONT REPORT A statement of basic ethical principles governing research involving human subjects issued by the National Commission for the Protection of Human Subjects in 1978.

BENEFICENCE An ethical principle discussed in the Belmont Report that entails an obligation to protect persons from harm. The principle of beneficence can be expressed in two general rules: (1) do not harm; and (2) protect from harm by maximizing possible benefits and minimizing possible risks of harm.

BENEFIT A valued or desired outcome; an advantage.

BEST INTEREST means that the burden to the individual resulting from participation in research are determined by the individual's legally authorized representative to be reasonable in relation to the individual resulting from individual's participation in research, taking into account:



IRB STANDARD OPERATING PROCEDURES

1. The potential short and long term effects of the participation in research on the physical, emotional, and cognitive functions of the individual;
2. The degree of physical pain or discomfort, psychological distress, or loss of dignity caused to the individual by participation in research;
3. The prognosis of the individual; and
4. The risks, side effects, and benefits of participation in research, compared to the risks, side effects, and benefits of standard treatment, if any, or of not participating in the research

BIOLOGIC any therapeutic serum, toxin, anti-toxin, or analogous microbial product applicable to the prevention, treatment, or cure of diseases or injuries.

BLIND STUDY DESIGNS *See: Masked Study Designs; Double-Masked Design; and Single-Masked Design.*

CADAVER The body of a deceased person.

CAPACITY (Capacity to consent to a research participation) The ability to understand the purpose, procedures, risks, benefits of and alternatives (including non participation) to a research study, including the ability to express a choice about participation and to understand that a refusal to participate involves no penalty or loss of benefits to which the person is otherwise entitled

CASE-CONTROL STUDY A study comparing persons with a given condition or disease (the cases) and persons without the condition or disease (the controls) with respect to antecedent factors. (*See also: Retrospective Studies.*)

CAT SCAN Abbreviation for Computerized Axial Tomography, an X-ray technique for producing images of internal bodily structures through the assistance of a computer.

CHILDREN Persons who have not attained the legal age for consent to treatment or procedures involved in the research, as determined under the applicable law of the jurisdiction in which the research will be conducted [45 CFR 46.401(a)].

CDC Centers for Disease Control and Prevention; an agency within the Public Health Service, Department of Health and Human Services.

CLASS I, II, III DEVICES Classification by the Food and Drug Administration of medical devices according to potential risks or hazards.

CLINICAL TRIAL A controlled study involving human subjects, designed to evaluate prospectively the safety and effectiveness of new drugs or devices or of behavioral interventions.

CLOSE RELATIVE any person, eighteen years of age or older who is related to the prospective subject and has maintained such regular contact with the prospective subject to be familiar with his or her activities, health, and religious or moral beliefs

COGNITIVELY IMPAIRED Having either a psychiatric disorder (*e.g.*, psychosis, neurosis, personality or behavior disorders, or dementia) or a developmental disorder (*e.g.*, mental retardation) that affects cognitive or emotional functions to the extent that capacity for judgment and reasoning is significantly diminished. Others, including persons under the influence of or dependent on drugs or alcohol, those suffering from degenerative diseases affecting the brain,



IRB STANDARD OPERATING PROCEDURES

terminally ill patients, and persons with severely disabling physical handicaps, may also be compromised in their ability to make decisions in their best interests.

COHORT A group of subjects initially identified as having one or more characteristics in common who are followed over time. In social science research, this term may refer to any group of persons who are born at about the same time and share common historical or cultural experiences.

COMMON RULE the federal regulations governing the protection of human subjects in research. Refer to 45 CFR 46.

COMPENSATION Payment or medical care provided to subjects injured in research; does not refer to payment (remuneration) for participation in research. (*Compare: Remuneration.*)

COMPETENCE Technically, a legal term, used to denote capacity to act on one's own behalf; the ability to understand information presented, to appreciate the consequences of acting (or not acting) on that information, and to make a choice. (*See also: Incompetence, Incapacity.*)

CONFIDENTIALITY Pertains to the treatment of information that an individual has disclosed in a relationship of trust and with the expectation that it will not be divulged to others without permission in ways that are inconsistent with the understanding of the original disclosure.

CONSENT *See: Informed Consent.*

CONTRACT An agreement; as used here, an agreement that a specific research activity will be performed at the request, and under the direction, of the agency providing the funds. Research performed under contract is more closely controlled by the agency than research performed under a grant. (*Compare: Grant.*)

CONTROL (SUBJECTS) or CONTROLS Subject(s) used for comparison who are not given a treatment under study or who do not have a given condition, background, or risk factor that is the object of study. Control conditions may be concurrent (occurring more or less simultaneously with the condition under study) or historical (preceding the condition under study). When the present condition of subjects is compared with their own condition on a prior regimen or treatment, the study is considered historically controlled.

CONTRAINDICATED Disadvantageous, perhaps dangerous; a treatment that should not be used in certain individuals or conditions due to risks (e.g., a drug may be contraindicated for pregnant women and persons with high blood pressure).

CORRELATION COEFFICIENT A statistical index of the degree of relationship between two variables. Values of correlation coefficients range from -1.00 through zero to +1.00. A correlation coefficient of 0.00 indicates no relationship between the variables. Correlations approaching -1.00 or +1.00 indicate strong relationships between the variables. However, causal inferences about the relationship between two variables can never be made on the basis of correlation coefficients, no matter how strong a relationship is indicated.

CROSSOVER DESIGN A type of clinical trial in which each subject experiences, at different times, both the experimental and control therapy. For example, half of the subjects might be randomly assigned first to the control group and then to the experimental intervention, while the other half would have the sequence reversed.

DATA AND SAFETY MONITORING BOARD A committee of scientists, physicians, statisticians, and others that collects and analyzes data during the course of a clinical trial to monitor for adverse effects and other trends (such as an indication that one treatment is



IRB STANDARD OPERATING PROCEDURES

significantly better than another, particularly when one arm of the trial involves a placebo control) that would warrant modification or termination of the trial or notification of subjects about new information that might affect their willingness to continue in the trial.

DEAD FETUS An expelled or delivered fetus that exhibits no heartbeat, spontaneous respiratory activity, spontaneous movement of voluntary muscles, or pulsation of the umbilical cord (if still attached) [45 CFR 46.203(f)]. Generally, some organs, tissues, and cells (referred to collectively as fetal tissue) remain alive for varying periods of time after the total organism is dead.

DEBRIEFING Giving subjects previously undisclosed information about the research project following completion of their participation in research. (Note that this usage, which occurs within the behavioral sciences, departs from standard English, in which debriefing is obtaining rather than imparting information.)

DECISIONALLY INCAPACITATED INDIVIDUAL an individual who is at least 18 years of age, and who cannot give a valid informed consent to participate as the subject of research because the individual cannot sufficiently understand the nature, extent, or probable consequence of the proposed research participation, cannot make a sufficient evaluation of burdens, risks, and benefits of the proposed research participation, or cannot communicate a research participation decision by a court. An adult individual who is able to communicate by means other than speech shall not be deemed incapacitated solely by reason of inability to speak

DECLARATION OF HELSINKI A code of ethics for clinical research approved by the World Medical Association in 1964 and widely adopted by medical associations in various countries. It was revised in 1975 and 1989.

DEPENDENT VARIABLES The outcomes that are measured in an experiment. Dependent variables are expected to change as a result of an experimental manipulation of the independent variable(s).

DESCRIPTIVE STUDY Any study that is not truly experimental (e.g., quasi-experimental studies, correlational studies, record reviews, case histories, and observational studies).

DEVICE (MEDICAL) *See: Medical Device.*

DHEW A federal agency: U.S. Department of Health, Education and Welfare; reorganized in 1980 as the Department of Health and Human Services (DHHS) and the Department of Education.

DHHS A federal agency: U.S. Department of Health and Human Services; formerly the Department of Health, Education and Welfare (DHEW).

DIAGNOSTIC (PROCEDURE) Tests used to identify a disorder or disease in a living person.

DISINTERESTED means:

1. Not being in a position to gain personal benefit from:
2. Not participating in any way, including authorship of publications, in the research concerning which an individual performs duties under these regulations; and
3. Not having any investment or other financial interest in any business entity sponsoring the research



IRB STANDARD OPERATING PROCEDURES

DOUBLE-MASKED DESIGN A study design in which neither the investigators nor the subjects know the treatment group assignments of individual subjects. Sometimes referred to as "double-blind."

DRUG Any chemical compound that may be used on or administered to humans as an aid in the diagnosis, treatment, cure, mitigation, or prevention of disease or other abnormal conditions.

EMANCIPATED MINOR A legal status conferred upon persons who have not yet attained the age of legal competency as defined by state law (for such purposes as consenting to medical care), but who are entitled to treatment as if they had by virtue of assuming adult responsibilities such as being self-supporting and not living at home, marriage, or procreation. (*See also: Mature Minor.*)

EMBRYO Early stages of a developing organism broadly used to refer to stages immediately following fertilization of an egg through implantation and very early pregnancy (*i.e.*, from conception to the eighth week of pregnancy). (*See also: Fetus.*)

EPIDEMIOLOGY A scientific discipline that studies the factors determining the causes, frequency, and distribution of diseases in a community or given population.

EQUITABLE Fair or just; used in the context of selection of subjects to indicate that the benefits and burdens of research are fairly distributed [Federal Policy §____.111(a)(3)].

ETHICS ADVISORY BOARD An interdisciplinary group that advises the Secretary, HHS, on general policy matters and on research proposals (or classes of proposals) that pose ethical problems.

ETHNOGRAPHIC RESEARCH Ethnography is the study of people and their culture. Ethnographic research, also called fieldwork, involves observation of and interaction with the persons or group being studied in the group's own environment, often for long periods of time. (*See also: Fieldwork.*)

EXPANDED AVAILABILITY Policy and procedure that permits individuals who have serious or life-threatening diseases for which there are no alternative therapies to have access to investigational drugs and devices that may be beneficial to them. Examples of expanded availability mechanisms include Treatment INDs, Parallel Track, and open study protocols.

EXPEDITED REVIEW Review of proposed research by the IRB Chairperson or a designated voting member or group of voting members rather than by the entire IRB. Federal rules permit expedited review for certain kinds of research involving no more than minimal risk and for minor changes in approved research [Federal Policy §____.110].

EXPERIMENTAL Term often used to denote a therapy (drug, device, procedure) that is unproven or not yet scientifically validated with respect to safety and efficacy. A procedure may be considered "experimental" without necessarily being part of a formal study (research) to evaluate its usefulness. (*See also: Research.*)

EXPERIMENTAL STUDY A true experimental study is one in which subjects are randomly assigned to groups that experience carefully controlled interventions manipulated by the experimenter according to a strict logic allowing causal inference about the effects of the interventions under investigation. (*See also: Quasi-Experimental Study.*)

EXPERIMENTAL SUBJECT *See "Human Subject."*



IRB STANDARD OPERATING PROCEDURES

FALSE NEGATIVE When a test wrongly shows an effect or condition to be absent (e.g., that a woman is not pregnant when, in fact, she is).

FALSE POSITIVE When a test wrongly shows an effect or condition to be present (e.g. that is woman is pregnant when, in fact, she is not).

FDA Food and Drug Administration; an agency of the federal government established by Congress in 1912 and presently part of the Department of Health and Human Services.

FEDERAL POLICY (THE) The federal policy that provides regulations for the involvement of human subjects in research. The Policy applies to all research involving human subjects conducted, supported, or otherwise subject to regulation by any federal department or agency that takes appropriate administrative action to make the Policy applicable to such research. Currently, sixteen federal agencies have adopted the Federal Policy. (Also known as the "Common Rule.")

FETAL MATERIAL The placenta, amniotic fluid, fetal membranes, and umbilical cord.

FETUS The product of conception from the time of implantation until delivery. If the delivered or expelled fetus is viable, it is designated an infant [45 CFR 46.203(c)]. The term "fetus" generally refers to later phases of development; the term "embryo" is usually used for earlier phases of development. (*See also: Embryo.*)

FIELDWORK Behavioral, social, or anthropological research involving the study of persons or groups in their own environment and without manipulation for research purposes (distinguished from laboratory or controlled settings). (*See also: Ethnographic Research.*)

510(K) DEVICE A medical device that is considered substantially equivalent to a device that was or is being legally marketed. A sponsor planning to market such a device must submit notification to the FDA 90 days in advance of placing the device on the market. If the FDA concurs with the sponsor, the device may then be marketed. 510(k) is the section of the Food, Drug and Cosmetic Act that describes premarket notification; hence the designation "510(k) device."

FULL BOARD REVIEW Review of proposed research at a convened meeting at which a majority of the membership of the IRB is present, including at least one member whose primary concerns are in nonscientific areas. For the research to be approved, it must receive the approval of a majority of those members present at the meeting [Federal Policy §____.108].

GENE THERAPY The treatment of genetic disease accomplished by altering the genetic structure of either somatic (non-reproductive) or germline (reproductive) cells.

GENERAL ASSURANCE Obsolete term previously used to denote an institutional assurance covering multiple research projects. (*See also: Assurance.*)

GENERAL CONTROLS Certain FDA statutory provisions designed to control the safety of marketed drugs and devices. The general controls include provisions on adulteration, misbranding, banned devices, good manufacturing practices, notification and record keeping, and other sections of the Medical Device Amendments to the Food, Drug and Cosmetic Act [21 U.S. Code §360(c) (Food, Drug and Cosmetic Act §513)].

GENETIC SCREENING Tests to identify persons who have an inherited predisposition to a certain phenotype or who are at risk of producing offspring with inherited diseases or disorders.

GENOTYPE The genetic constitution of an individual.



IRB STANDARD OPERATING PROCEDURES

GRANT Financial support provided for research study designed and proposed by the principal investigator(s). The granting agency exercises no direct control over the conduct of approved research supported by a grant. (*Compare: Contract.*)

GUARDIAN An individual who is authorized under applicable state or local law to give permission on behalf of a child to general medical care [45 CFR 46.402(3)].

HEALTH CARE AGENT a legally authorized representative to whom authority to make health decisions delegate under a health care proxy as authorized by Public Health Law Article 29-C

HEALTH CARE PROXY a document delegating authority to make health care decisions executed in accordance with the requirements of Public Health Law Article 29-C

HELSINKI DECLARATION *See: Declaration of Helsinki.*

HISTORICAL CONTROLS Control subjects (followed at some time in the past or for whom data are available through records) who are used for comparison with subjects being treated concurrently. The study is considered historically controlled when the present condition of subjects is compared with their own condition on a prior regimen or treatment.

HUMAN IN VITRO FERTILIZATION Any fertilization involving human sperm and ova that occurs outside the human body.

HUMAN SUBJECTS: See Section II.2 of this policy.

IDE *See: Investigational Device Exemptions.*

INCAPACITY Refers to a person's mental status and means inability to understand information presented, to appreciate the consequences of acting (or not acting) on that information, and to make a choice. Often used as a synonym for incompetence. (*See also: Incompetence.*)

INCOMPETENCE Technically, a legal term meaning inability to manage one's own affairs. Often used as a synonym for incapacity. (*See also: Incapacity.*)

IND *See: Investigational New Drug.*

INDEPENDENT CONSENT MONITOR a disinterested adult who is designated by an IRB, to monitor the informed consent process when a legally authorized representative is considering whether to give informed consent to the participation by decisional incapacitated individuals in research. The role of the independent consent monitor is:

1. To confirm to the IRB that:
 - a. The risk/benefit category of the proposed research is unambiguously included in an advance research directive authorizing research participation, if one exists;
 - b. The legally authorized representative understand the goals and risks of the research; and
2. To witness the process by which an investigator provides the legally authorized representative with the information required by an IRB for informed consent

INDEPENDENT DATA AND SAFETY MONITORING BOARD two or more disinterested individuals, independent of the research, authorized by an IRB to monitor data from a specific research study to ensure safety of subjects and to periodically report findings to the IRB

INDEPENDENT VARIABLES The conditions of an experiment that are systematically manipulated by the investigator.



IRB STANDARD OPERATING PROCEDURES

INFORMED CONSENT A person's voluntary agreement, based upon adequate knowledge and understanding of relevant information, to participate in research or to undergo a diagnostic, therapeutic, or preventive procedure. In giving informed consent, subjects may not waive or appear to waive any of their legal rights, or release or appear to release the investigator, the sponsor, the institution or agents thereof from liability for negligence [Federal Policy §116; 21 CFR 50.20 and 50.25].

INSTITUTION (1) Any public or private entity or agency (including federal, state, and local agencies) [Federal Policy §____.102(b)].

INSTITUTION (2) A residential facility that provides food, shelter, and professional services (including treatment, skilled nursing, intermediate or long-term care, and custodial or residential care). Examples include general, mental, or chronic disease hospitals; inpatient community mental health centers; halfway houses and nursing homes; alcohol and drug addiction treatment centers; homes for the aged or dependent, residential schools for the mentally or physically handicapped; and homes for dependent and neglected children.

INSTITUTIONAL REVIEW BOARD A specially constituted review body established or designated by an entity to protect the welfare of human subjects recruited to participate in biomedical or behavioral research [Federal Policy §§____.102(g), _____.108, _____.109].

INSTITUTIONALIZED Confined, either voluntarily or involuntarily (e.g., a hospital, prison, or nursing home).

INSTITUTIONALIZED COGNITIVELY IMPAIRED Persons who are confined, either voluntarily or involuntarily, in a facility for the care of the mentally or otherwise disabled (e.g., a psychiatric hospital, home, or school for the retarded).

INVESTIGATIONAL DEVICE EXEMPTIONS (IDE) Exemptions from certain regulations found in the Medical Device Amendments that allow shipment of unapproved devices for use in clinical investigations [21 CFR 812.20].

INVESTIGATIONAL NEW DRUG OR DEVICE A drug or device permitted by FDA to be tested in humans but not yet determined to be safe and effective for a particular use in the general population and not yet licensed for marketing.

INVESTIGATOR In clinical trials, an individual who actually conducts an investigation [21 CFR 312.3]. Any interventions (e.g., drugs) involved in the study are administered to subjects under the immediate direction of the investigator. (*See also: Principal Investigator.*)

IN VITRO Literally, "in glass" or "test tube;" used to refer to processes that are carried out outside the living body, usually in the laboratory, as distinguished from in vivo.

IN VIVO Literally, "in the living body;" processes, such as the absorption of a drug by the human body, carried out in the living body rather than in a laboratory (in vitro).

IRB *See: Institutional Review Board.*

JUSTICE An ethical principle discussed in the Belmont Report requiring fairness in distribution of burdens and benefits; often expressed in terms of treating persons of similar circumstances or characteristics similarly.

LACTATION The period of time during which a woman is providing her breast milk to an infant or child.



IRB STANDARD OPERATING PROCEDURES

LEGALLY AUTHORIZED REPRESENTATIVE A person authorized either by statute or by court appointment to make decisions on behalf of another person. In human subjects research, an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research [Federal Policy §____.102(c)].

LOD SCORE An expression of the probability that a gene and a marker are linked.

LONGITUDINAL STUDY A study designed to follow subjects forward through time.

MASKED STUDY DESIGNS Study designs comparing two or more interventions in which either the investigators, the subjects, or some combination thereof do not know the treatment group assignments of individual subjects; sometimes called "blind" study designs. (*See also: Double-Masked Design; Single-Masked Design.*)

MATURE MINOR Someone who has not reached adulthood (as defined by state law) but who may be treated as an adult for certain purposes (e.g., consenting to medical care). Note that a mature minor is not necessarily an emancipated minor. (*See also: Emancipated Minor.*)

MEDICAL DEVICE A diagnostic or therapeutic article that does not achieve any of its principal intended purpose through chemical action within or on the body. Such devices include diagnostic test kits, crutches, electrodes, pacemakers, arterial grafts, intraocular lenses, and orthopedic pins or other orthopedic equipment.

MEDICAL DEVICE AMENDMENTS (MDA) Amendments to the Federal Food, Drug and Cosmetic Act passed in 1976 to regulate the distribution of medical devices and diagnostic products.

MEDICALLY RESPONSIBLE CLINICIAN a licensed medical doctor or other practitioner skilled and knowledgeable about caring for persons with the kinds of conditions/disease represented by the specific study population, who is designated by an investigator and approved by and IRB to evaluate whether decisionally incapable subjects' continued participation is appropriate in research that presents a minor increase over minimal risk is more than a minor increase over minimal risk

MENTALLY DISABLED *See: Cognitively Impaired.*

METABOLISM (OF A DRUG) The manner in which a drug is acted upon (taken up, converted to other substances, and excreted) by various organs of the body.

MINIMAL RISK A risk is minimal where the probability and magnitude of harm or discomfort anticipated in the proposed research are not greater, in and of themselves, than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests [Federal Policy §____.102(i)]. For example, the risk of drawing a small amount of blood from a healthy individual for research purposes is no greater than the risk of doing so as part of routine physical examination.

The definition of minimal risk for research involving prisoners differs somewhat from that given for non-institutionalized adults. [*See 45 CFR 46.303(d) and Guidebook Chapter 6, Section E, "Prisoners."*]

MINOR INCREASE OVER MINIMAL RISK the probability and magnitude of harm or discomfort anticipated in the research, including psychological harm and loss of privacy or other aspects of personal dignity, are only slightly greater in and of themselves than those ordinarily encountered during the performance of routine physical or psychological examination or tests



IRB STANDARD OPERATING PROCEDURES

MONITORING the collection and analysis of data as the project progresses to assure the appropriateness of the research, its design and subject protections.

MORE THAN MINOR INCREASE OVER MINIMAL RISK subjects, as a result of research participation, would be exposed to more than remote possibility of:

1. Substantial or prolonged pain, discomfort, or distress; or
2. Clinically significant deterioration of medical or mental condition

NATIONAL COMMISSION National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. An interdisciplinary advisory body, established by Congressional legislation in 1974, which was in existence until 1978, and which issued a series of reports and recommendations on ethical issues in research and medicine, many of which are now embodied in federal regulations.

NDA See: *New Drug Application*.

NEW DRUG APPLICATION Request for FDA approval to market a new drug.

NIAAA National Institute on Alcohol Abuse and Alcoholism; an institute in NIH.

NIDA National Institute on Drug Abuse; an institute in NIH.

NIH National Institutes of Health: a federal agency within the Public Health Service, DHHS, comprising 21 institutes and centers. It is responsible for carrying out and supporting biomedical and behavioral research.

NIMH National Institute of Mental Health; an institute in NIH.

NONAFFILIATED MEMBER Member of an Institutional Review Board who has no ties to the parent institution, its staff, or faculty. This individual is usually from the local community (e.g., minister, business person, attorney, teacher, homemaker).

NONSIGNIFICANT RISK DEVICE An investigational medical device that does not present significant risk to the patient. (*See also: Significant Risk Device.*)

NONTHERAPEUTIC RESEARCH Research that has no likelihood or intent of producing a diagnostic, preventive, or therapeutic benefit to the current subjects, although it may benefit subjects with a similar condition in the future.

NONVIABLE FETUS An expelled or delivered fetus which, although it is living, cannot possibly survive to the point of sustaining life independently, even with the support of available medical therapy [45 CFR 46.203 (d) and (e)]. Although it may be presumed that an expelled or delivered fetus is nonviable at a gestational age less than 20 weeks and weight less than 500 grams [Federal Register 40 (August 8, 1975): 33552], a specific determination as to viability must be made by a physician in each instance. (*See also: Viable Infant.*)

NORMAL VOLUNTEERS Volunteer subjects used to study normal physiology and behavior or who do not have the condition under study in a particular protocol, used as comparisons with subjects who do have the condition. "Normal" may not mean normal in all respects. For example, patients with broken legs (if not on medication that will affect the results) may serve as normal volunteers in studies of metabolism, cognitive development, and the like. Similarly, patients with heart disease but without diabetes may be the "normals" in a study of diabetes complicated by heart disease.

NULL HYPOTHESIS The proposition, to be tested statistically, that the experimental intervention has "no effect," meaning that the treatment and control groups will not differ as a



IRB STANDARD OPERATING PROCEDURES

result of the intervention. Investigators usually hope that the data will demonstrate some effect from the intervention, thereby allowing the investigator to reject the null hypothesis.

NUREMBERG CODE A code of research ethics developed during the trials of Nazi war criminals following World War II and widely adopted as a standard during the 1950s and 1960s for protecting human subjects.

OFFICE FOR PROTECTION FROM RESEARCH RISKS (OPRR) The office within the National Institutes of Health, an agency of the Public Health Service, Department of Health and Human Services, responsible for implementing DHHS regulations (45 CFR Part 46) governing research involving human subjects.

OPEN DESIGN An experimental design in which both the investigator(s) and the subjects know the treatment group(s) to which subjects are assigned.

OPRR See: *Office for Protection from Research Risks*.

PATERNALISM Making decisions for others against or apart from their wishes with the intent of doing them good.

PERMISSION The agreement of parent(s) or guardian to the participation of their child or ward in research [45 CFR 46.402(c)].

PHARMACOLOGY The scientific discipline that studies the action of drugs on living systems (animals or human beings).

PHASE 1, 2, 3, 4 DRUG TRIALS Different stages of testing drugs in humans, from first application in humans (Phase 1) through limited and broad clinical tests (Phase 3), to post marketing studies (Phase 4).

- **PHASE 1 DRUG TRIAL** Phase 1 trial include the initial introduction of an investigational new drug into humans. These studies are typically conducted with healthy volunteers; sometimes, where the drug is intended for use in patients with a particular disease, however, such patients may participate as subjects. Phase 1 trials are designed to determine the metabolic and pharmacological actions of the drug in humans, the side effects associated with increasing doses (to establish a safe dose range), and, if possible, to gain early evidence of effectiveness; they are typically closely monitored. The ultimate goal of Phase 1 trials is to obtain sufficient information about the drug's pharmacokinetics and pharmacological effects to permit the design of well-controlled, sufficiently valid Phase 2 studies. Other examples of Phase 1 studies include studies of drug metabolism, structure-activity relationships, and mechanisms of actions in humans, as well as studies in which investigational drugs are used as research tools to explore biological phenomena or disease processes. The total number of subjects involved in Phase 1 investigations is generally in the range of 20-80.
- **PHASE 2 DRUG TRIAL** Phase 2 trials include controlled clinical studies conducted to evaluate the drug's effectiveness for a particular indication in patients with the disease or condition under study, and to determine the common short-term side effects and risks associated with the drug. These studies are typically well controlled, closely monitored, and conducted with a relatively small number of patients, usually involving no more than several hundred subjects.
- **PHASE 3 DRUG TRIAL** Phase 3 trials involve the administration of a new drug to a larger number of patients in different clinical settings to determine its safety, efficacy, and appropriate dosage. They are performed after preliminary evidence of effectiveness



IRB STANDARD OPERATING PROCEDURES

has been obtained, and are intended to gather necessary additional information about effectiveness and safety for evaluating the overall benefit-risk relationship of the drug, and to provide an adequate basis for physician labeling. In Phase 3 studies, the drug is used the way it would be administered when marketed. When these studies are completed and the sponsor believes that the drug is safe and effective under specific conditions, the sponsor applies to the FDA for approval to market the drug. Phase 3 trials usually involve several hundred to several thousand patient-subjects.

- **PHASE 4 DRUG TRIAL** Concurrent with marketing approval, FDA may seek agreement from the sponsor to conduct certain post marketing (Phase 4) studies to delineate additional information about the drug's risks, benefits, and optimal use. These studies could include, but would not be limited to, studying different doses or schedules of administration than were used in Phase 2 studies, use of the drug in other patient populations or other stages of the disease, or use of the drug over a longer period of time [21 CFR §312.85].

PHENOTYPE The physical manifestation of a gene function.

PHS Public Health Service. Part of the U.S. Department of Health and Human Services, it includes FDA, NIH, CDC, SAMHSA, and HRSA.

PLACEBO A chemically inert substance given in the guise of medicine for its psychologically suggestive effect; used in controlled clinical trials to determine whether improvement and side effects may reflect imagination or anticipation rather than actual power of a drug.

POSTAMENDMENTS DEVICES Medical devices marketed after enactment of the 1976 Medical Device Amendments.

PREAMENDMENTS DEVICES Medical devices marketed before enactment of the 1976 Medical Device Amendments.

PRECLINICAL INVESTIGATIONS Laboratory and animal studies designed to test the mechanisms, safety, and efficacy of an intervention prior to its applications to humans.

PREDICATE DEVICES Currently legally marketed devices to which new devices may be found substantially equivalent under the 510(k) process.

PREGNANCY The period of time from confirmation of implantation of a fertilized egg within the uterus until the fetus has entirely left the uterus (*i.e.*, has been delivered). Implantation is confirmed through a presumptive sign of pregnancy such as missed menses or a positive pregnancy test [45 CFR 46.203(b)]. This "confirmation" may be in error, but, for research purposes, investigators would presume that a living fetus was present until evidence to the contrary was clear. Although fertilization occurs a week or more before implantation, the current inability to detect the fertilization event or the presence of a newly fertilized egg makes a definition of pregnancy based on implantation necessary.

PREMARKET APPROVAL Process of scientific and regulatory review by the FDA to ensure the safety and effectiveness of Class III devices.

PRESIDENT'S COMMISSION President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research. An interdisciplinary advisory group, established by congressional legislation in 1978, which was in existence until 1983, and which issued reports on ethical problems in health care and in research involving human subjects.



IRB STANDARD OPERATING PROCEDURES

PRINCIPAL INVESTIGATOR The scientist or scholar with primary responsibility for the design and conduct of a research project. (See also: Investigator.)

PRISONER An individual involuntarily confined in a penal institution, including persons: (1) sentenced under a criminal or civil statute; (2) detained pending arraignment, trial, or sentencing; and (3) detained in other facilities (e.g., for drug detoxification or treatment of alcoholism) under statutes or commitment procedures providing such alternatives to criminal prosecution or incarceration in a penal institution [45 CFR 46.303(c)].

PRIVACY Control over the extent, timing, and circumstances of sharing oneself (physically, behaviorally, or intellectually) with others.

PROBAND The person whose case serves as the stimulus for the study of other members of the family to identify the possible genetic factors involved in a given disease, condition, or characteristic.

PROPHYLACTIC Preventive or protective; a drug, vaccine, regimen, or device designed to prevent, or provide protection against, a given disease or disorder.

PROSPECT OF DIRECT BENEFIT on the basis of scientific evidence, a realistic possibility exists that some subjects physical, medical or mental conditions and related functioning might be improved as a direct result of participation in research, including ameliorating symptoms or avoiding side effects of standard therapy

PROSPECTIVE STUDIES Studies designed to observe outcomes or events that occur subsequent to the identification of the group of subjects to be studied. Prospective studies need not involve manipulation or intervention but may be purely observational or involve only the collection of data.

PROTOCOL The formal design or plan of an experiment or research activity; specifically, the plan submitted to an IRB for review and to an agency for research support. The protocol includes a description of the research design or methodology to be employed, the eligibility requirements for prospective subjects and controls, the treatment regimen(s), and the proposed methods of analysis that will be performed on the collected data.

PURITY The relative absence of extraneous matter in a drug or vaccine that may or may not be harmful to the recipient or deleterious to the product.

QUASI-EXPERIMENTAL STUDY A study that is similar to a true experimental study except that it lacks random assignments of subjects to treatment groups. (See also: *Experimental Study*.)

RADIOACTIVE DRUG Any substance defined as a drug in §201(b)(1) of the Federal Food, Drug and Cosmetic Act that exhibits spontaneous disintegration of unstable nuclei with the emission of nuclear particles or photons [21 CFR 310.3(n)]. Included are any nonradioactive reagent kit or nuclide generator that is intended to be used in the preparation of a radioactive drug and "radioactive biological products," as defined in 21 CFR 600.3(ee). Drugs such as carbon-containing compounds or potassium-containing salts containing trace quantities of naturally occurring radionuclides are not considered radioactive drugs.

RADIOACTIVE DRUG RESEARCH COMMITTEE (RDRC) An institutional committee responsible for the use of radioactive drugs in human subjects for research purposes. Research involving human subjects that proposes to use radioactive drugs must meet various FDA requirements, including limitations on the pharmacological dose and the radiation dose. Furthermore, the exposure to radiation must be justified by the quality of the study and the importance of the information it seeks to obtain. The committee is also responsible for



IRB STANDARD OPERATING PROCEDURES

continuing review of the drug use to ensure that the research continues to comply with FDA requirements, including reporting obligations. The committee must include experts in nuclear medicine and the use of radioactive drugs, as well as other medical and scientific members [21 CFR 36.1].

RADIOPAQUE CONTRAST AGENTS Materials that stop or attenuate radiation that is passed through the body, creating an outline on film of the organ(s) being examined. Contrast agents, sometimes called "dyes," do not contain radioisotopes. When such agents are used, exposure to radiation results only from the X-ray equipment used in the examination. The chemical structure of radiopaque contrast agents can produce a variety of adverse reactions, some of which may be severe — and possibly life-threatening — in certain individuals.

RADIOPHARMACEUTICALS Drugs (compounds or materials) that may be labeled or tagged with a radioisotope. These materials are largely physiological or subpharmacological in action, and, in many cases, function much like materials found in the body. The principal risk associated with these materials is the consequent radiation exposure to the body or to specific organ systems when they are injected into the body.

RANDOM, RANDOM ASSIGNMENT, RANDOMIZATION, RANDOMIZED Assignment of subjects to different treatments, interventions, or conditions according to chance rather than systematically (e.g., as dictated by the standard or usual response to their condition, history, or prognosis, or according to demographic characteristics). Random assignment of subjects to conditions is an essential element of experimental research because it makes more likely the probability that differences observed between subject groups are the result of the experimental intervention.

RECOMBINANT DNA TECHNOLOGY "The ability to chop up DNA, the stuff of which genes are made, and move the pieces, [which] permits the direct examination of the human genome," and the identification of the genetic components of a wide variety of disorders [Holtzman (1989), p. 1]. Recombinant DNA technology is also used to develop diagnostic screens and tests, as well as drugs and biologics for treating diseases with genetic components. See Guidebook Chapter 5, Section H, "Human Genetic Research."

REM Acronym for Roentgen Equivalent in Man; the unit of measurement for a dose of an ionizing radiation that produces the same biological effect as a unit of absorbed dose (1 rad) of ordinary X-rays. One millirem is equal to 1/1000 of a rem.

REMISSION A period in which the signs and symptoms of a disease are diminished or in abeyance. The term "remission" is used when one cannot say with confidence that the disease has been cured.

REMUNERATION Payment for participation in research. (NOTE: It is wise to confine use of the term "compensation" to payment or provision of care for research-related injuries.) (*Compare: Compensation.*)

RESPECT FOR PERSONS An ethical principle discussed in the Belmont Report requiring that individual autonomy be respected and that persons with diminished autonomy be protected.

RETROSPECTIVE STUDIES Research conducted by reviewing records from the past (e.g., birth and death certificates, medical records, school records, or employment records) or by obtaining information about past events elicited through interviews or surveys. Case control studies are an example of this type of research.



IRB STANDARD OPERATING PROCEDURES

REVIEW (OF RESEARCH) The concurrent oversight of research on a periodic basis by an IRB. In addition to the at least annual reviews mandated by the federal regulations, reviews may, if deemed appropriate, also be conducted on a continuous or periodic basis [Federal Policy §____.108(e)].

RISK The probability of harm or injury (physical, psychological, social, or economic) occurring as a result of participation in a research study. Both the probability and magnitude of possible harm may vary from minimal to significant. Federal regulations define only "minimal risk." (See also: *Minimal Risk*.)

SAMHSA Substance Abuse and Mental Health Services Administration; includes the Center for Substance Abuse Prevention, the Center for Substance Abuse Treatment and the Center on Mental Health Services. Previously the Alcohol, Drug Abuse, and Mental Health Administration (ADAMHA). (See also: *ADAMHA*.)

SCIENTIFIC REVIEW GROUP A group of highly regarded experts in a given field, convened by NIH to advise NIH on the scientific merit of applications for research grants and contracts. Scientific review groups are also required to review the ethical aspects of proposed involvement of human subjects. Various kinds of scientific review groups exist, and are known by different names in different institutes of the NIH (e.g., Study Sections, Initial Review Groups, Contract Review Committees, or Technical Evaluation Committees).

SECRETARY A U.S. Cabinet Officer. In the context of DHHS-conducted or -supported research, usually refers to the Secretary of Health and Human Services.

SIGNIFICANT RISK DEVICE An investigational medical device that presents a potential for serious risk to the health, safety, or welfare of the subject.

SINGLE-MASKED DESIGN Typically, a study design in which the investigator, but not the subject, knows the identity of the treatment assignment. Occasionally the subject, but not the investigator, knows the assignment. Sometimes called "single-blind design."

SITE VISIT A visit by agency officials, representatives, or consultants to the location of a research activity to assess the adequacy of IRB protection of human subjects or the capability of personnel to conduct the research.

SOCIAL EXPERIMENTATION Systematic manipulation of, or experimentation in, social or economic systems; used in planning public policy.

SPONSOR (OF A DRUG TRIAL) A person or entity that initiates a clinical investigation of a drug — usually the drug manufacturer or research institution that developed the drug. The sponsor does not actually conduct the investigation, but rather distributes the new drug to investigators and physicians for clinical trials. The drug is administered to subjects under the immediate direction of an investigator who is not also a sponsor. A clinical investigator may, however, serve as a sponsor-investigator. The sponsor assumes responsibility for investigating the new drug, including responsibility for compliance with applicable laws and regulations. The sponsor, for example, is responsible for obtaining FDA approval to conduct a trial and for reporting the results of the trial to the FDA.

SPONSOR-INVESTIGATOR An individual who both initiates and actually conducts, alone or with others, a clinical investigation. Corporations, agencies, or other institutions do not qualify as sponsor-investigators.

STATISTICAL SIGNIFICANCE A determination of the probability of obtaining the particular distribution of the data on the assumption that the null hypothesis is true. Or, more simply put,



IRB STANDARD OPERATING PROCEDURES

the probability of coming to a false positive conclusion. [See *McLarty (1987), p. 2.*] If the probability is less than or equal to a predetermined value (e.g., 0.05 or 0.01), then the null hypothesis is rejected at that significance level (0.05 or 0.01).

STERILITY (1) The absence of viable contaminating microorganisms; aseptic state.

STERILITY (2) The inability to procreate; the inability to conceive or induce conception.

STUDY SECTION See: *Scientific Review Group.*

SUBJECTS (HUMAN) See: *Human Subjects.*

SURROGATE a family member or close friend authorized by these regulations to make human subject research decisions for n adults without capacity to consent to research participation in the absence of a health care agent and a research agent. The surrogate for an adult without capacity to consent to research participation would be one person from the following list, chosen from the class highest in priority when persons in prior class are not reasonably available, willing, and competent to act:

1. The spouse, if not legally separated from the adult;
2. A son or daughter eighteen years or older;
3. A parent;
4. A brother or sister eighteen years or older;
5. A close friend or relative eighteen years or older.

SURVEYS Studies designed to obtain information from a large number of respondents through written questionnaires, telephone interviews, door-to-door canvassing, or similar procedures.

THERAPEUTIC INTENT The research physician's intent to provide some benefit to improving a subject's condition (e.g., prolongation of life, shrinkage of tumor, or improved quality of life, even though cure or dramatic improvement cannot necessarily be effected.) This term is sometimes associated with Phase 1 drug studies in which potentially toxic drugs are given to an individual with the hope of inducing some improvement in the patient's condition as well as assessing the safety and pharmacology of a drug.

THERAPY Treatment intended and expected to alleviate a disease or disorder.

UNIFORM ANATOMICAL GIFT ACT Legislation adopted by all 50 States and the District of Columbia that indicates procedures for donation of all or part of a decedent's body for such activities as medical education, scientific research, and organ transplantation.

VACCINE A biologic product generally made from an infectious agent or its components — a virus, bacterium, or other microorganism — that is killed (inactive) or live attenuated (active, although weakened). Vaccines may also be biochemically synthesized or made through recombinant DNA techniques.

VARIABLE (NOUN) An element or factor that the research is designed to study, either as an experimental intervention or a possible outcome (or factor affecting the outcome) of that intervention.

VIABLE INFANT When referring to a delivered or expelled fetus, the term "viable infant" means likely to survive to the point of sustaining life independently, given the benefit of available medical therapy [45 CFR 46.203(d)]. This judgment is made by a physician. In accordance with DHHS regulations, the Secretary, HHS, may publish guidelines to assist in the determination of



IRB STANDARD OPERATING PROCEDURES

viability. Such guidelines were published in 1975, and specify an estimated gestational age of 20 weeks or more and a body weight of 500 grams or more as indices of fetal viability [Federal Register 40 (August 8, 1975): 33552]. These indices depend on the state of present technology and may be revised periodically. (See *also: Nonviable Fetus.*)

VOLUNTARY Free of coercion, duress, or undue inducement. Used in the research context to refer to a subject's decision to participate (or to continue to participate) in a research activity.



IRB STANDARD OPERATING PROCEDURES

Appendix 5 – BRANY IRB Standard Operating Procedures

Glossary of Lay Terms for Use in Preparing Informed Consent Documents

Abdominal	Pertaining to body cavity below diaphragm which contains stomach, intestines, liver, and other organs
Absorb	Take up fluids, take into the body
Acidosis	Condition when blood contains more acid than normal
Acuity	Clearness, keenness, especially of vision, hearing
Acute	New, recent, sudden
Adenopathy	Swollen lymph nodes
Adjunct	Additional substance, treatment or procedure used for increasing the effectiveness of the primary substance, treatment or procedure
Adjuvant	Helpful, assisting, aiding
Adjuvant treatment	Added treatment
Adverse	Unfavorable (we define “Adverse Event”)
Adverse Effect	Side effect of a drug that is undesirable; examples include discomfort or harm to an organ or tissue
Allergic Reaction	May include rash, trouble breathing, fever, and/or diarrhea
Ambulate/-ation/-ory	Walk, able to walk
Ameliorate	Improve
Analysis	to study thoroughly
Anaphylaxis	Serious, potentially life threatening allergic reaction including reduced blood pressure and difficulty breathing
Anemia	Decreased red blood cells; low red blood cell count which can cause tiredness or fatigue
Anesthetic (general)	A drug or agent used to produce unconsciousness and to decrease the feeling of pain; it puts you to sleep to allow surgery
Anesthetic (local)	A drug or agent used to numb an area of your body to permit surgery or biopsy
Angina	Chest pain from too little blood flow to the heart
Angina Pectoris	Chest pain from too little blood flow to the heart
Antecubital	Area inside the elbow
Antibiotic	Drug that kills bacteria and other germs
Antibody	Protein made in the body in response to a foreign substance; attacks the foreign substance and protects you from infection



IRB STANDARD OPERATING PROCEDURES

Anticonvulsant	Drug used to prevent or treat seizures
Antilipidemic	A drug that decreases the level of fat(s) in the blood
Antimicrobial	Drug that kills bacteria and other germs
Antiretroviral	Drug used to treat HIV or other diseases caused by viruses
Antiviral	Drug used to treat diseases caused by viruses
Antitussive	A drug used to reduce coughing
Anorexia	Condition in which person will not eat; lack of appetite
Arrhythmia	Any change from the normal heartbeat (abnormal heartbeat)
Aspiration	Material entering the lungs following vomiting
Assay	Lab test
Assent	Agreement (usually used for very young children's approval, followed by parent/guardian's consent in the form of signature in the consent form)
Assess	To learn about
Asthma	A lung disease associated with narrowing of the breathing passages in the lungs
Asymptomatic	Without symptoms
Axilla	Armpit
Baseline	A measurement to serve as the basis to compare subsequent measurements
Benign	Not harmful, usually without serious consequences, but with some exceptions, e.g. benign brain tumor may have serious consequences
b.i.d.	Twice a day
Binding/Bound	Carried by/stuck together/transported
Bioavailability	The portion of a drug that enters the blood – relates to drugs taken by mouth
Biopsy	A small sample of tissue removed for evaluation
Blood Amounts	To be defined in teaspoons or tablespoons (a teaspoon is approximately 5 ml)
Blood Profile	Series of blood tests
Bolus	An amount given all at once
Bone mass/density	The amount of calcium in a given amount of bone
Bradyarrhythmias	Slow, irregular heartbeats
Bradycardia	Slow heartbeat
Bronchoalveolar Lavage	Wash out part of the lung with salt water to obtain lung cells for laboratory tests



IRB STANDARD OPERATING PROCEDURES

Bronchoscopy	Insertion of a flexible tube through the nose and voice box to examine the inside of the lung
Bronchospasm	Narrowing of the breathing passages of the lung causing difficulty breathing and wheezing
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Carcinogenic	Capable of causing cancer
Carcinoma	Type of cancer
Cardiac	Refers to the heart
Cardioversion	Return of the normal heartbeat by electric shock or drugs
Catheter	A tube inserted into the body for withdrawing or introducing fluids (i.e. a Foley Catheter)
Catheter (Indwelling Epidural)	A tube placed near the nerves in the spinal cord used to administer anesthesia during an operation
Cell Culture	Keep cells alive and allow to grow under artificial conditions in the lab
Central Nervous System	(CNS) Brain and spinal cord
Cerebral	Brain (we define "cerebral trauma")
Cerebral Trauma	Damage to the brain
Cessation	Stopping
Chemotherapy	Treatment of disease, usually cancer, by drugs
Chronic	Continuing for a long time
Cisplatin	A drug used to kill cancer cells
Clinical	Referring to medical care
Clinically Significant	Of major importance for treating or evaluating patients
Clinical Trial	An experiment involving patients
Closeout	The final procedure that will conclude the study
Colonoscopy	Examination of the interior parts of the body by introducing a small instrument (endoscope) a flexible tube inserted through the rectum to examine the intestines
Coma	Unconscious State
Complete Response	Total disappearance of disease
Congenital	Occurring prior to birth, due to parent's genetic input
Congestive Heart Disease	Hardening of the Arteries of the Heart
Cognitive Tests	Tests of thinking abilities
Conjunctivitis	Irritation and redness of the thin membrane covering the eye
Consent	Agreement
Consolidation Phase	Treatment phase intended to make a remission permanent follows induction



IRB STANDARD OPERATING PROCEDURES

Contraindicated	Should not be used
Control	Healthy volunteer
Controlled Trial	Study in which the experimental treatment or procedure is compared to a standard (control) treatment or procedure
Cooperative Group	Association of multiple hospitals and doctors to perform clinical trials together
Coronary	Refers to the blood vessels that supply the heart
Coronary Heart Disease	Hardening of the arteries of the heart
CT Scan (CAT)	(Computerized Tomography) Computerized series of X-Rays
Culture	Test for infection or germs that could cause infection
Cumulative	Total sum (of individual events, experiences, treatments)
Cutaneous	Relating to the skin
CVA (Cerebrovascular Accident)	Stroke
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Dermal	Skin
Dermatologic	Pertaining to the skin
Diagnosis	To determine the cause
Diastolic	Lower number in blood pressure reading
Distal	Toward the end, away from the center of the body
Diuretic	“Water Pill” or drug that causes an increase in urination
Doppler	Sound waves
Double Blind	Study in which neither investigators nor subjects know what drug the subject is receiving
Dysfunction	State of improper function
Dysplasia	Abnormal Cells
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Echocardiogram	Sound wave test of the heart
Edema	Increased fluid in body tissues, swelling
EEG (Electroencephalogram)	Recording of the electric waves in the brain
Efficacy	Effectiveness; how well something works
Electrocardiogram	ECG or EKG, electrical tracing of the heart
Electrolyte Imbalance	Imbalance of minerals in the blood (i.e. potassium, sodium)
Emesis	Vomiting
Empiric	Based on experience
End Point	The event observed in a subject that would determine ending or changing the treatment
Endoscopic	Insertion of a flexible tube with a light to examine an internal part of the body



IRB STANDARD OPERATING PROCEDURES

Endoscopy	Examination of the interior parts of the body by introducing a small instrument (endoscope) in flexible tubing inserted through the nose or mouth (we define "endoscope")
Enteral	Given through the stomach or intestines
Epidemiologic	Referring to the study or the distribution and populations of characteristics and diseases
Epidural	A tube placed near the nerves in the spinal cord to administer anesthesia during operation
Eradicating	Getting rid of (such as disease)
Evaluated	Assessed; examined for medical condition
Expedited Review	Rapid review of a protocol by human subjects committee Chairperson or designated IRB member without full committee approval, permitted with certain low-risk research
External	Outside the body
Extravasate	To leak outside of a blood vessel
Fast	To go without food
FDA	U.S. Food and Drug Administration, the branch of the federal government, which approves new drugs
Fibrillation	Irregular beat of the heart or other muscle
Fibrous	Having many fibers, such as scar tissue
Gastrointestinal	Relating to the stomach and intestines
Gastroscopy	Examination of the interior parts of the body by introducing a small instrument (endoscope) in a flexible tubing inserted through the nose or mouth to examine the stomach
General Anesthesia	A drug or agent used to produce unconsciousness and to decrease the feeling of pain; it puts you to sleep to allow surgery
Gestational	Pertaining to pregnancy
Glucose	A sugar
Gout	A disease that causes a painful inflammation of the joints
Hematocrit	Amount of red blood cells in the blood
Hematoma	A bruise; a black and blue mark
Hemodynamic Measuring	Measuring of blood flow
Hemoglobin	A substance in the blood that carries oxygen
Hemolysis	Breakdown of red blood cells
Heparin Lock	A plastic tube filled with blood thinner that is placed in a vein to give injections or take out blood
Hepatic	Refers to the liver



IRB STANDARD OPERATING PROCEDURES

Hepatoma	Cancer or tumor of the liver
Heritable Disease	A disease which can be transmitted to one's offspring resulting in damage to future children
Histopathologic	Pertaining to the disease status of body tissues or cells
Holter Monitor	A portable machine for recording heartbeats over a period of time
Hypercalcemia	Increased level of calcium in the blood
Hyperkalemia	Increased level of potassium in the blood
Hyponatremia	Increased level of sodium in the blood
Hyperemesis	Excessive vomiting
Hypertension	High blood pressure
Hypocalcemia	Reduced level of calcium in the blood
Hyponatremia	Reduced level of sodium in the blood
Hypotension	Low blood pressure
Hypoxemia	A decrease of oxygen in the blood
Hypoxia	A decrease of oxygen in the blood
<hr/>	
Iatrogenic	Cause by a physician or by treatment
IDE	Investigational Device Exemption; the license to test an unapproved new medical device
Idiopathic	A disorder for which the cause is unknown
Illicit Drugs/Substances	Illegal drugs
Immune System	The system in the body that reacts to foreign or occasionally one's own proteins
Immunoglobulin	A substance produced by the body that binds to a foreign substance
Immunosuppressive	Drug, which reduces the body's immune response, used in transplantation and diseases caused by disordered immunity
Immunotherapy	Use of drugs to help the body's immune (protective) system; usually used to destroy cancer cells
Impaired Function	Abnormal function
Implanted	Placed in the body
IND	Investigational New Drug; the license to test an unapproved new drug
Induction Phase	Beginning phase or stage of a treatment
Induration	Hardening
Indwelling	Remaining in a given location, such as a catheter
Infarct	Death of tissue because of lack of blood supply



IRB STANDARD OPERATING PROCEDURES

Infectious Disease	Disease, which is transmitted from one person to next
Inflammation	Swelling which is generally painful, red and warm
Infusaport	A device surgically placed under the skin in order to give fluids and medication
Infusion	Introduction of a substance into the body, usually into the blood through a vein
Ingestion	Eating; taking by mouth
Interferon	Agent, which acts against viruses; antiviral agent
Interior	Inside of the body
Intermittent	Occurring (regularly or irregularly) between two time points; alternatively ceasing and beginning
Internal	Within the body
Intramuscular	Into the muscle; within the muscle
Intraperitoneal	Into the abdominal cavity
Intrathecal	Injected into the space around the spinal cord
Intravenous (IV)	Injected into a vein
Intravesical	In the bladder
Intubate	Insertion of a tube into a body part (we have the same definition for "Tracheal Intubation")
Tracheal Intubation	The placement of a tube into the throat (trachea) to assist breathing
Invasive Procedure	Puncture, opening or cutting of the skin
Investigational Method	A treatment method, which has not been proven to be beneficial or has not been accepted as standard care
Ischemia	Decreased oxygen in a tissue (usually because of decreased blood flow)
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Lactating	Nursing or breast-feeding
Laparotomy	A procedure in which an incision is made in the abdominal wall to enable a physician to look at the organs
Lethargy	Sleepiness
Lipid	Fat
Lipid Profile	(panel) fat and cholesterol levels in the blood
Lumbar Puncture	After the skin is numbed, a needle is inserted into the back to withdraw fluid for analysis
Leukopenia	Low white blood cell count, which can increase the possibility of infection
Lipid Content	Fat content in the blood



IRB STANDARD OPERATING PROCEDURES

Local Anesthesia	A drug or agent used to numb an area of your body to permit surgery or biopsy
Localized	Restricted to one area, limited to one area
Lumen	The cavity of an organ or tube (e.g. blood vessel)
Lymphangiography	An x-ray of the lymph nodes or tissues after injection of dye in lymph vessels (e.g. in feet)
Lymphocyte	A type of white blood cell important in immunity and defense against infection
Lymphoma	A cancer of the lymph nodes (or tissues)
Lumbar Puncture	Spinal Tap; Placement of a needle between the bones in the back to remove some of the fluid around the spinal cord
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Malaise	A vague feeling of bodily discomfort, feeling bad
Malfunction	Condition in which something is not functioning properly
Malignancy	Cancer or other progressively enlarging and spreading tumor, usually fatal if not successfully treated
Medulloblastoma	A type of brain tumor
Megaloblastosis	Change in red blood cells
Metabolize	Process of breaking down substances in cells to obtain energy
Metastasis	Spread of cancer cells from one part of the body to another
Metronidazole	A drug used to treat infection caused by parasites or other causes of anaerobic infections
MI	Myocardial infarction; heart attack
Microorganism	Germ
Minimal	Slight
Minimize	Reduce
Monitor	Check on; keep track of; watch carefully
Mobility	Ease of movement
Morbidity	Undesired result or complication
Mortality	Death or death rate
Motility	The ability to move
MRI	Magnetic resonance imaging; body pictures created using magnetic rather than x-ray energy
Mucosa/Mucous Membrane	Moist lining of digestive, respiratory, reproductive and urinary tracts
Multi-center	The same study being carried out at several centers
Myalgia	Muscle aches
Myocardial	Referring to the heart



IRB STANDARD OPERATING PROCEDURES

Myocardial Infarction	Heart Attack
Nasogastric Tube	Tube from the nose to the stomach
NCI	National Cancer Institute
Necrosis	Death of tissue
Neonatal	Referring to the newborn period
Neoplasia	Tumor, may be benign or malignant
Neuroblastoma	A cancer of the nerve tissue
Neurological	Pertaining to the nervous system
Neutropenia	Decrease in the main part of the white blood cells
NIH	National Institutes of Health
Non-compliance	Deviate from agreement or to not follow the set procedure
Non-Invasive	Not breaking, cutting or entering the skin
Normal Subject	Healthy volunteer
Nosocomial Pneumonia	Pneumonia acquired in the hospital
Objective	Aim or goal
Occlusion	Closing; obstruction
Oncology	The study of tumors or cancer
Ophthalmic	Referring to the eye
Optimal	Best, most favorable or desirable
Oral Administration	By mouth
Orthopedic	Referring to the bones
Osteopetrosis	Rare bone disorder characterized dense bone
Osteoporosis	Softening of the bones
Outcome	An observed event in a subject (usually used to determine the effectiveness of a treatment)
Ovaries	Female sex glands
Parenteral	Injection of a drug into a vein or into the skin
Patency	Condition of being open
Pathogenesis	Causative mechanism in disease
Percutaneous	Through the skin
Perforation	A tear or a hole
Perinatal	Referring to the pregnancy and newborn period
Peripheral	Not central
Peritoneal	Inside the body cavity
Per Os (PO)	By mouth



IRB STANDARD OPERATING PROCEDURES

Pharmacodynamics	Study of how a drug acts on the body
Pharmacokinetics	The study of the way the body absorbs, distributes, metabolizes, and gets rid of a drug
Phase I	Initial study of a new drug in humans to determine the limits of tolerance and its safety
Phase II	Second phase of a study of a new drug intended to obtain initial information
Phase III	Large scale trials to confirm and expand information on safety and usefulness of a new drug
Phlebitis	Irritation or inflammation of the vein
Pilot Study	An introductory (usually small) study before the actual (usually larger) study
Placebo	A substance with no active medication
Placebo Effect	The perception of improvement when a placebo is given
Platelets	Small particles in the blood that help with clotting
Polyurai	Excessive urination
Post-Operative	After surgery
Potential	Possible
Potentiate	Increase or multiply the effect of a drug or toxin by administration of another drug or toxin at the same time
Potentiator	An agent that helps another agent work better
Prenatal	Before birth
Pre-Operative	Before surgery
PRN	As needed
Prophylaxis	A drug given to prevent disease or infection
Prognosis	Chances for recovery
Progresses	Worsens or gets worse
Prone	Lying on the stomach
Prorated	Describe the payment schedule
Prospective	Study following patients forward in time
Prosthesis	Artificial limb, such as arms and legs
Protocol	Plan of study
Proximal	Closer to the center of the body, away from the end
Pulmonary	Referring to the lungs
q.d.	Everyday
q.i.d	Four times a day
Radiation Therapy	X-Ray or Cobalt treatment



IRB STANDARD OPERATING PROCEDURES

Random	By chance
Randomization	Chance selection, like flipping a coin
RBC	Red Blood Cell
Recombinant	Formation of new combinations of genes resulting from the manipulation of genes in the laboratory
Reconstitution	Putting back together the original parts or elements; for drugs: preparation of a drug for administration by adding liquid to a dry, powdered drug
Recur	Happen again
Refractory	Not responding to treatment
Regimen	Pattern of administering treatment
Regeneration	Regrowth of a structure or of lost tissue
Relapse	The return of a disease
Remission	Disappearance of evidence of cancer or other disease
Renal	Referring to the kidneys
Replicable	Possible to duplicate
Resect	Remove or cut out surgically
Resolve	Go away
Retrospective Study	Study looking back over past experience
Review	Reexamination or revise or go over again
Revoke	Cancel or take back
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Sample Size	Number of people enrolled in the study
Sarcoma	A type of cancer
Sedation	Giving medicine to make someone sleepy or less anxious
Sedative	A drug to calm or make less anxious
Seizures	Intense uncontrollable movements
Seminoma	A type of testes cancers
Sequelae	A condition following as a consequence of a disease
Sequential	In a row
Serum	Blood
Software	Computer program
Somnolence	Sleepiness
Spirometry/PFT	Measurement of how well you breathe and how well your lungs function
Standard of Care	Treatment plan, which the majority of the medical community would accept as appropriate
Staging	A determination of the extent of the disease



IRB STANDARD OPERATING PROCEDURES

Stenosis	Narrowing of a duct, tube, or one of the heart valves
Stomatitis	Mouth sores; inflammation of the mouth
Stratify	Arrange in groups for analysis of results (e.g., stratify by age, sex, etc.)
Stupor	Stunned state in which it is difficult to get a response or the attention of the subject
Subcutaneous	Under the skin
Subclavian	Under the collarbone
Supine	Lying on the back
Supportive Care	General medical care aimed at symptoms not intended to improve or cure underlying disease
Symptomatic	Having symptoms
Syndrome	A condition characterized by a set of symptoms
Systemically	Distributed throughout the body
Systolic	Top number in blood pressure reading
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Teratogenic	Capable of causing malformations in unborn fetuses
Terminate	Stop
Testes	Male sex gland; male organs which produce sperm
Therapeutic	Treatment of condition, disease, or disorder
Thoracic	Relating to the chest
Thrombocytopenia	A condition in which there is an abnormally small amount of platelets in the blood
Thrombosis	Blood clot
t.i.d	Three times a day
Titration	Gradual alteration of drug dose to determine desired effect or most beneficial strength of drug
Tissue	A collection of similar cells that perform a function
T-lymphocytes	Type of white blood cells involved in immune reactions
Topical	Surface; on the skin
Topical Anesthetic	Applied to certain area of the skin to reduce pain to specific (limited) area to which applied
Toxicity	An unwanted side effect resulting in injury to a tissue or organ
Toxicology Test	A test for illegal drugs
Transdermal	Through the skin
Transient	Lasting or staying only a short time
Transiently	Temporarily
Trauma	Injury; wound
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IRB STANDARD OPERATING PROCEDURES

Treadmill	Walking machine often used to determine heart function
Uptake	Absorption and incorporation of a substance by living tissue; absorb and incorporate a substance, taking in of a substance by living tissue
Valvuloplasty	Plastic repair of a valve, especially in the heart
Varices	Enlarged veins, usually in legs or lining of tube between mouth and stomach
Vasospasm	Narrowing of blood vessels due to spasm of vessel walls
Vector	A carrier, usually an insect that carries and transmits disease-causing microorganisms
Venipuncture	Blood drawing
Vertical Transmission	Spread of disease
Vertigo	Dizziness
WBC	White blood cell



IRB STANDARD OPERATING PROCEDURES

Appendix 6 – BRANY IRB Standard Operating Procedures

Reviewer Checklist [xForm #17]

Reviewer Checklist Data Entry

-- Reviewer Instructions --

ATTESTATION: NO CONFLICT OF INTEREST (COI) BY IRB REVIEWER:

IRB members who have an interest in a project that is being reviewed **MUST:**

- a) Decline assignment as a reviewer
- b) Remove him/herself from the meeting during discussion & voting
⇒ Please check here to attest you have no Conflict of Interest (COI) for the research considered for this review.

REVIEWER INSTRUCTIONS

1. Select the Review Type. **If an ICF is part of the review assignment, select Yes to review the ICF.** Proper review type selection is essential as the responses guide you to the appropriate questions on the xForm Reviewer Checklist.
2. Each of the protocol components noted in the next questions should be characterized as adequate or inadequate. If a component is considered inadequate, a short description of the inadequacies should be noted. An overall comment may be included at the end.
3. *****The "No Change to Prior Board Determination" option can NOT be selected for any initial review!*****
4. Any documents you may need to attach to complete this review will be requested *at the end of the review question pages.*
5. Pressing the "Save for Later" button or closing the xForm will save all the responses you have entered thus far.

If you have any questions regarding completing this xForm, please contact the BRANY IRB at 516.470.6900, and we will be happy to assist you!

Thank You!
BRANY IRB

Select appropriate Reviewer/Review Type

Choices:

- PRIMARY Reviewer - Initial Full Board
 - PRIMARY Reviewer - Initial Expedited
 - SECONDARY Reviewer (Initial)
 - CONTINUING Reviewer - Full Board
 - CONTINUING Reviewer – Expedited
 - MODIFICATION Reviewer - Full Board
 - MODIFICATION Reviewer - Expedited
-



IRB STANDARD OPERATING PROCEDURES

Complete the Consent Form Checklist for this review (i.e. Are you required to or do you need to complete the Consent Form checklist for the review you are assigned)?

OPTIONAL: For Primary Reviewers when a Secondary Reviewer has been assigned to review the study.

ALL Secondary Reviewers will go directly to the Consent Form checklist.

⇒Select either 'Yes' or 'No'

When **YES**, you will be required to complete the Consent Form checklist.

-- Modification Qualify for Expedited --

DOES MODIFICATION QUALIFY FOR EXPEDITED REVIEW

Does this Modification Review qualify for Expedited Review?

When **NO**, you will jump to IRB Action page at the end of the xForm.

⇒Select either 'Yes' or 'No'

Does this modification qualify for expedited review?

To qualify for an expedited review, ALL of the following conditions MUST be true. Please check the conditions, if any, that are true. (If this DOES NOT qualify for an Expedited Review, you will be required to explain in another question.)

⇒Check *one or more* of the following items from the list of check boxes presented:

- Modification represents a minor change to previously approved research
- Modification does not alter the risk-to-benefit analysis for this research
- Modification does not fall into one of the categories (1-13) listed below:

Modification Categories:

- (1) Addition of a new drug;**
 - (2) Addition of a new device;**
 - (3) Addition of an invasive procedure;**
 - (4) Increase in medication dose or a decrease in dose that may increase the risk;**
 - (5) Addition of vulnerable subjects as a study population;**
 - (6) Prolongation of the patient's participation in the study other than for observational purpose;**
 - (7) Change in the inclusion/exclusion criteria which may involve incorporation of populations at greater risk;**
 - (8) Identification of new potentially significant risks;**
 - (9) Collection of additional blood samples that exceed the limits set in expedited category 2;**
 - (10) Unanticipated problem involving risks to participants of others;**
 - (11) Substantial changes in the level of risks, the research design or methodology, the number of subjects enrolled in the research, the qualifications of the research team, the facilities available to support the safe conduct of the research;**
 - (13) Any item deemed to warrant full board review by the Chair or designee.**
-



IRB STANDARD OPERATING PROCEDURES

-- Assessment of Submission --

BACKGROUND:

The Background/Introduction should provide an adequate rationale for the conduct of the study.

⇒Select *one* of the following options from the list of radio buttons presented:

- Adequate
- Inadequate
- No Change to Prior Board Determination

SCIENTIFIC MERIT VALIDITY:

a) The available nonclinical & clinical information on an investigational product is adequate to support the proposed clinical trial.

⇒Select *one* of the following options from the list of radio buttons presented:

- Adequate
- Inadequate
- No Change to Prior Board Determination

Comments:

⇒Enter an unlimited amount of text.

b) Clinical trials are scientifically sound & described in a clear, detailed protocol.

⇒Select *one* of the following options from the list of radio buttons presented:

- Adequate
- Inadequate
- No Change to Prior Board Determination

Comments

⇒Enter an unlimited amount of text.

AIMS/HYPOTHESES:

The aims should be logical, concrete, & capable of being accomplished. If the hypotheses are presented they should flow logically from the Background. Required)

⇒Select *one* of the following options from the list of radio buttons presented:

- Adequate
- Inadequate
- No Change to Prior Board Determination

METHODOLOGY:

The methodology should be capable of producing meaningful data (e.g. the approach is valid & adequate). The procedures should be feasible & there should be a logistical timetable or sequence of events.

⇒Select *one* of the following options from the list of radio buttons presented:

- Adequate
- Inadequate
- No Change to Prior Board Determination

RISK vs. BENEFITS:

In reviewing the protocol for the assessment of risk benefit ratio, please make sure that the proposal meets all of the following requirements:



IRB STANDARD OPERATING PROCEDURES

Risks to subjects are minimized:

- a) **By using procedures which are consistent with sound research design & which do not unnecessarily expose subjects to risk AND**
- b) **Whenever appropriate, by using procedures already being performed on subjects for diagnostic or treatment purposes.**
- c) **In considering risks, consider physical, psychological, social, economic, & legal risks?**

⇒Select *one* of the following options from the list of radio buttons presented:

- Adequate
- Inadequate
- No Change to Prior Board Determination

Comments

⇒Enter an unlimited amount of text.

Risks to subjects are reasonable in relation to anticipated benefits, if any, AND to the importance of the knowledge reasonably expected to result from the research.

Consider only those risks & benefits that may result from the research (as distinguished from risks & benefits of therapies subjects would receive even if not participating in the research). DO not consider possible long-range effects of applying knowledge gained in research (e.g. the possible effects of the research on public policy) as among those research risks that fall within the purview of the IRBs responsibility.

⇒Select *one* of the following options from the list of radio buttons presented:

- Adequate
- Inadequate
- No Change to Prior Board Determination

Comments (Also consider the impact of the study design on risk (e.g. randomization process, dosing schedule, placebo control, etc.)

⇒Enter an unlimited amount of text.

SELECTION OF SUBJECTS IS EQUITABLE.

Take into account the purposes of the research & the setting in which the research will be conducted. Consider the effect of inclusion/exclusion criteria, recruitment methods, & payment arrangements on selection of subjects.

⇒Select *one* of the following options from the list of radio buttons presented:

- Proceed to Evaluation of Subject Selection (*When "Proceed to Evaluation of Subject Selection" is selected you will be required to answer additional questions on another page.*)
- No Change to Prior Board Determination

EVALUATION OF SUBJECT SELECTION

Take into account the purposes of the research & the setting in which the research will be conducted. Consider the effect of inclusion/exclusion criteria, recruitment methods, & payment arrangements on selection of subjects.

Based on the ethnic makeup of the anticipated subject population, is there a need for a translated ICF?

⇒Select either 'Yes' or 'No'



IRB STANDARD OPERATING PROCEDURES

Has the investigator provided an adequate plan for consenting & maintaining ongoing communication for subjects whose primary language is not English?

⇒Select *one* of the following options from the list of radio buttons presented:

- Yes
- No
- Not Applicable

Will military personnel be involved in this research?

⇒Select *one* of the following options from the list of radio buttons presented:

- Yes
- No
- Not Applicable

If YES, confirm the research application provides for the following provisions:

- Officers are not permitted to influence the decision of their subordinates.
- Officers and senior non-commissioned officers may not be present at the time of recruitment.
- Officers and senior non-commissioned officers have a separate opportunity to participate.
- When recruitment involves a percentage of a unit, an independent ombudsman is present.
- There are limitations on dual compensation, including:
 - Prohibit an individual from receiving pay of compensation for research during duty hours.
 - An individual may be compensated for research if the participant is involved in the research when not on duty.
 - Federal employees while on duty and non-Federal persons may be compensated for blood draws for research up to \$50 for each blood draw.
 - Non-Federal persons may be compensated for research participating other than blood draws in a reasonable amount as approved by the IRB according to local prevailing rates and the nature of the research.

Are the above criteria satisfied?

⇒Select *one* of the following options from the list of radio buttons presented:

- Yes
- No
- Not Applicable

Participant recruitment & enrollment procedures are adequate.

⇒Select either 'Yes' or 'No'

Does the subject reimbursement plan (payment for participation) have the potential to coerce or unduly influence subjects?

⇒Select either 'Yes' or 'No'

Is subject selection equitable?

When No you will be required to explain/comment.

⇒Select either 'Yes' or 'No'

Comments regarding the subject selection



IRB STANDARD OPERATING PROCEDURES

⇒Enter an unlimited amount of text.

-- Subject Provisions --

WHERE APPROPRIATE, THE RESEARCH PLAN MAKES ADEQUATE PROVISION FOR MONITORING THE DATA COLLECTED TO ENSURE THE SAFETY OF SUBJECTS.

- All clinical trials require safety monitoring, but not all trials require monitoring by a formal committee. For FDA-regulated studies, Data Monitoring Committees (DMC) have generally been established for large, randomized, multi-center studies with mortality or major morbidity as a primary or secondary endpoint.
- NIH requires data & safety monitoring, generally in the form of Data Safety Monitoring Boards (DSMBs), for Phase 3 of clinical trials. For earlier trials (Phases 1, 2), a DSMB may be appropriate if the study has multiple clinical sites, if it is blinded (masked) or if it employs particularly high-risk interventions or involves vulnerable populations.
- **Attention should be given to Investigator-initiated trials and the plan for data safety monitoring, especially when the investigator is also the IND or IDE holder (i.e., Sponsor-investigator). Data safety monitoring for investigator-initiated clinical research should be undertaken by a qualified individual external to the study team. In such circumstances, the IRB should confirm that the Sponsor-Investigator has established a **plan for data safety monitoring**.**

⇒Select *one* of the following options from the list of radio buttons presented:

- Yes
- No
- No Change to Prior Board Determination

FOR INVESTIGATOR-INITIATED TRIALS WHEN THE INVESTIGATOR IS ALSO THE IND OR IDE HOLDER (I.E., SPONSOR-INVESTIGATOR), THERE IS A PLAN TO MONITOR THE CONDUCT AND PROGRESS OF THE CLINICAL INVESTIGATION:

- **Attention should be given to Investigator-initiated trials when the investigator is also the IND or IDE holder (i.e., Sponsor-Investigator) and the plan for **monitoring the conduct and progress of the clinical investigation(s)**. Monitoring the conduct and progress of the research should be undertaken by a qualified individual external to the study team. In such circumstances, the IRB should confirm that the Sponsor-Investigator has established a **plan for monitoring the conduct and progress of the clinical investigation(s)**.**

⇒Select *one* of the following options from the list of radio buttons presented:

- Yes
- No
- No Change to Prior Board Determination
- Not applicable

For research subject to the requirements of the **Department of Defense** that is greater than minimal risk, the IRB must require the appointment of a **research monitor independent of the team conducting the research**. Department of Defense requirements also permit the IRB to require this for research or studies involving no more than minimal risk, if appropriate. **Is this**



IRB STANDARD OPERATING PROCEDURES

research subject to requirements of the Department of Defense (i.e., funded or conducted by the DoD) and greater than minimal risk?

⇒Select *one* of the following options from the list of radio buttons presented:

- Yes
- No - not DOD research
- No – not greater than minimal risk
- No – not greater than minimal risk but the IRB wants to require a monitor anyway (see above)
- No Change to Prior Board Determination

If YES (or if this is minimal risk DoD supported research and the IRB wants to require a monitor anyway), confirm by checking the following 3 criteria are met:

- The research monitor is appointed by name
- The research monitor must be **independent of the team conducting the research**. There may be more than one research monitor (e.g. if different skills or experience are needed). The monitor may be an ombudsman or a member of the data safety monitoring board.
- The IRB must approve a written summary of the monitors' duties, authorities, and responsibilities. The IRB will communicate with research monitors to confirm their duties, authorities, and responsibilities. The duties of the research monitor are determined on the basis of specific risks or concerns about the research. The monitor may:
 - perform oversight functions (e.g. observe recruitment, enrollment procedures, and the consent process, oversee study interventions and interactions, review monitoring plans and unanticipated problems involving risks to participants or others, oversee data matching, data collection and analysis).
 - discuss the research protocol with researchers, interview human subjects, and consult with others outside of the study.
 - report observations and findings to the IRB or a designated official.
- The consent form specifies that the research monitor will have the authority to, stop a research study in progress, remove individuals from study, and take any steps to protect the safety and well-being of participants until the IRB can assess.

WHERE APPROPRIATE THERE ARE ADEQUATE PROVISIONS TO PROTECT THE PRIVACY OF SUBJECTS.

- Consider the plan for protecting the privacy interests of subjects (e.g. private interviews, use of barriers when subject is required to disrobe, private room for performing research interventions, consideration of whether teen subjects should be interviewed without parents when sensitive subject matter is involved).

⇒Select *one* of the following options from the list of radio buttons presented:

- Yes
- No
- No Change to Prior Board Determination



IRB STANDARD OPERATING PROCEDURES

WHERE APPROPRIATE THERE ARE ADEQUATE PROVISIONS TO MAINTAIN THE CONFIDENTIALITY OF DATA.

- Evaluate the methods proposed to obtain & record information about subjects (e.g. questionnaires, data collection tools, surveys, direct assessments/observation, laboratory tests, etc.)
- Also consider the provisions in place to maintain the confidentiality of data, such as blinding results (removing identifying information), coding data & securing access to the code list, limiting access to data, & offering Certificates of Confidentiality.

⇒Select *one* of the following options from the list of radio buttons presented:

- Yes
- No
- No Change to Prior Board Determination

CONSENT PROCESS - Method and Documentation

METHOD FOR OBTAINING CONSENT: Consider who will be obtaining consent & other elements of the consent process as described in the protocol & research application & whether:

- **The investigator would obtain the legally effective consent of the participant or the participant's legally authorized representative.**
- **The circumstances of the consent process provided the prospective participant or the legally authorized representative sufficient opportunity to consider whether to participate.**
- **The circumstances of the consent process minimized the possibility of coercion or undue influence.**
- **The individuals communicating information to the participant or the legally authorized representative during the consent process would provide the information in language understandable to the participant of the representative.**

⇒Select *one* of the following options from the list of radio buttons presented:

- Proceed to Evaluation of Consent Method and Documentation (*When "Proceed to Evaluation of Consent Method and Documentation" is selected you will be required to answer additional questions on another page and the opportunity to modify the informed consent form.*)
- Study Includes a Waiver of Consent
- No Change to Prior Board Determination

-- Consent Process --

Does the research include one or more of the following? (Select ALL that apply):

⇒Check *one or more* of the following items from the list of check boxes presented:

- Request for waiver of documentation of informed consent
- Request for waiver OR alteration of elements of informed consent
- NONE of the above

-- Waiver of Document of Informed Consent --

Waiver of Document of Informed Consent

Instructions: The IRB can only approve a request to waive documentation of informed consent if all



IRB STANDARD OPERATING PROCEDURES

of the items under either Condition 1 or 2 below are true. The researcher must provide adequate justification for either case.

Condition 1

1.a. This research is NOT subject to FDA regulation.

⇒Select *one* of the following options from the list of radio buttons presented:

- True
- False

1.b. The investigator has provided adequate explanation/justification to demonstrate that the only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality.

⇒Select *one* of the following options from the list of radio buttons presented:

- True (*When **TRUE**, you will be required to respond to question 1.b.i. below.*)
- False

1.b.i. When 1.b. is **TRUE, has the investigator provided adequate explanation/justification to demonstrate that each subject will be asked if s/he wants documentation linking him/her with the research? (The subject's wishes would govern.)**

⇒Enter an unlimited amount of text.

- OR -

Condition 2

2. The investigator has provided adequate explanation/justification to demonstrate that the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside the research context.

⇒Select *one* of the following options from the list of radio buttons presented:

- True
- False

-- Waiver or Alteration of Elements of Informed Consent --

Waiver or Alteration of Elements of Informed Consent

1. For which elements of consent has the investigator requested a waiver or alteration?

⇒Enter an unlimited amount of text.

2. Is the request to waive or alter elements of informed consent appropriate?



IRB STANDARD OPERATING PROCEDURES

Either A or B **MUST** be satisfied in order for a waiver/alteration of consent elements to be approvable:

A. All THREE (3) criteria MUST be met:

1. The research or demonstration project is to be conducted by or subject to the approval of state of local government officials & is designed to study, evaluate or otherwise examine:

- public benefit or service programs;
- procedures for obtaining benefits or services under those programs;
- possible changes in or alternatives to those programs or procedures, or
- possible changes in methods or levels of payment for benefits or services under those programs;

⇒Select either 'Yes' or 'No'

2. The research could not practicably be carried out without the waiver or alteration.

⇒Select either 'Yes' or 'No'

3. The research is not subject to FDA regulation.

⇒Select either 'Yes' or 'No'

B. All FIVE (5) criteria must be met:

⇒Check *one or more* of the following items from the list of check boxes presented:

- 1. The research involves no more than minimal risk to the subjects;
- 2. The waiver or alteration will not adversely affect the rights & welfare of the subjects;
- 3. The research could not practicably be carried out without the waiver or alteration; AND
- 4. Whenever appropriate, the subjects will be provided with additional pertinent information after participation.
- 5. The research is not subject to FDA regulation.
- NONE of the above.

-- Consent Process Evaluation --

CONSENT PROCESS

METHOD FOR OBTAINING CONSENT

Consider who will be obtaining consent & other elements of the consent process as described in the protocol & research application & whether:

- The investigator would obtain the legally effective consent of the participant or the participant's legally authorized representative.
- The circumstances of the consent process provided the prospective participant or the legally authorized representative sufficient opportunity to consider whether to participate.
- The circumstances of the consent process minimized the possibility of coercion or undue influence.
- The individuals communicating information to the participant or the legally authorized representative during the consent process would provide the information in language understandable to the participant or the representative.

Is this method for obtaining consent appropriate?



IRB STANDARD OPERATING PROCEDURES

⇒Select either 'Yes' or 'No'

Consent Method Comment

⇒Enter an unlimited amount of text.

Consent Documentation

⇒Check *one or more* of the following items from the list of check boxes presented:

- The consent document embodies the basic & appropriate additional elements of disclosure.
- The participant or the participant's legally authorized representative will sign & date the consent document.
- A copy of the consent document will be given to the person signing the consent document.
- The investigator will give either the participant or the representative adequate opportunity to read the consent document before it was signed.

Consent Documentation Comment

⇒Enter an unlimited amount of text.

If a Consent Form was part of this review (you selected Yes on the first page of this xForm), you will proceed to the Consent Form Checklist portion of the xForm next.

-- Consent Waiver --

Consent Waiver

If the project includes a request to waive the requirement to obtain consent, is it appropriate?

Either A or B **MUST** be satisfied in order for a consent waiver to be approvable:

A. All THREE (3) criteria MUST be met:

1. The research or demonstration project is to be conducted by or subject to the approval of state or local government officials & is designed to study, evaluate, or otherwise examine:
 - (i) public benefit or service programs;
 - (ii) procedures for obtaining benefits or services under those programs;
 - (iii) possible changes in or alternatives to those programs or procedures, or
 - (iv) possible changes in methods or levels of payment for benefits or services under those programs;
2. The research could not practicably be carried out without the waiver or alteration,
3. The research is not subject to FDA regulation.

B. All FIVE (5) criteria must be met:

1. The research involves no more than minimal risk to the subjects;
2. The waiver or alteration will not adversely affect the rights & welfare of the subjects;
3. The research could not practicably be carried out without the waiver or alteration; and
4. Whenever appropriate, the subjects will be provided with additional pertinent information after participation.
5. The research is not subject to FDA regulation.

⇒Select *one* of the following options from the list of radio buttons presented:



IRB STANDARD OPERATING PROCEDURES

- Yes
- No
- N/A

Consent Form Checklist -- General Protocol Questions --

GENERAL PROTOCOL QUESTIONS (for secondary reviewers at IRB meeting only)

To attach an electronic, informed consent form that includes the changes you are specifying in this review, you **MUST** select "**See Attached**" for the item(s) that you are modifying the request form for.

Is there a clearly defined rationale for the study? ⇒Select either 'Yes' or 'No'

Explain study rationale: ⇒Enter an unlimited amount of text.

Are eligibility and exclusionary criteria clearly detailed? ⇒Select either 'Yes' or 'No'

Explain eligibility and exclusionary details: ⇒Enter an unlimited amount of text.

Are there any populations that you feel are unfairly excluded? ⇒Select either 'Yes' or 'No'

Explain populations unfairly excluded: ⇒Enter an unlimited amount of text.

Do the risks to subjects appear reasonable in relation to anticipated benefits, if any?
⇒Select either 'Yes' or 'No'

Explain why the risks to subjects appear reasonable in relation to anticipated benefits. ⇒Enter an unlimited amount of text.

-- Consent Form Elements Part I (1-11) --

CONSENT FORM CHECKLIST PART I

Instructions: Please check that the following requirements are contained in the consent document. *If any item is missing from the informed consent document, provide a comment in the comment area for that question indicating the item to be added to the document and where it should be added.*

You may also attach a copy of the informed consent form electronically with edit changes included on another page that follows at the end of the Consent Form evaluation process. Circle words or phrases that need to be rewritten in lay language. Whenever possible, recommend acceptable language for the Principal Investigator to incorporate in the consent document.

To attach an electronic, informed consent form that includes the changes you are specifying in this review, you **MUST select "**See Attached**" for the item(s) that you are modifying.**

1. Statement that the study involves research:

IRB STANDARD OPERATING PROCEDURES

⇒Select *one* of the following options from the list of radio buttons presented:

- Yes
- No *When No, you must specify language to be added or revised in the following question.*
- See Attached

Statement that that study involves research: language to be added or revised ⇒Enter an unlimited amount of text.

2. Purpose of the research stated in lay terminology:

⇒Select *one* of the following options from the list of radio buttons presented:

- Yes
- No *When No, you must specify language to be added or revised in the following question.*
- See Attached

Purpose of the research stated in lay terminology: language to be added or revised ⇒Enter an unlimited amount of text.

3. Reason subject asked to participate:

⇒Select *one* of the following options from the list of radio buttons presented:

- Yes
- No *When No, you must specify language to be added or revised in the following question.*
- See Attached

Reason subject asked to participate: language to be added or revised ⇒Enter an unlimited amount of text.

4. Expected duration of subject's participation:

⇒Select *one* of the following options from the list of radio buttons presented:

- Yes
- No *When No, you must specify language to be added or revised in the following question.*
- See Attached

Expected duration of subject's participation: language to be added or revised ⇒Enter an unlimited amount of text.

5. Study design described in lay language (e.g. randomization, double-blind, placebo-controlled):

⇒Select *one* of the following options from the list of radio buttons presented:

- Yes
- No *When No, you must specify language to be added or revised in the following question.*
- See Attached

Study design described in lay language: language to be added or revised ⇒Enter an unlimited amount of text.

6. Study procedures/treatments clearly described and match the protocol:

⇒Select *one* of the following options from the list of radio buttons presented:

- Yes
- No *When No, you must specify language to be added or revised in the following question.*
- See Attached

Study procedures/treatments clearly described and match the protocol: language to be added or revised ⇒Enter an unlimited amount of text.

7. Description of the drug/device:

⇒Select *one* of the following options from the list of radio buttons presented:



IRB STANDARD OPERATING PROCEDURES

- Yes
- No *When **No**, you must specify language to be added or revised in the following question.*
- See Attached

Description of the drug/device: language to be added or revised ⇒Enter an unlimited amount of text.

8. Statement that the drug/device is experimental and not approved by the FDA (if applicable)

⇒Select *one* of the following options from the list of radio buttons presented:

- Yes
- No *When **No**, you must specify language to be added or revised in the following question.*
- See Attached

Statement that the drug/device is experimental and not approved by FDA (if applicable): language to be added or revised ⇒Enter an unlimited amount of text.

9. Compensation for injury:

⇒Select *one* of the following options from the list of radio buttons presented:

- Yes
- No *When **No**, you must specify language to be added or revised in the following question.*
- See Attached

Compensation for injury: language to be added or revised ⇒Enter an unlimited amount of text.

10. Compensation for injury for research subject to the Department of Defense Requirements

⇒Select *one* of the following options from the list of radio buttons presented:

- The DoD Component conducting the research has provided a disclosure, and the text in the consent **is consistent** with the DoD Component's requirements
- The DoD Component conducting the research has provided a disclosure, and the text in the consent **is NOT consistent** with the DoD Component's requirements
- NOT APPLICABLE

Compensation for injury: language to be added or revised per DoD Component's requirements⇒Enter an unlimited amount of text.

11. Costs to the subject, if any, for study related procedures, study medication etc. If there are no costs does it say so?

⇒Select *one* of the following options from the list of radio buttons presented:

- Yes
- No *When **No**, you must specify language to be added or revised in the following question.*
- See Attached

Costs to the subject, if any, for study related procedures. study medication etc.: language to be added or revised ⇒Enter an unlimited amount of text.

12. Number of subjects in the trial (at the site and for other sites in multi-center studies):

⇒Select *one* of the following options from the list of radio buttons presented:

- Yes
- No *When **No**, you must specify language to be added or revised in the following question.*
- See Attached

Number of subjects in the trial (at the site and for other sites in multi-center studies): language to be added or revised ⇒Enter an unlimited amount of text.



IRB STANDARD OPERATING PROCEDURES

-- Consent Form Elements Part II (12-21) --

CONSENT FORM PART II

To attach an electronic, informed consent form that includes the changes you are specifying in this review, you MUST select "See Attached" for the item(s) that you are modifying.

*****If you select "See Attached" for any of the consent form questions, you will be required to attach an electronic copy of the consent form with the edit changes **at the end of the Consent Form Evaluation xForm question process.*******

13. Potential risks and discomforts to the subject:

⇒Select *one* of the following options from the list of radio buttons presented:

- Yes
- No *When No, you must specify language to be added or revised in the following question.*
- See Attached

Potential risks and discomforts to the subject: language to be added or revised ⇒Enter an unlimited amount of text.

14. Potential for direct benefit to the subject and/or benefits to society:

⇒Select *one* of the following options from the list of radio buttons presented:

- Yes
- No *When No, you must specify language to be added or revised in the following question.*
- See Attached

Potential for direct benefit to the subject and/or benefits to society: language to be added or revised ⇒Enter an unlimited amount of text.

15. Alternatives available:

⇒Select *one* of the following options from the list of radio buttons presented:

- Yes
- No *When No, you must specify language to be added or revised in the following question.*
- See Attached

Alternatives available: language to be added or revised ⇒Enter an unlimited amount of text.

16. Statement that participation is voluntary and subjects may refuse to participate or withdraw at any time:

⇒Select *one* of the following options from the list of radio buttons presented:

- Yes
- No *When No, you must specify language to be added or revised in the following question.*
- See Attached

Statement that participation is voluntary and subject may refuse to participate or withdraw at any time: language to be added or revised ⇒Enter an unlimited amount of text.

17. Statement regarding confidentiality of research records:

⇒Select *one* of the following options from the list of radio buttons presented:

- Yes
- No *When No, you must specify language to be added or revised in the following question.*
- See Attached



IRB STANDARD OPERATING PROCEDURES

Statement regarding confidentiality of research records: language to be added or revised

⇒Enter an unlimited amount of text.

18. For studies involving drugs, the dosage and route of administration:

⇒Select *one* of the following options from the list of radio buttons presented:

- Yes
- No *When No, you must specify language to be added or revised in the following question.*
- See Attached

For studies involving drugs, the dosage and route of administration: language to be added or revised ⇒Enter an unlimited amount of text.

19. Contact information if the subject has questions about the trial regarding rights as a research subject:

⇒Select *one* of the following options from the list of radio buttons presented:

- Yes
- No *When No, you must specify language to be added or revised in the following question.*
- See Attached

Contact information if the subject has questions about the trial regarding rights as a research subject: language to be added or revised ⇒Enter an unlimited amount of text.

20. Contact information if the subject has questions about the trial regarding research related injuries:

⇒Select *one* of the following options from the list of radio buttons presented:

- Yes
- No *When No, you must specify language to be added or revised in the following question.*
- See Attached

Contact information if the subject has questions about the trial regarding research related injuries: language to be added or revised ⇒Enter an unlimited amount of text.

21. Is any coercive language used in the informed consent document?

⇒Select *one* of the following options from the list of radio buttons presented:

- Yes *If Yes, where? Please specify where and provide alternative language in the following question.*
- No
- See Attached

Is any coercive language used in the informed consent document: alternative language to be added⇒Enter an unlimited amount of text.

22. Is any exculpatory language used in the informed consent document?

- **OPRR (now OHRP) Guidance (November 1996):**
<http://www.hhs.gov/ohrp/policy/exculp.html>
- **FDA Draft Guidance (August 2011):**
www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM271036.pdf

⇒Select *one* of the following options from the list of radio buttons presented:

- Yes *If Yes, where? Please specify where and provide alternative language in the following question.*



IRB STANDARD OPERATING PROCEDURES

- No
- See Attached

Exculpatory language used in the informed consent document: alternative language to be added or revised ⇒Enter an unlimited amount of text.

-- Consent Form Elements Part III (22-29) --

IF APPLICABLE, DOES THE CONSENT INCLUDE:

You may also attach a copy of the advertisement, public service announcement, other subject material, and/or assent form(s) electronically with edit changes included on another page that follows at the end of the Consent Form evaluation process. Circle words or phrases that need to be rewritten in lay language. Whenever possible, recommend acceptable language for the Principal Investigator to incorporate in the appropriate document.

To attach an electronic, informed consent form that includes the changes you are specifying in this review, you MUST select "See Attached" for the item(s) that you are modifying.

If you select "See Attached" for any of the consent form questions, you will be required to attach an electronic copy of the consent form with the edit changes **at the end of the Consent Form Evaluation xForm question process.**

23. Anticipated circumstance under which a subject's participation may be terminated is in the consent

⇒Select *one* of the following options from the list of radio buttons presented:

- Yes
- No *When No, you must specify language to be added or revised in the following question.*
- See Attached

Please specify language to be added or revised re: Anticipated circumstance under which a subject's participation may be terminated is in the consent ⇒Enter an unlimited amount of text.

24. Statement that significant new findings will be disclosed is in the consent

⇒Select *one* of the following options from the list of radio buttons presented:

- Yes
- No *When No, you must specify language to be added or revised in the following question.*
- See Attached

Please specify language to be added or revised re: Statement that significant new findings will be disclosed ⇒Enter an unlimited amount of text.

25. Medical consequences of withdrawing from the trial is in the consent

⇒Select *one* of the following options from the list of radio buttons presented:

- Yes
- No *When No, you must specify language to be added or revised in the following question.*
- See Attached

Please specify language to be added or revised re: Medical consequences of withdrawing from the trial ⇒Enter an unlimited amount of text.



IRB STANDARD OPERATING PROCEDURES

26. If subject will receive reimbursement, is a reimbursement schedule provided (i.e., when and how the subjects will receive reimbursement) is the consent

***Reimbursement should generally not be listed in the "Benefits" section of the consent.**

⇒Select *one* of the following options from the list of radio buttons presented:

- Yes
- No *When **No**, you must specify language to be added or revised in the following question.*
- See Attached

Please specify language to be added or revised re: If subject will receive reimbursement, is a reimbursement schedule provided (i.e., when and how the subjects will receive reimbursement)

⇒Enter an unlimited amount of text.

27. For applicable clinical trials, as defined in 42 U.S.C. 282(j)(1)(A), is required statement added?

Required statement:

"A description of this clinical trial will be available on <http://www.ClinicalTrials.gov> as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time."

- Trials of Drugs and Biologics: controlled clinical investigations, other than Phase I investigations, of a product subject to FDA regulation (not generics)
- Trials of Devices: Controlled trials with health outcomes of devices subject to FDA regulation, other than small feasibility studies, and pediatric postmarket surveillance
-

⇒Select *one* of the following options from the list of radio buttons presented:

- Yes
- No
- See Attached
- N/A

28. ASSENT FORM: Are there recommended changes to the Assent form(s)?

⇒Select *one* of the following options from the list of radio buttons presented:

- Yes *If Yes, where? Please specify where and provide alternative language in the following question.*
- No
- See Attached

28a. Assent Form Comments ⇒Enter an unlimited amount of text.

29. ADDITIONAL CONSENT DOCUMENTS or ADDENDUM REQUIRED?

**Does the study have/need additional Consent documents and/or Addendum?
(e.g., genetic or pharmacokinetic sub-study)**

⇒Select *one* of the following options from the list of radio buttons presented:

- Yes *If Yes, you will be required to answer additional questions.*
- No
- N/A



IRB STANDARD OPERATING PROCEDURES

30. Are there Advertisements and/or Subject Materials included with this review?

⇒Select *one* of the following options from the list of radio buttons presented:

- Yes *If Yes, you will be required to answer additional questions.*
- No

-- Advertisements and Subject Materials --

Advertisements and Subject Materials

If you select "See Attached" for any of the consent form questions, you will be required to attach an electronic copy of the consent form with the edit changes **at the end of the Consent Form Evaluation xForm question process.**

INTERNET AD: If the submission includes an Internet ad, are any modifications required?

⇒Select *one* of the following options from the list of radio buttons presented:

- Yes *When Yes, you will be required to supply language to be added or revised.*
- No
- See Attached
- N/A

Internet Ad Comments: ⇒Enter an unlimited amount of text.

PUBLIC SERVICE ANNOUNCEMENT (PSA): If the submission includes a public service announcement, are any modifications required?

⇒Select *one* of the following options from the list of radio buttons presented:

- Yes *When Yes, you will be required to supply language to be added or revised.*
- No
- See Attached
- N/A

Public Service Announcement Comments⇒Enter an unlimited amount of text.

OTHER SUBJECT MATERIALS: Are there other subject materials that require modification (e.g., subject dairy, dosing instructions, flyer, brochure, pamphlet, wallet card, etc.)?

⇒Select *one* of the following options from the list of radio buttons presented:

- Yes *When Yes, you will be required to supply language to be added or revised.*
- No
- See Attached
- N/A

Other Subject Material Comments⇒Enter an unlimited amount of text.

-- Consent Form Additional/Addendum --

ADDITIONAL CONSENT DOCUMENTS or ADDENDUM (e.g. genetic or pharmacokinetic sub-study)

To attach an electronic, informed consent form that includes the changes you are specifying in this review, you **MUST** select "**See Attached**" for the item(s) that you are modifying the request form for.



IRB STANDARD OPERATING PROCEDURES

You may also attach a copy of the informed consent form electronically with edit changes included on another page that follows at the end of the Consent Form evaluation process. Circle words or phrases that need to be rewritten in lay language. Whenever possible, recommend acceptable language for the Principal Investigator to incorporate in the consent document.

If you select "**See Attached**" for any of the consent form questions, you will be required to attach an electronic copy of the consent form with the edit changes **at the end of the Consent Form Evaluation xForm question process.**

Any additional modifications required for the additional Consent documents and/or Addendum?

⇒Select *one* of the following options from the list of radio buttons presented:

- Yes *When **Yes**, you will be required to supply language to be added or revised.*
- No
- See Attached
- N/A

Additional modifications required to Consent documents and/or Addendum: language to be added or revised⇒Enter an unlimited amount of text.

If a Consent Addendum, does it:

- a. Refer to main/other consent? and**
 - b. Contain appropriate additional info in readily understandable language?**
- Select N/A if NOT a consent Addendum.

⇒Select *one* of the following options from the list of radio buttons presented:

- Yes *When **Yes**, you will be required to supply language to be added or revised.*
- No
- See Attached
- N/A

Consent Addendum additional info: language to be added or revised⇒Enter an unlimited amount of text.

-- Consent Form Additional Comments --

CONSENT FORM ADDITIONAL COMMENT(S):

Please enter any additional comments regarding the consent form here⇒Enter an unlimited amount of text.

-- Consent Form Modified Attachment(s) --

CONSENT FORM MODIFIED ATTACHMENT(S)

Attach ANY documents that need modifications/edits and/or to be included with this review. Consent Form, Advertisements, PSAs, Subject Materials, etc., attachment(s) with edit changes included.

Attach a copy of the modified form(s) with edit changes included. Circle words or phrases that need to be rewritten in lay language. Whenever possible, recommend acceptable language for the Principal Investigator to incorporate in the appropriate document.



IRB STANDARD OPERATING PROCEDURES

If you selected "See Attached" for ANY of the Consent Form Checklist questions, you will be **REQUIRED** to submit at least one (1) document showing the edit changes.

You may attach up to twenty-five (25) separate documents.
⇒ Attach 1 to 25 files of type "ICF w/IRB-Directed Changes" to this xForm.

-- Vulnerable Populations Consideration Questions --

HIPAA WAIVER

In order for a waiver of the requirement to obtain HIPAA authorization to apply, the following must be true:

1. The use or disclosure of PHI involves no more than minimal risk to the privacy of individuals, based on, at least, the following:
 - An adequate plan to protect identifiers
 - An adequate plan to destroy identifiers (unless retention is required by law)
 - Adequate assurances that the PHI will not be reused or disclosed
2. The research could not be conducted without the waiver
3. The research could not be conducted without access to the PHI

⇒ Select *one* of the following options from the list of radio buttons presented:

- N/A - CHECK HERE IF NOT APPLICABLE
- No Change to Prior Board Determination
- Request to waive HIPAA authorization for recruitment is appropriate
- Request to waive HIPAA authorization for recruitment IS NOT appropriate

CONSIDERATIONS FOR VULNERABLE POPULATIONS

When "Proceed to Evaluation of..." choice is selected, you will be required to answer additional questions on another page.

RESEARCH INVOLVING CHILDREN

⇒ Select *one* of the following options from the list of radio buttons presented:

- **Proceed to Evaluation of Research Involving Children** (*When "Proceed to Evaluation of Research Involving Children" is selected, you will be required to answer additional questions on another page.*)
- N/A - CHECK HERE IF NOT APPLICABLE
- No Change to Prior Board Determination

RESEARCH INVOLVING PREGNANT WOMEN OR FETUSES OR RESEARCH TO COLLECT DATA ON PREGNANT PARTNERS AS SUBJECTS

⇒ Select *one* of the following options from the list of radio buttons presented:

- **Proceed to Evaluation of Research involving Pregnant Women or Fetuses** (*When "Proceed to Evaluation of Research involving Pregnant Women or Fetuses" is selected, you will be required to answer additional questions on another page.*)
- N/A - CHECK HERE IF NOT APPLICABLE
- No Change to Prior Board Determination



IRB STANDARD OPERATING PROCEDURES

RESEARCH INVOLVING NEONATES AS SUBJECTS

⇒Select *one* of the following options from the list of radio buttons presented:

- **Proceed to Evaluation of Research Involves Neonates** (*When "Proceed to Evaluation of Research Involves Neonates" is selected, you will be required to answer additional questions on another page.*)
- **N/A - CHECK HERE IF NOT APPLICABLE**
- **No Change to Prior Board Determination**

RESEARCH INVOLVING PRISONERS

⇒Select *one* of the following options from the list of radio buttons presented:

- **Proceed to Evaluation of Research Involves Prisoners** (*When "Proceed to Evaluation of Research Involves Prisoners" is selected, you will be required to answer additional questions on another page.*)
- **N/A - CHECK HERE IF NOT APPLICABLE**
- **No Change to Prior Board Determination**

RESEARCH INVOLVING COGNITIVELY IMPAIRED PERSONS

⇒Select *one* of the following options from the list of radio buttons presented:

- **Proceed to Evaluation of Research Involving Cognitively Impaired** (*When "Proceed to Evaluation of Research Involving Cognitively Impaired" is selected, you will be required to answer additional questions on another page.*)
- **N/A - CHECK HERE IF NOT APPLICABLE**
- **No Change to Prior Board Determination**

RESEARCH INVOLVING ADULT SUBJECTS WHO MAY LACK THE CAPACITY TO CONSENT

⇒Select *one* of the following options from the list of radio buttons presented:

- **Proceed to Evaluation of Adults Lacking Capacity to Consent** (*When "Proceed to Evaluation of Adults Lacking Capacity to Consent" is selected, you will be required to answer additional questions on another page.*)
- **N/A - CHECK HERE IF NOT APPLICABLE**
- **No Change to Prior Board Determination**

RESEARCH INVOLVING SURROGATE CONSENT (*Legally Authorized Representative*)

When reviewing research for which an investigator seeks the use of a legally authorized representative, please use this definition when determining who can serve as a "Legally Authorized Representative".

Legally Authorized Representative (LAR):

FDA regulation 21 CFR § 312.61 & DHHS regulation 45 CFR 102(c) define a legally authorized representative as an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research. However, State & local law would control over the regulations stated above. If a subject is medically incapable and/or legally incompetent, then a legally authorized representative, as determined under state or local law, must consent on the subject's behalf. A legally authorized representative may be a parent or legal guardian of a child, someone having durable power of attorney for health care (a health care proxy) for the subject, or some other court order authorizing him/her to be the legal representative.



IRB STANDARD OPERATING PROCEDURES

Since state & local law may vary in this regard, the BRANY IRB will seek legal consult on this matter when reviewing research for investigators in states other than New York.

⇒Select *one* of the following options from the list of radio buttons presented:

- **Proceed to Evaluation of Surrogate Consent** (*When "Proceed to Evaluation of Surrogate Consent" is selected, you will be required to answer additional questions on another page.*)
- **N/A - CHECK HERE IF NOT APPLICABLE**
- **No Change to Prior Board Determination**

RESEARCH IN ANY "VULNERABLE" SUBJECTS

(E.g. Children, Pregnant Women, Cognitively Impaired Persons, Prisoners, Students, Economically or Educationally Disadvantaged, Etc.)

Are the safeguards afforded to all subjects sufficient to protect vulnerable subjects in this study, or are special safeguards needed to protect vulnerable subjects?

⇒Select *one* of the following options from the list of radio buttons presented:

- **N/A - CHECK HERE IF NOT APPLICABLE**
- **No Change to Prior Board Determination**
- **Safeguards are sufficient**
- **Special Safeguards are needed to protect vulnerable subjects (SPECIFY):**

Specify Special Safeguards: ⇒Enter an unlimited amount of text.

-- Research Involving Children --

Definitions:

- **"Children"** are persons who have not attained the legal age for consent to treatments or procedures involved in the research under the applicable law or the jurisdiction in which the research will be conducted. A person is deemed to be a "child" in New York State if he is under 18 years old (age of majority is reached the day prior to the individual's birth date) A person is deemed to be a "child" in New York State if he is under 18 years old & not married or a parent. State laws may vary with regard to the definition of "child".
- **"Emancipated Minors"** are persons who have not yet attained the age of legal majority as defined by state or local law (18 years of age in New York), but who are entitled to treatment as if they had by virtue of assuming adult responsibilities, such as marriage, or procreation are considered emancipated minors. While emancipated minors do not meet the regulatory definition of "child", the BRANY IRB will review & process projects that plan to include emancipated minors in accordance with 45 CFR 46, subpart D requirements as described above.
- **"Guardian"** means an individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care. In New York State, a guardian is appointed either by parent pursuant to a designation, deed of guardianship or will approved by a Family Court or Surrogate's Court judge; or by a Family Court or Surrogate's Court judge pursuant to a letter or order of guardianship. State laws may vary with regard to the definition of "child".
- **The BRANY IRB will seek legal consult on this matter when reviewing research for investigators in states other than New York.**



IRB STANDARD OPERATING PROCEDURES

RISKS VS. BENEFITS FOR RESEARCH INVOLVING CHILDREN

⇒Select *one* of the following options from the list of radio buttons presented:

- **Proceed to Evaluation of Risk vs. Benefits for Research Involving Children**
- **No Change to Prior Board Determination**

ASSENT & PARENT/GUARDIAN PERMISSION

In additions to the determinations above, the IRB must determine whether adequate provisions are made for soliciting the assent of children, when in the judgment of the IRB the children are capable of providing assent.

⇒Select *one* of the following options from the list of radio buttons presented:

- **Proceed to Evaluation of Assent and Parent/Guardian Permission**
- **No Change to Prior Board Determination**

IS THE PROPOSED REIMBURSEMENT TO PARENTS/GUARDIANS AND/OR THE CHILD APPROPRIATE?

Indicate whether the proposed reimbursement to the parents/guardians and/or to the child is appropriate given the context of the study & the parent/guardian/subject involvement in the research. Consider whether study-related procedures/visits are within the realm of routine medical care, or whether extra time/convenience will be required of the parent/guardian/subject that they should be reasonably compensated for.

⇒Select *one* of the following options from the list of radio buttons presented:

- **Proceed to Evaluation of Proposed Reimbursement to Parents/Guardians and/or to the Child Appropriate**

No Change to Prior Board Determination

DOES THE RESEARCH APPLICATION INDICATE THAT THE RESEARCH MAY INCLUDE EMANCIPATED MINORS?

⇒Select *one* of the following options from the list of radio buttons presented:

- **Proceed to Evaluation of Research That May Include Emancipated Minors**
- **No Change to Prior Board Determination**

-- Risks vs. Benefits for Research Involving Children --

The federal regulations require IRBs to classify research involving children into one of 4 categories & to document their considerations of the risks & benefits of the study. The 4 categories of research involving children that may be approved by IRBs, based on the degree of risk & benefit to individual subjects are as follows. Choose the category that pertains to the protocol under review.

⇒Select *one* of the following options from the list of radio buttons presented:

- **(A) Research not involving greater than minimal risk (45CFR46.404 / 21CFR50.51)**
- **(B) Research involving greater than minimal risk, but presenting the prospect of direct benefits to an individual subject (45CFR46.405 / 21CFR50.52). Research in this category is approvable provided: a) the risk is justified by the anticipated benefit to the subject; and b) the relationship of risk to benefit is at least as favorable as any available alternative approach**
- **(C) Research involving greater than minimal risk with no prospect of direct benefits to individual subjects, but likely to yield generalizable knowledge about the subject's disease or condition (45CFR46.406 / 21CFR50.53). *****DO NOT SELECT THIS CHOICE IF****



IRB STANDARD OPERATING PROCEDURES

RESEARCH INVOLVES HEALTHY CONTROLS***• Research in this category is approvable provided: a) The risk presents a minor increase over minimal risk; b) The intervention or procedure presents experiences to subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social or educational settings; and c) The intervention or procedure is likely to yield generalizable knowledge about the subject's disorder or condition that is of vital importance for the understanding or amelioration of the subject's disorder or condition

- (D) Research that is not otherwise approvable, but which presents an opportunity to understand, prevent or alleviate a serious problem affecting the health or welfare of children (45CFR46.407/21CFR50.54). Research that is not approvable may be conducted provided that the IRB, the Secretary & consultation with a panel of experts finds that the research presents a reasonable opportunity to further understanding, etc.

If (C) or (D) is Yes, Does the research involve children who are WARDS?

- *The IRB shall require appointment of an advocate for each child who is a ward
- Research in this category is approvable for children who are **wards** of the state or any other agency, institution, or entity provided the research is:
 - a) Related to their status as wards; **or**
 - b) Conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of the children involved as subjects are not wards

⇒Select either 'Yes' or 'No'

Describe the rationale for your classification (Category A, B, C or D) indicated above ⇒Enter an unlimited amount of text.

-- Assent & Parent/Guardian Permission --

Should assent be obtained from all subjects capable of giving it?

Take into account the ages, maturity, & psychological state of the children involved.

⇒Select either 'Yes' or 'No' (If **Yes**, you will be required to answer additional questions.)

If Yes, Is the assent procedure suggested by the investigator adequate?

⇒Select either 'Yes' or 'No'(If **No**, you will be required to answer the next question.)

If Assent procedure suggested by the investigator is NOT adequate, specify modifications required

⇒Enter an unlimited amount of text.

Specify how Assent should be documented (Required when assent should be obtained from all subjects capable of giving it is Yes.)

⇒Select *one* of the following options from the list of radio buttons presented:

- Separate assent form signed by subject.
- Assent statement appended to document of informed consent.
- Other (SPECIFY)

Other (SPECIFY) ⇒Enter an unlimited amount of text.

Assent is a requirement of (select one):

⇒Select *one* of the following options from the list of radio buttons presented:

- All Children
- Some Children (Explain)
- None of the Children



IRB STANDARD OPERATING PROCEDURES

If assent is a requirement of some children, which children DO NOT have to provide assent?

⇒Enter an unlimited amount of text.

Indicate why assent is not required of these children:

⇒Check *one or more* of the following items from the list of check boxes presented:

- The children are not capable of providing assent based on age, maturity, or psychological state.
- The capability of the children is so limited that they could not reasonably be consulted or that the intervention.
- The research holds out a prospect of direct benefit that is important to the health or well being of the children & is available only in the context of the research.
- The assent can be waived using the following criteria for waiver of informed consent: a) The research involves no more than minimal risk to the participants; b) The waiver will not adversely affect the rights & welfare of the participants; c) The research could not practicably be carried out without the waiver; and d) Whenever appropriate, the participants will be provided with additional pertinent information after participation.

May the permission from the parents or guardians be waived? The IRB shall determine that adequate provisions are made for soliciting the permission of each child's parents or guardian.

⇒Select *one* of the following options from the list of radio buttons presented:

- No - Permission of ONE parent is sufficient (even if both parents are alive, known, competent & reasonably available & both have the legal responsibility for the care & custody of the child). (Only allowed if research does not involved greater than minimal risk to the child, or if the research involved greater than normal risk but presents the prospect of direct benefit to the individual subjects.)
- No - Permission of BOTH parents is required (unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has the legal responsibility for the care & custody of the child.
- Yes - Research protocol is designed for conditions or for a subject population for which parental or guardian permission is not a reasonable requirement to protect subjects (e.g., neglected or abused children). An appropriate mechanism for protecting children who will participate as subjects must be substituted, and the waiver parent/guardian permission must not be inconsistent with Federal, state, or local law.

-- Reimbursement Appropriate --

IS THE PROPOSED REIMBURSEMENT TO PARENTS/GUARDIANS AND/OR TO THE CHILD APPROPRIATE?

Indicate whether the proposed reimbursement to the parents/guardians and/or to the child is appropriate given the context of the study & the parent/guardian/subject involvement in the research. Consider whether study-related procedures/visits are within the realm of routine medical care, or whether extra time/convenience will be required of the parent/guardian/subject that they should be reasonably compensated for.

⇒Select *one* of the following options from the list of radio buttons presented:



IRB STANDARD OPERATING PROCEDURES

- Yes - Proposed Reimbursement is appropriate.
- No - Proposed Reimbursement is not appropriate. (Explain)
- Not Applicable - Study does not propose to reimburse the parents/guardians/child.

Specify reason (e.g., coercive, excessive, etc.) proposed reimbursement is not appropriate
⇒Enter an unlimited amount of text.

-- Emancipated Minors --

DOES THE RESEARCH APPLICATION INDICATE THAT THE RESEARCH MAY INCLUDE EMANCIPATED MINORS?

⇒Select *one* of the following options from the list of radio buttons presented:

- Yes - It is appropriate to include emancipated minors with an informed consent.
- Yes - It is appropriate to include emancipated minors, BUT the following modifications to the protocol and/or informed consent are required (PLEASE SPECIFY)
- No - It is not appropriate to include emancipated minors.
- Not Applicable - Study does not propose to include emancipated minors.

Modifications to the Protocol and/or Informed Consent to include Emancipated Minors ⇒Enter an unlimited amount of text.

-- Research Involves Pregnant Women or Fetuses --

PREGNANT WOMEN OR FETUSES

Pregnant women or fetuses may be involved in research if ALL of the following conditions are met:

(A) Where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies, including studies on non-pregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses;

⇒Select *one* of the following options from the list of radio buttons presented

- Yes
- No (Explain)
- Not Applicable (Explain)

Explain ⇒Enter an unlimited amount of text.

(B) Either (1) or (2) must apply for the research to be approvable:

(1) The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus

⇒Select *one* of the following options from the list of radio buttons presented

- Yes
- No (Explain)
- Not Applicable (Explain)

Explain ⇒Enter an unlimited amount of text.

(2) If there is no such prospect of benefit, the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge (or generalizable knowledge when research is subject to DoD requirements) which cannot be obtained by any other means;

⇒Select *one* of the following options from the list of radio buttons presented

- Yes



IRB STANDARD OPERATING PROCEDURES

- No (Explain)
 - Not Applicable (Explain)
- Explain** ⇒Enter an unlimited amount of text.

(C) Risk is the least possible for achieving the objectives of the research;
⇒Select *one* of the following options from the list of radio buttons presented

- Yes
 - No (Explain)
 - Not Applicable (Explain)
- Explain** ⇒Enter an unlimited amount of text.

(D) One of the following (1, 2, 3 or 4) must apply for the research to be approvable:
(1) The research holds out the prospect of direct benefit to the pregnant woman, and the woman's consent will be obtained.

- ⇒Select *one* of the following options from the list of radio buttons presented
- Yes
 - No (Explain)
 - Not Applicable (Explain)

Explain ⇒Enter an unlimited amount of text.

(2) The research holds out the prospect of direct benefit both to the pregnant women and the fetus, and the woman's consent will be obtained.

- ⇒Select *one* of the following options from the list of radio buttons presented
- Yes
 - No (Explain)
 - Not Applicable (Explain)

Explain ⇒Enter an unlimited amount of text.

(3) The research holds out no prospect of benefit for the woman nor the fetus, the risk to the fetus is no greater than minimal, the purpose of the research is the development of important biomedical knowledge (or generalizable knowledge when research is subject to DoD requirements) that cannot be obtained by any other means, and the woman's consent will be obtained.

- ⇒Select *one* of the following options from the list of radio buttons presented
- Yes
 - No (Explain)
 - Not Applicable (Explain)

Explain ⇒Enter an unlimited amount of text.

(4) The research holds out the prospect of direct benefit solely to the fetus, and the consent of the pregnant woman and the father will be obtained, except that the father's consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity or the pregnancy resulted from rape or incest.

- ⇒Select *one* of the following options from the list of radio buttons presented
- Yes
 - No (Explain)
 - Not Applicable (Explain)

Explain ⇒Enter an unlimited amount of text.



IRB STANDARD OPERATING PROCEDURES

(E) Each individual providing consent under paragraph (d) or (e) of this section is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate;

⇒Select *one* of the following options from the list of radio buttons presented

- Yes
- No (Explain)
- Not Applicable (Explain)

Explain ⇒Enter an unlimited amount of text.

(F) For children as defined in §46.402(a) who are pregnant, assent and permission are obtained in accord with the provisions of 45CFR46 Subpart D (see Reviewer Checklist section);

⇒Select *one* of the following options from the list of radio buttons presented

- Yes
- No (Explain)
- Not Applicable (Explain)

Explain ⇒Enter an unlimited amount of text.

(G) No inducements, monetary or otherwise, will be offered to terminate a pregnancy;

⇒Select *one* of the following options from the list of radio buttons presented

- Yes
- No (Explain)
- Not Applicable (Explain)

Explain ⇒Enter an unlimited amount of text.

(H) Individuals engaged in the research will have no part in any decisions as to timing, method, or procedures used to terminate a pregnancy;

⇒Select *one* of the following options from the list of radio buttons presented

- Yes
- No (Explain)
- Not Applicable (Explain)

Explain ⇒Enter an unlimited amount of text.

(I) Individuals engaged in the research will have no part in determining the viability of a neonate.

⇒Select *one* of the following options from the list of radio buttons presented

- Yes
- No (Explain)
- Not Applicable (Explain)

Explain ⇒Enter an unlimited amount of text.

Check that all criteria above (A - I) are met.

Comments: ⇒Enter an unlimited amount of text.

⇒Select *one* of the following options from the list of radio buttons presented:

- **Research is approvable.**
- **Research is NOT approvable.**



IRB STANDARD OPERATING PROCEDURES

-- Research Involves Neonates --

NEONATES

ALL of the following must be true:

(A) The research involves neonates where it will not be ascertained whether a neonate is viable

⇒Select either 'Yes' or 'No' (*When No, you will be required to explain.*)

Explain ⇒Enter one line of text.

(B) Either (1) or (2) applies:

(1) Preclinical and clinical studies to provide data for assessing potential risks to neonates are not scientifically appropriate. Required)

⇒Select *one* of the following options from the list of radio buttons presented:

- Yes
- No (Explain)
- Not Applicable (Explain)

Explain ⇒Enter one line of text.

(2) Preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates.

⇒Select *one* of the following options from the list of radio buttons presented:

- Yes
- No (Explain)
- Not Applicable (Explain)

Explain ⇒Enter one line of text.

(C) Each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the neonate.

⇒Select either 'Yes' or 'No' (*When No, you will be required to explain.*)

Explain ⇒Enter one line of text.

(D) Individuals engaged in the research will have no part in determining the viability of a neonate.

⇒Select either 'Yes' or 'No' (*When No, you will be required to explain.*)

Explain ⇒Enter one line of text.

(E) One of the following (1) or (2) is true:

(1) The research holds out the prospect of enhancing the probability of survival of the neonate to the point of viability, and any risk is the least possible for achieving the objective.

⇒Select *one* of the following options from the list of radio buttons presented:

- Yes
- No (Explain)
- Not Applicable (Explain)

Explain ⇒Enter one line of text.

(2) The purpose of the research is the development of important biomedical knowledge (or generalizable knowledge when research is subject to DoD



IRB STANDARD OPERATING PROCEDURES

requirements) which cannot be obtained by other means, and there will be no added risk to the neonate resulting from the research.

⇒Select *one* of the following options from the list of radio buttons presented:

- Yes
- No (Explain)
- Not Applicable (Explain)

Explain ⇒Enter one line of text.

(F) One of the following (1) or (2) is true:

(1) The legally effective informed consent of either parent or neonate will be obtained, except that consent of the father or his legally authorized representative need not be obtained if the pregnancy resulted from rape or incest.

⇒Select *one* of the following options from the list of radio buttons presented:

- Yes
- No (Explain)
- Not Applicable (Explain)

Explain ⇒Enter one line of text.

(2) If neither parent is able to consent because of unavailability, incompetence, or temporary incapacity, the legally effective informed consent of either parent's legally authorized representative will be obtained, except that the consent of the father or his legally authorized representative need not be obtained if the pregnancy resulted from rape or incest.

⇒Select *one* of the following options from the list of radio buttons presented:

- Yes
- No (Explain)
- Not Applicable (Explain)

Explain ⇒Enter one line of text.

Select one:

You will be required to answer additional questions if research involves **non-viable neonates**.

⇒Select *one* of the following options from the list of radio buttons presented:

- Research involves non-viable neonates.
- NOT APPLICABLE

Select one:

You will be required to answer additional questions if research involves **viable neonates**.

⇒Select *one* of the following options from the list of radio buttons presented:

- Research involves viable neonates.
- NOT APPLICABLE

-- Research Involves Non-Viable Neonates --

NON-VIABLE NEONATES

ALL of the following must be true

(A) The research involves neonates ascertained to be non-viable

⇒Select either 'Yes' or 'No'

Explain ⇒Enter an unlimited amount of text.



IRB STANDARD OPERATING PROCEDURES

(B) Either (1) or (2) applies:

(1) Preclinical and clinical studies to provide data for assessing potential risks to neonate are not scientifically appropriate.

⇒Select *one* of the following options from the list of radio buttons presented:

- Yes
- No (Explain)
- Not Applicable (Explain)

Explain ⇒Enter an unlimited amount of text.

(2) Preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates

⇒Select *one* of the following options from the list of radio buttons presented:

- Yes
- No (Explain)
- Not Applicable (Explain)

Explain⇒Enter an unlimited amount of text.

(C) Each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the neonate.

⇒Select either 'Yes' or 'No'

Explain ⇒Enter an unlimited amount of text.

(D) Individuals engaged in the research will have no part in determining the viability of a neonate.

⇒Select either 'Yes' or 'No'

Explain ⇒Enter an unlimited amount of text.

(E) Vital functions of the neonate will not be artificially maintained.

⇒Select either 'Yes' or 'No'

Explain ⇒Enter an unlimited amount of text.

(F) The research will not terminate the heartbeat or respiration of the neonate.

⇒Select either 'Yes' or 'No'

Explain ⇒Enter an unlimited amount of text.

(G) There will be no added risk to the neonate resulting from the research.

⇒Select either 'Yes' or 'No'

Explain ⇒Enter an unlimited amount of text.

(H) The purpose of the research is the development of important biomedical knowledge (or generalizable knowledge when research is subject to DoD requirements) that cannot be obtained by other means.

⇒Select either 'Yes' or 'No'

Explain ⇒Enter an unlimited amount of text.

(I) The legally effective informed consent of both parents will be obtained, except that the consent of the father or his legally authorized representative need not be obtained if the



IRB STANDARD OPERATING PROCEDURES

pregnancy resulted from rape or incest and the informed consent of one parent will suffice if either parent is unable to consent because of unavailability, incompetence, or temporary incapacity. (The consent of a legally authorized representative of either or both of the parents of a nonviable neonate will not suffice.) Refer to Reviewer Checklist.

⇒Select either 'Yes' or 'No'

Explain ⇒Enter an unlimited amount of text.

-- Research Involves Viable Neonates --

VIABLE NEONATES

BOTH of the following must be true in order for research involving viable neonates to be approved:

(A) The research involves neonates ascertained to be viable.

⇒Select either 'Yes' or 'No' (*When No, you will be required to explain.*)

Explain ⇒Enter an unlimited amount of text.

(B) The research meets the requirements for research involving children (see Reviewer Checklist)

⇒Select either 'Yes' or 'No' (*When No, you will be required to explain.*)

Explain ⇒Enter an unlimited amount of text.

-- Research Involves Neonate IRB Determinations --

IRB Determinations

Comments⇒Enter an unlimited amount of text.

Check to indicate whether:

⇒Select *one* of the following options from the list of radio buttons presented:

- Research is approvable.
- Research is NOT approvable.

-- Research Involves Prisoners --

RESEARCH INVOLVING PRISONERS

The BRANY IRB does not routinely review research involving prisoners. When the IRB reviews research that involves prisoners, the majority of the board (exclusively of prisoner members) shall have no association with the prison involved and at least one member of the board shall be a prisoner or a prisoner advocate, in keeping with 45CFR46.304. The IRB Coordinator(s) will ensure that one or more individuals who were prisoners or prisoner representative will be present at the IRB meeting.

A. Only research studies meeting one of the four categories described below may be approved to include prisoners as research participants. Check the appropriate category for the submitted research:

⇒Select *one* of the following options from the list of radio buttons presented:

- Category A: Studies of the possible causes, effects and processes of incarceration and of criminal behavior, provided that the study presents no more than minimal risk and no more than inconvenience to the participants;



IRB STANDARD OPERATING PROCEDURES

- Category B: Studies of prisons as instituted structures or of prisoners as incarcerated persons, provided that the study presents no more than minimal risk and no more than inconvenience to the participants;
- Category C: Research on conditions particularly affecting prisoners as a class (for example, vaccine trials and other research on hepatitis which is more prevalent in prisons than elsewhere; and research on social and psychological problems such as alcoholism, drug addiction and sexual assaults) provided that the study may proceed only after the Secretary of the Department of Health & Human Services (DHHS) has consulted with appropriate experts including experts in penology, medicine, and ethics, and published notice, in the Federal Register, of the intent to approve such research; or
- Category D: Research on practices, both innovative and accepted, which have the intent and reasonable probability of improving the health or well-being of the participant. In cases in which those studies require the assignment of prisoners in a manner consistent with protocols approved by the IRB to control groups which may not benefit from the research, the study may proceed only after the Secretary of DHHS has consulted with appropriate experts, including experts in penology, medicine, and ethics, and published notice, in the Federal Register, of the intent to approve such research.

B. In addition, the IRB can only approve research studies involving prisoners if it finds that ALL of the following criteria apply:

1) Any possible advantages accruing to the prisoner through his or her participation in the research, when compared to the general living conditions, medical care, quality of food, amenities and opportunity for earnings in prison, are not of such magnitude that his or her ability to weigh the risks of the research against the value of such advantages in the limited choice environment of the prison is impaired;

⇒Select either 'Yes' or 'No' (*When No, you will be required to explain.*)

Explain ⇒Enter an unlimited amount of text.

2) The risks involved in the research are commensurate with risks that would be accepted by non-prisoner volunteers;

⇒Select either 'Yes' or 'No' (*When No, you will be required to explain.*)

Explain ⇒Enter an unlimited amount of text.

3) Procedures for the selection of participants within the prison are fair to all prisoners and immune from arbitrary intervention by prison authorities or prisoners. Unless the principal investigator provides to the Board justification in writing for following some other procedures, control participants must be selected randomly from the group of available prisoners who meet the characteristics needed for that particular research study;

⇒Select either 'Yes' or 'No' (*When No, you will be required to explain.*)

Explain ⇒Enter an unlimited amount of text.

4) The information is presented in a language and reading level that is understandable to the participant population;

⇒Select either 'Yes' or 'No' (*When No, you will be required to explain.*)

Explain ⇒Enter an unlimited amount of text.

5) Adequate assurance exists that parole boards will not take into account a prisoner's participation in the research in making decisions regarding parole, and each prisoner is



IRB STANDARD OPERATING PROCEDURES

clearly informed in advance that participation in the research will have no effect on his or her parole;

⇒Select either 'Yes' or 'No' (*When No, you will be required to explain.*)

Explain ⇒Enter an unlimited amount of text.

6) Where the IRB finds there may be a need for follow-up examination or care of participants after the end of their participation, adequate provision has been made for such examination or care, taking into account the varying lengths of individual prisoners' sentences and for informing participants of this fact.

⇒Select either 'Yes' or 'No' (*When No, you will be required to explain.*)

Explain ⇒Enter an unlimited amount of text.

C. If a study utilizing prisoners as research participants is federally funded, a letter must be sent from the IRB to the DHHS Secretary through the Office for Human Research Protections (OHRP) indicating it has approved a study that will include prisoners in accordance with 45 CFR part 46 subpart C. The research may not begin until written approval is received from OHRP on behalf of the DHHS Secretary confirming that the proposed research involved solely one of the permissible categories.

- ⇒Check *one or more* of the following items from the list of check boxes presented:
Check here if the research is federally funded.

-- Research Involves Prisoners IRB Determination --

- **Section A: Only one (1) of the categories applies.**
- **Section B: All six (6) criteria apply.**
- **Section C: Determine whether research is federally funded.**

Comments ⇒Enter an unlimited amount of text.

Check to indicate whether:

⇒Select *one* of the following options from the list of radio buttons presented:

- Research is approvable.
- Research is NOT approvable.

-- Research Involving Cognitively Impaired Persons --

RESEARCH INVOLVING COGNITIVELY IMPAIRED PERSONS

Cognitively Impaired is defined in the OPRR Guidebook as having either a psychiatric disorder (e.g. psychosis, neurosis, personality or behavior disorder), an organic impairment (e.g. dementia), or a developmental disorder (e.g. mental retardation) that affects cognitive or emotional functions to the extent that capacity for judgment & reasoning is significantly diminished.

IRB considerations may include:

Is there a washout period (e.g. withdrawing current anti-depression therapy to enroll subject in trial)?

⇒Select either 'Yes' or 'No' (*If Yes, you will be required to answer another question.*)

If Yes, are there appropriate rescues or other precautions in place?

⇒Select either 'Yes' or 'No' (*If No, you will be required to answer an additional question.*)



IRB STANDARD OPERATING PROCEDURES

If No, describe additional precautions required

⇒Enter an unlimited amount of text.

Is there need for an independent clinical monitor?

⇒Select either 'Yes' or 'No' (*If you select No, an explanation will be required.*)

If No, explain ⇒Enter an unlimited amount of text.

-- Research Adult Subjs May Lack Capacity to Consent --

RESEARCH INVOLVING ADULT SUBJECTS WHO MAY LACK THE CAPACITY TO CONSENT

Is the investigator's plan for determining capacity to consent appropriate?

⇒Select either 'Yes' or 'No' (*When No, you will be required to enter a comment.*)

Comment ⇒Enter an unlimited amount of text.

Should assent be obtained from this category of subjects?

⇒Select either 'Yes' or 'No' (*When No, you will be required to enter a comment.*)

Comment ⇒Enter an unlimited amount of text.

If the investigator will obtain assent, has an adequate plan been provided?

⇒Select either 'Yes' or 'No' (*When No, you will be required to enter a comment.*)

Comment ⇒Enter an unlimited amount of text.

-- Research Involving Surrogate Consent --

RESEARCH INVOLVING SURROGATE CONSENT (LEGALLY AUTHORIZE REPRESENTATIVE)

When reviewing research for which an investigator seeks the use of a legally authorized representative, please use this definition when determining who can serve as a "Legally Authorized Representative".

Legally Authorized Representative (LAR):

FDA regulation 21 CFR § 50.3 § 50.3 & DHHS regulation 45 CFR 102(c) define a legally authorized representative as an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research. However, State & local law would control over the regulations stated above. If a subject is medically incapable and/or legally incompetent, then a legally authorized representative, as determined under state or local law, must consent on the subject's behalf. A legally authorized representative may be a parent or legal guardian of a child, someone having durable power of attorney for health care (a health care proxy) for the subject, or some other court order authorizing him/her to be the legal representative.

Since state & local law may vary in this regard, the BRANY IRB will seek legal consult on this matter when reviewing research for investigators in states other than New York.

Where a patient is incapacitated & unable to consent, the patient may be enrolled as a research subject by the patient's legally authorized representative as follows:



IRB STANDARD OPERATING PROCEDURES

Where a patient is deemed incompetent or is incapacitated and unable to consent, the patient may be enrolled as a research subject by the patient's surrogate (*legally authorized representative*) as follows:

A **non-therapeutic clinical trial (i.e., a trial in which there is no anticipated direct clinical benefit to the subject) should be conducted in subjects who personally give consent and who sign and date the written consent document.**

For research that is **not subject to the requirements of the Department of Defense**, consent to participate in **non-therapeutic research** may be obtained from a **healthcare proxy authorized to consent for research** (or, if the proxy is silent with respect to research, it is acceptable for another legally authorized representative) if the following conditions are fulfilled:

- (f) The objectives of the trial cannot be met by means of a trial in subjects who can give consent personally.
- (g) The foreseeable risks to the subject are low.
- (h) The negative impact on the subject's well-being is minimized and low.
- (i) The trial is not prohibited by law.
- (j) The opinion of the IRB is expressly sought on the inclusion of such subjects, and the written opinion covers this aspect.
- (k) The investigator would obtain the legally effective consent of the participant or the participant's legally authorized representative.
- (l) The circumstances of the consent process provided the prospective participant or the legally authorized representative sufficient opportunity to consider whether to participate.
- (m) The individuals communicating information to the participant or the legally authorized representative during the consent process would provide the information in language understandable to the participant or the representative.

Such trials (**non-therapeutic trials**), unless an exception is justified, should be conducted in patients having a disease or condition for which the investigational product is intended. Subjects in these trials should be particularly closely monitored and should be withdrawn if they appear to be unduly distressed.

Consent to participate in **therapeutic research** may be obtained from a **healthcare proxy authorized to consent for research**. If the proxy is silent with respect to research, it is acceptable for a health care proxy (or other legally authorized representative) to sign the consent if:

- (f) There is potential benefit over standard treatment; and



IRB STANDARD OPERATING PROCEDURES

- (g) Standard treatment is not being withheld; and
- (h) There is no alternative standard treatment; and
- (i) Enrollment in the study is in the best interest of the patient; and
- (j) Participation in the research would not be contrary to the known wishes of the patient
- (k) The investigator would obtain the legally effective consent of the participant or the participant's legally authorized representative.
- (l) The circumstances of the consent process provided the prospective participant or the legally authorized representative sufficient opportunity to consider whether to participate.
- (m) The individuals communicating information to the participant or the legally authorized representative during the consent process would provide the information in language understandable to the participant or the representative.

THIS POLICY SHOULD ONLY BE FOLLOWED IF CONSISTENT WITH THE POLICY OF THE INVESTIGATOR'S INSTITUTION. In the event an Institution's policies are more stringent, the more stringent policies should be followed.

Please indicate whether surrogate consent (consent by a legally authorized representative) is appropriate for this study:

⇒Select *one* of the following options from the list of radio buttons presented:

- The use of surrogate consent is appropriate for this study.
- The use of surrogate consent IS NOT appropriate for this study.

Rationale for answer ⇒Enter an unlimited amount of text.

Submission to Review III

-- Other Research Consideration Questions --

Please complete the following sections. Your answer will determine which pages you will be displayed during the remainder of the Reviewer Checklist Entry Form

When "Proceed to Evaluation of..." choice is selected, you will be required to answer additional questions on another page.

LOCAL RESEARCH CONTEXT CONSIDERATIONS

⇒Select *one* of the following options from the list of radio buttons presented:

- **Proceed to Evaluation of Local Research Context Considerations**
- **No Change to Prior Board Determination**

SITE RESOURCE CONSIDERATIONS

⇒Select *one* of the following options from the list of radio buttons presented:

- **Proceed to Evaluation of Site Resource Considerations**



IRB STANDARD OPERATING PROCEDURES

- **No Change to Prior Board Determination**

IND (INVESTIGATIONAL NEW DRUG) CONSIDERATIONS

Please consider whether the study drug or biologic should be investigated under an IND. If there is any question about requirements for INDs, the IRB administrative staff can provide you with the IND determination form.

⇒Select *one* of the following options from the list of radio buttons presented:

- **Proceed to Evaluation of IND Considerations**
- **No Change to Prior Board Determination**
- **N/A - CHECK HERE IF NOT APPLICABLE**

DEVICE CONSIDERATIONS

Please consider whether the device has been classified as a Significant Risk (SR) device or a Non-Significant Risk (NSR) device. (Refer to the [Research Application](#).) If there is any question about criteria for classifying devices, the IRB administrative staff can provide you with the IDE determination form.

⇒Select *one* of the following options from the list of radio buttons presented:

- **Proceed to Evaluation of Device Considerations**
- **No Change to Prior Board Determination**
- **N/A - CHECK HERE IF NOT APPLICABLE**

CONSIDERATION FOR MULTI-CENTER RESEARCH PROJECTS FOR WHICH THE INVESTIGATOR OR THE ORGANIZATION WILL SERVE AS THE LEAD INVESTIGATOR

⇒Select *one* of the following options from the list of radio buttons presented:

- **Proceed to Evaluation of Multi-Center Research Considerations**
- **No Change to Prior Board Determination**
- **N/A - CHECK HERE IF NOT APPLICABLE**

Unanticipated Problem Involving Risks to Subjects or Others

Any event that:

- **is unforeseen**
- **suggests that research places subjects at greater risk than was previously known or recognized, and;**
- **is related or possibly related to a subject's participation in research.**

Related or possibly related to the research: An event is "related or possibly related to the research" if in the opinion of the investigator it is more likely than not related to a subject's participation in research.

Unexpected: An event is "unexpected" when its specificity and severity are not accurately reflected in the informed consent document or other study-related documents (e.g., protocol, IB, safety updates, etc.).

Unanticipated: An event is "unanticipated" when it was unforeseeable at the time of occurrence. The word unanticipated, is NOT a synonym for unexpected. A research protocol can monitor for an unexpected event, but cannot monitor for an unforeseen event. All unanticipated events are unexpected, but NOT vice versa.



IRB STANDARD OPERATING PROCEDURES

If reviewing **adverse event** or **deviation reports**, **monitoring reports**, or **reports of any other events or possible problems**, consider whether the submission also represents a **UP**.

⇒Select *one* of the following options from the list of radio buttons presented:

- Possible UP - Proceed to Evaluation of Unanticipated Problems (UP) Involving Risks to Participants or Others
- N/A - CHECK HERE IF NOT APPLICABLE

Serious or Continuing Non-Compliance

Failure of the investigator or any member of the research staff to adhere to applicable laws or regulations, IRB policies and procedures, and any requirements or determinations made by the IRB as part of the review of a research project, and such failure increases risk to subjects, or adversely affects the rights & welfare of research subjects. A single instance of non-compliance may be serious. Any failure to comply may be serious or continuing if it either actually, or potentially, increases risks or adversely affects the rights & welfare of the participants. Examples of serious non-compliance include, but are not limited to:

1. Failure to obtain IRB approval prior to initiation of research project;
2. Continuation of research when the IRB approval has expired (i.e., failed to file for continuing review);
3. Failure to notify the IRB of changes in ongoing research (e.g., deviations, amendments, SAEs);
4. Failure to obtain informed consent;
5. Failure to document informed consent; or
6. Failure to properly document the research and research procedures.

Continuing non-compliance: a pattern of reports of non-compliance that, if unaddressed, may compromise the integrity of the human research protection program. The pattern may reflect a lack of knowledge on the part of the investigator or a lack of commitment by the investigator or the research staff to human subject protection.

Minor non-compliance: is neither serious nor continuing.

If reviewing adverse event or deviation reports, monitoring reports, or reports of any other events or possible problems, consider whether the submission also represents a serious OR continuing non-compliance.

⇒Select *one* of the following options from the list of radio buttons presented:

- Possible Serious or Continuing Non-Compliance - Proceed to Evaluation of Serious or Continuing Non-Compliance
- N/A - CHECK HERE IF NOT APPLICABLE

-- Local Research Considerations Continuing Review --

Local Research Considerations

Are any modifications to the research project recommended as a result of the evaluation of the local research context? (Please refer to the [Research Application](#).)

⇒Select either 'Yes' or 'No' (*When **Yes**, you will be required to explain.*)

Explain ⇒Enter an unlimited amount of text.



IRB STANDARD OPERATING PROCEDURES

For CONTINUING REVIEW ONLY: have there been any changes to the local research context that warrant modification to the research?

⇒Select either 'Yes' or 'No' (*When Yes, you will be required to specify the changes.*)

Specify ⇒Enter an unlimited amount of text.

-- Local Research Considerations --

Are any modifications to the research project recommended as a result of the evaluation of the local research context? (Please refer to the [Research Application](#).)

⇒Select either 'Yes' or 'No' (*When Yes, you will be required to explain.*)

Explain ⇒Enter an unlimited amount of text.

-- Site Research Considerations --

SITE RESOURCE CONSIDERATIONS

Does the investigator have appropriate mechanisms in place to ensure that adequate staffing & resources are available for each research project conducted so that the rights & welfare of research subjects will be protected? Staff should be sufficiently trained to administer the research protocol without impacting on subject safety or data integrity. Staff should have sufficient time available to interact with subjects as needed. Trained staff should be available to provide backup coverage in emergency situations. (Please refer to the [Research Application](#).)

If **NO**, you will be required to explain.

⇒Select either 'Yes' or 'No'

Explain ⇒Enter an unlimited amount of text.

-- Investigational New Drug (IND) Considerations --

IND (INVESTIGATIONAL NEW DRUG) CONSIDERATIONS

Please consider whether the study drug or biologic should be investigated under an IND. If there is any question about requirements for INDs, the IRB administrative staff can provide you with the IND determination form.

Does the research being conducted require an IND?

⇒Select *one* of the following options from the list of radio buttons presented:

- No
- Yes (*When YES, you will be required to answer the question regarding evidence of valid IND number.*)
- Not Applicable

If this research was NOT submitted under an IND, should the investigator apply for an IND?

⇒Select *one* of the following options from the list of radio buttons presented:

- No
- Yes
- Not Applicable

Rationale ⇒Enter an unlimited amount of text.



IRB STANDARD OPERATING PROCEDURES

If this research was submitted under an IND, is there evidence of a valid IND number?

⇒Select either 'Yes' or 'No' (*Required when research being conducted requires an IND is YES.*)

Comment ⇒Enter an unlimited amount of text.

-- Device Considerations --

DEVICE CONSIDERATIONS

Please consider whether the device has been classified as a Significant Risk (SR) device, a Non-Significant Risk (NSR) device or Neither Category. (Refer to the [Research Application](#).) If there is any question about criteria for classifying devices, the IRB administrative staff can provide you with the IDE determination form.

Select the device designation then xForms will proceed to that section of the form to answer specific questions.

Device Type

⇒Select *one* of the following options from the list of radio buttons presented:

- Non-Significant Risk Device
- Significant Risk Device
- Neither Category

-- NSR Device Considerations --

Non-Significant Risk (NSR) Device

For NSR devices, is a letter from the sponsor indicating why the device is considered NSR included?

⇒Select *one* of the following options from the list of radio buttons presented:

- Yes
- No

Does the IRB agree with this designation?

⇒Select *one* of the following options from the list of radio buttons presented:

- Yes
- No

Explain ⇒Enter an unlimited amount of text.

-- SR Device Considerations --

Significant Risk (SR) Device

For SR devices, does the research application include an Investigational Device Exemption (IDE) from FDA?

⇒Select *one* of the following options from the list of radio buttons presented:

- Yes
- No

If research was submitted under an IDE, is there evidence of a valid IDE?

⇒Select *one* of the following options from the list of radio buttons presented:

- Yes



IRB STANDARD OPERATING PROCEDURES

- No

Comment ⇒Enter an unlimited amount of text.

Does the IRB agree with this designation?

⇒Select *one* of the following options from the list of radio buttons presented:

- Yes
- No

-- Neither Device Considerations --

NEITHER CATEGORY

If neither category above applies, has a letter explaining why the investigation is exempt from the IDE requirements under 21 CFR 812.2(c) or otherwise exempt been provided?

⇒Select *one* of the following options from the list of radio buttons presented:

- Yes
- No

Does the IRB agree with this designation?

⇒Select *one* of the following options from the list of radio buttons presented:

- Yes
- No

Explain⇒Enter an unlimited amount of text.

-- Multi-Center Research --

MULTI-CENTER RESEARCH PROJECTS

BRANY IRB will expect that the lead investigator/organization be responsible to obtain & manage the information obtained from the multi-center research that might be relevant to participate protections, including but not limited to:

- Unanticipated problems involving risks to participants or others.
- Interim results
- Protocol modifications

Is the investigator's plan for managing the above information adequate?

⇒Select either 'Yes' or 'No'

Explain ⇒Enter an unlimited amount of text.

-- Unanticipated Problems (UP) Involving Risks --

Unanticipated Problems (UP) Involving Risks to Subjects or Others

Any event that is:

- unforeseen
- suggests that research places subjects at greater risk than was previously known or recognized, and;
- related or possibly related to a subject's participation in research.

Related or possibly related to the research: An event is "related or possibly related to the research" if in the opinion of the investigator it is more likely than not related to a subject's participation in



IRB STANDARD OPERATING PROCEDURES

research.

Unexpected: An event is "unexpected" when its specificity and severity are not accurately reflected in the informed consent document or other study-related documents (e.g., protocol, IB, safety updates, etc.).

Unanticipated: An event is "unanticipated" when it was unforeseeable at the time of occurrence. The word unanticipated, is NOT a synonym for unexpected. A research protocol can monitor for an unexpected event, but cannot monitor for an unforeseen event. All unanticipated events are unexpected, but NOT vice versa.

Select one of the following:

Comment/Explanation required when Submission Represents:

- Possible UP *or*
- DOES NOT Represent a UP

⇒ Select *one* of the following options from the list of radio buttons presented:

- Submission Represents possible UP: *select only if reviewed by expedited review*
- Notify IRB staff to obtain further information and forward to CHAIR & FULL BOARD REVIEW
- Submission Represents a UP: items (1)-(3) above are ALL TRUE → *only if at convened meeting*
- Submission DOES NOT Represent a UP - some/all of items (1)-(3) above do not apply (explain)

Comments/Explanation ⇒ Enter an unlimited amount of text.

-- Serious and/or Continuing Non-Compliance --

SERIOUS AND/OR CONTINUING NON-COMPLIANCE

If reviewing adverse event or deviation reports, monitoring reports, or reports of any other events or possible problems, consider whether the submission also represents a serious AND/OR continuing non-compliance.

Failure of the investigator or any member of the research staff to adhere to applicable laws or regulations, IRB policies and procedures, and any requirements or determinations made by the IRB as part of the review of a research project, and such failure increases risk to subjects, or adversely affects the rights & welfare of research subjects. A single instance of non-compliance may be serious. Any failure to comply may be serious or continuing if it either actually, or potentially, increases risks or adversely affects the rights & welfare of the participants.

Examples of serious non-compliance include, but are not limited to:

1. Failure to obtain IRB approval prior to initiation of research project;
2. Continuation of research when the IRB approval has expired (i.e., failed to file for continuing review);
3. Failure to notify the IRB of changes in ongoing research (e.g., deviations, amendments, SAEs);
4. Failure to obtain informed consent;
5. Failure to document informed consent; or
6. Failure to properly document the research and research procedures.



IRB STANDARD OPERATING PROCEDURES

Continuing non-compliance: a pattern of reports of non-compliance that, if unaddressed, may compromise the integrity of the human research protection program. The pattern may reflect a lack of knowledge on the part of the investigator or a lack of commitment by the investigator or the research staff to human subject protection.

Minor non-compliance: is neither serious nor continuing.

Submission represents *possible* non-compliance

- Notify IRB staff to forward to IRB Chairperson to determine whether the non-compliance is serious or continuing. If it's minor non-compliance, specify in comments below.

When Yes, you will be required to specify/explain in the following question.

⇒Select either 'Yes' or 'No'

If Yes, specify if it's minor non-compliance, or provide other comments:

⇒Enter an unlimited amount of text.

If reviewing submission already determined to be serious or continuing non-compliance at convened meeting (check ALL that apply):

⇒Check *one or more* of the following items from the list of check boxes presented:

- Submission represents SERIOUS non-compliance
- Submission represents CONTINUING non-compliance

Additional IRB Actions to Consider:

Is suspension or termination of the research warranted?

⇒Select either 'Yes' or 'No'

Is additional investigation of the Investigator warranted?

⇒Select either 'Yes' or 'No'

Is a corrective action plan required?

If Yes, you will be required to answer additional questions.

⇒Select either 'Yes' or 'No'

Comments ⇒Enter an unlimited amount of text.

Corrective Action Plan is required. Will the IRB require any of the following?

Modification to the research protocol

⇒Select either 'Yes' or 'No'

Modification to the informed consent document

⇒Select either 'Yes' or 'No'

Subjects to be re-consented

⇒Select either 'Yes' or 'No'

Earlier continuing review of the project

⇒Select either 'Yes' or 'No'

Monitoring of the consent process

⇒Select either 'Yes' or 'No'

Increased monitoring of the research

⇒Select either 'Yes' or 'No'

Comment (include any other corrective action measures you may want to suggest)



IRB STANDARD OPERATING PROCEDURES

⇒Enter an unlimited amount of text.

-- Continuing Review Considerations --

CONTINUING REVIEW CONSIDERATIONS

Have there been any significant new findings that arose from the continuing review process that may relate to participants' willingness to continue participation?

⇒Select either 'Yes' or 'No'

If YES, please specify how the information should be provided to subjects.

⇒Check *one or more* of the following items from the list of check boxes presented:

- **Revise consent form**
- **PI must draft letter to subjects**
- **Other (Describe)**

Describe Other Method ⇒Enter an unlimited amount of text.

Review subject experiences. Does the summary of subject experiences, including (if applicable), summary of AEs, minor deviation log, previously reported major deviations, and SAE reports at this site warrant any modifications to the research?

⇒Select either 'Yes' or 'No'

If YES, specify modifications requested regarding Subject Experiences:

⇒Enter an unlimited amount of text.

Review unanticipated problems. Have there been any unanticipated problems that warrant any modification to the research?

⇒Select either 'Yes' or 'No'

If YES, specify modifications requested regarding Unanticipated Problems:

⇒Enter an unlimited amount of text.

DATA SAFETY MONITORING PROVISIONS

Does the research plan continue to make adequate provisions for monitoring data collected to ensure the safety of subjects? (Required)

⇒Select either 'Yes' or 'No'

Has the Sponsor established a Data Safety Monitoring Board (DSMB), DMC or safety monitoring committee?

⇒Select *one* of the following options from the list of radio buttons presented:

- **NO**
- **Yes – The report was not provided**
- **YES - The report was provided**

Does the IRB require any additional information about or want to suggest modification to the data safety monitoring plan? When Yes, enter a comment in next question. When No, click Next. (Required)

⇒Select either 'Yes' or 'No'



IRB STANDARD OPERATING PROCEDURES

CR Additional Suggestion - Modification Data Safety Monitoring Plan

⇒Enter an unlimited amount of text.

SITE RESOURCES - Are site staffing resources sufficient to continue the conduct of this study?

⇒Select either 'Yes' or 'No' (When **NO**, you will be required to explain your answer.)

Site Resources Explanation: ⇒Enter an unlimited amount of text.

SITE PERFORMANCE EVALUATION

Based on your review of the site's most recent monitoring report & attached copies of signed informed consent documents (signed, dated & all lines completed) do you recommend a more detailed site audit by the BRANY Audit Staff?

⇒Select either 'Yes' or 'No' (When **YES**, you will be required to explain your answer.)

Site Performance Evaluation Explanation:⇒Enter an unlimited amount of text.

Informed Consent

Is the informed consent document accurate & complete?

When **YES** or **Not Applicable**, click **Next**.

⇒Select *one* of the following options from the list of radio buttons presented:

- NO (When **NO**, you are required to explain in the following question.)
- YES
- Not Applicable

Informed Consent Accurate and Complete Explanation ⇒Enter an unlimited amount of text.

-- Expedited Review Checklist-Continuing Review --

INSTRUCTIONS: This checklist is for determining whether NEW or CONTINUING research applications qualify for expedited review. If you are reviewing a modification to previously approved research, please refer to the **REVIEWER CHECKLIST** for appropriate expedited review criteria. Please complete this in addition to the Reviewer Checklist.

NO MORE THAN MINIMAL RISK: "Minimal Risk" means the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves from those ordinarily encountered in daily life or during the performance of routine physical or psychological examination of tests [45 CFR 46.102(i)].

For research subject to the requirements of the **Department of Defense**, the definition of minimal risk based on the phrase "ordinarily encountered in daily life or during the performance of routine physical or physiological examinations or tests" must not be interpreted to include the inherent risks certain categories of human subjects face in their everyday life. For example, the risks imposed in research involving human subjects focused on a special population should not be evaluated against the inherent risks encountered in their work environment (e.g., emergency responder, pilot, soldier in a combat zone) or having a medical condition (e.g., frequent medical tests or constant pain).

A. CATEGORY OF EXPEDITED REVIEW: PLEASE CHECK ONE OR MORE APPLICABLE CATEGORIES:

⇒Check *one or more* of the following items from the list of check boxes presented:



IRB STANDARD OPERATING PROCEDURES

- (1)(a) Clinical studies of drugs for which an investigational new drug application (21 CFR Part 312) is not required. (Note: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.)
- (1)(b) Research on medical devices for which (i) an investigational device exemption application (21 CFR Part 812) is not required or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.
- (2)(a) Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture from healthy, nonpregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week.
- (2)(b) Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture from other adults and children, considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week.
- (3) Prospective collection of biological specimens for research purposes by noninvasive means. Examples: (a) hair and nail clippings in a nondisfiguring manner; (b) deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction; (c) permanent teeth if routine patient care indicates a need for extraction; (d) excreta and external secretions (including sweat); (e) uncannulated saline collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or applying a dilute citric solution to the tongue; (f) placenta removed at delivery; (g) amniotic fluid obtained at the time of rupture of the membrane prior to or during labor; (h) supra- and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques; (i) mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings; (j) sputum collected after saline mist nebulization.
- (4) Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.) Examples: (a) physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject's privacy; (b) weighing or testing sensory acuity; (c) magnetic resonance imaging; (d) electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography; (e) moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.
- (5) Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely from nonresearch purposes (such as medical treatment or diagnosis). (NOTE: Some research in this category may be exempt from HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(4). This listing refers only to research that is not exempt.)
- (6) Collection of data from voice, video, digital or image recordings made for research purposes.
- (7) Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communications, cultural



IRB STANDARD OPERATING PROCEDURES

beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies. (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(2) and (b)(3). This listing refers only to research that is not exempt.)

- (8)(a) →→ CONTINUING REVIEW ONLY: Continuing review of research previously approved by the convened IRB where (i) the research is permanently closed to the enrollment of new subjects; (ii) all subjects have completed all research-related interventions; and (iii) the research remains active only for long-term follow-up of subjects.
- (8)(b) →→ CONTINUING REVIEW ONLY: Continuing review of research previously approved by the convened IRB where no subjects have been enrolled and no additional risks have been identified; ‡(8)(c) →→> CONTINUING REVIEW ONLY: Continuing review of research previously approved by the convened IRB where the remaining research activities are limited to data analysis. ‡(9) →→> CONTINUING REVIEW ONLY: Continuing review of research, not conducted under an investigational new drug application or investigational device exemption where categories two (2) through eight (8) do not apply but the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified.

B. INCLUDES RESEARCH ACTIVITIES THAT:

- (1) Present no more than minimal risk to human subjects and**
- (2) Involve only procedures listed in one or more of the categories above (see A 1-7):**

Note: The activities listed should not be deemed to be of minimal risk simply because they are included on this list. Inclusion on this list merely means that the activity is eligible for review through the expedited review procedure when the specific circumstances of the proposed research involve no more than minimal risk to human subjects.

⇒Select *one* of the following options from the list of radio buttons presented:

- Yes
- No - Explain
- Not Applicable - Submission is for continuing review of research previously approved by the convened IRB.

No - Explain ⇒Enter an unlimited amount of text.

C. REMINDER: THE CATEGORIES IN THE LIST in A ABOVE APPLY REGARDLESS OF THE AGE OF SUBJECTS, EXCEPT AS NOTED IN CATEGORY (2)(a) AND/OR CATEGORY (2)(b):

Note: Children are defined in the HHS regulations as "persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted." 45 CFR 46.402(a). **Source: 63 FR 60364-60367, November 9, 1998.**

D. The expedited review procedure may not be used where identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.



IRB STANDARD OPERATING PROCEDURES

You will be required to explain your response.

⇒Select *one* of the following options from the list of radio buttons presented:

- Identification of subjects and/or their responses WILL NOT reasonably place them at risk as noted above.
- Identification of subjects and/or their responses WILL reasonably place them at risk as noted about. Note: If this option is selected, this proposal must be reviewed by the convened IRB. Please contact IRB staff at 516-470-6900.

Explain (Explanation for D.) ⇒Enter an unlimited amount of text.

-- Expedited Review Checklist --

INSTRUCTIONS: This checklist is for determining whether **NEW** or **CONTINUING** research applications qualify for expedited review. If you are reviewing a modification to previously approved research, please refer to the **REVIEWER CHECKLIST** for appropriate expedited review criteria. Please complete this in addition to the Reviewer Checklist.

NO MORE THAN MINIMAL RISK: "Minimal Risk" means the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves from those ordinarily encountered in daily life or during the performance of routine physical or psychological examination of tests [45 CFR 46.102(i)].

A. CATEGORY OF EXPEDITED REVIEW: PLEASE CHECK ONE OR MORE APPLICABLE CATEGORIES:

⇒Check *one or more* of the following items from the list of check boxes presented:

- (1)(a) Clinical studies of drugs for which an investigational new drug application (21 CFR Part 312) is not required. (Note: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.)
- (1)(b) Research on medical devices for which (i) an investigational device exemption application (21 CFR Part 812) is not required or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.
- (2)(a) Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture from healthy, nonpregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week.
- (2)(b) Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture from other adults and children, considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week.
- (3) Prospective collection of biological specimens for research purposes by noninvasive means. Examples: (a) hair and nail clippings in a nondisfiguring manner; (b) deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction; (c) permanent teeth if routine patient care indicates a need for extraction; (d) excreta and external secretions (including sweat); (e) uncannulated saline collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or applying a dilute citric solution to the tongue; (f) placenta removed at delivery; (g) amniotic fluid obtained at the time of rupture of the membrane prior to or during

IRB STANDARD OPERATING PROCEDURES

labor; (h) supra- and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques; (i) mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings; (j) sputum collected after saline mist nebulization.

- (4) Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.) Examples: (a) physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject's privacy; (b) weighing or testing sensory acuity; (c) magnetic resonance imaging; (d) electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography; (e) moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.
- (5) Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely from nonresearch purposes (such as medical treatment or diagnosis). (NOTE: Some research in this category may be exempt from HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(4). This listing refers only to research that is not exempt.)
- (6) Collection of data from voice, video, digital or image recordings made for research purposes.
- (7) Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communications, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies. (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(2) and (b)(3). This listing refers only to research that is not exempt.)

B. INCLUDES RESEARCH ACTIVITIES THAT:

(1) Present no more than minimal risk to human subjects and

(2) Involve only procedures listed in one or more of the categories above (see A 1-7):

Note: The activities listed should not be deemed to be of minimal risk simply because they are included on this list. Inclusion on this list merely means that the activity is eligible for review through the expedited review procedure when the specific circumstances of the proposed research involve no more than minimal risk to human subjects.

When **No, you will be required to explain.**

⇒ Select *one* of the following options from the list of radio buttons presented:

- Yes
- No - Explain
- Not Applicable - Submission is for continuing review of research previously approved by the convened IRB.

B. is **No Explanation:**



IRB STANDARD OPERATING PROCEDURES

⇒Enter an unlimited amount of text.

C. REMINDER: THE CATEGORIES IN THE LIST in A ABOVE APPLY REGARDLESS OF THE AGE OF SUBJECTS, EXCEPT AS NOTED IN CATEGORY (2)(a) AND/OR CATEGORY (2)(b):

Note: Children are defined in the HHS regulations as "persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted." 45 CFR 46.402(a). Source: 63 FR 60364-60367, November 9, 1998.

D. The expedited review procedure may not be used where identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.

You will be required to explain your response.

⇒Select *one* of the following options from the list of radio buttons presented:

- Identification of subjects and/or their responses WILL NOT reasonably place them at risk as noted above.
- Identification of subjects and/or their responses WILL reasonably place them at risk as noted about. *Note: If this option is selected, this proposal must be reviewed by the convened IRB. Please contact IRB staff at 516-470-6900.*

Explanation for D: ⇒Enter an unlimited amount of text.

-- Expedited Checklist IRB Recommendation --

RECOMMENDATION FOR IRB ACTION:

When Submission Qualifies for Expedited Review you will be required to answer the next question.

⇒Select *one* of the following options from the list of radio buttons presented:

- Submission qualifies for expedited review →Make sure appropriate category is indicated in the following question.
- Submission DOES NOT qualify for expedited review.

If this is continuing review for which the initial review was completed by the convened IRB, in SECTION A on the previous page, did you select category 8a, 8b, 8c, or 9 (in addition to any other categories that may apply)?

Required when Submission Qualifies for Expedited Review.

⇒Select *one* of the following options from the list of radio buttons presented:

- NOT CONTINUING REVIEW FOR WHICH INITIAL REVIEW WAS BY CONVENED IRB
- YES
- NO - If not, please make sure the category 8a, 8b, 8c, or 9 applies, and check one of these categories (in addition to any other categories) before completing this form. Otherwise, the continuing review must be forwarded for review by the convened IRB.



IRB STANDARD OPERATING PROCEDURES

-- Continuing Review Interval --

In accordance with 45CFR46.109(e) and 21 CFR56.109(f), the IRB must conduct continuing review of approved projects at intervals appropriate to the degree of risk, but not less than once per year. You will be required to indicate the appropriate interval for continuing review with an explanation of the rationale for the stated time interval.

Some General Guidelines : In general, Phase I studies, Phase II studies enrolling pediatric subjects & all gene therapy trials should be considered for assignment of a 6 month approval period (or other approval period less than one year). When such trials are subsequently submitted for continuing review, the IRB as its discretion, will determine the approval period based on the adverse events reported & study activity/findings during the previous approval period. The rationale for determining the approval period must be documented.

RATIONALE - Indicate below. *Please check ALL that apply, or check "Other" & indicate rationale*

When ANY of the following choices are selected:

- Phase I study
- Phase II study involving pediatric subjects
- Study Involves Gene Transfer

AND the Continuing Review Interval is other than 6 months, you will be required to specify a reason why in another question.

⇒ Check *one or more* of the following items from the list of check boxes presented:

- Phase I study - if other than 6 months, specify REASON WHY below
- Phase II study involving pediatric subjects - if other than 6 months, specify REASON WHY below
- Study Involves Gene Transfer - if other than 6 months, specify REASON WHY below
- Safety Profile of the Study Agent is Well Established
- Sufficient Data to Support Efficacy of the Study Agent
- Study Population is "vulnerable" (e.g., children, minors, prisoners, pregnant women, mentally disabled persons, economically or educationally disadvantaged, etc.)
- First Time the Study Agent is being tested in Study Population
- Other (Describe Rationale)

Other Rationale ⇒ Enter an unlimited amount of text.

Reason Why (Required when Phase I, Phase II, and/or studies involve Gene Transfer have approval intervals other than 6 months.) ⇒ Enter an unlimited amount of text.

→ **APPROVAL INTERVAL (Check One)**

When Other, you will be required to specify the approval time interval; interval cannot be greater than one (1) year.



IRB STANDARD OPERATING PROCEDURES

Other (NOT greater than 1 year)

⇒Select *one* of the following options from the list of radio buttons presented:

- 6 Months
- 12 Months
- Other (NOT greater than 1 year)

Other Interval (Interval cannot be greater than one (1) year.) ⇒Enter one line of text.

-- IRB Action --

IRB ACTION (Check One)

⇒Select *one* of the following options from the list of radio buttons presented:

APPROVED AS SUBMITTED

- APPROVE PENDING REQUIRED, SPECIFIC CHANGES (Requires minor revisions or there are minor questions to be resolved) - SPECIFY
- DEFER (Required major revisions or there are major questions to be resolved) - SPECIFY
- DISAPPROVE (Concept/rationale unacceptable or protocol must be completely revised/rewritten):
→ REVIEW BY CONVENED IRB ONLY - SPECIFY

SPECIFY RATIONALE (NOT required when IRB Action is APPROVE AS SUBMITTED):

⇒Enter an unlimited amount of text.

Optional Attachment: (e.g. for when you make Consent Form changes and the Consent Form was NOT considered part of the review, etc.)

⇒Attach 1 to 5 files of type "ICF w/IRB-Directed Changes" to this xForm.

-- IRB Action Consent Documents Modified/Added --

MODIFIED CHOICES->>>

The RE-CONSENT Question has been broken up into two (2) parts:

- 1) The question below to specify what, if any, consent documents were modified, added, or if consent changes are not-applicable for this review.
- 2) If changes were made to the consent documents and/or new consent documents added to the consent process, you will be required in a subsequent question to specify the re-consent process.

Please call the BRANY IRB if you have any questions: 516.470.6900

When a review includes new OR revised consent/assent/addendum form(s) OR the IRB has directed revisions to the consent/assent form/addendum form(s), the reviewer needs to determine whether already-enrolled subjects need to be re-consented with the new/revised document(s).

IRB approval letters will indicate whether or not re-consent is necessary AND the method that should be used for re-consent. This information will also be documented in the IRB record.

Please select the appropriate choice(s):

- a) EXISTING consent(s)/assent(s)/addendum(s) modified.
- b) NEW consent(s)/assent(s)/addendum(s) added.
- c) GRANDFATHER – Re-Consent Not Applicable.
- d) NO CONSENT/ASSENT/ADDENDUM DOCUMENTATION CHANGES – NOT



IRB STANDARD OPERATING PROCEDURES

APPLICABLE

When a) or b) are selected, the method of re-consent question(s) will appear on a subsequent page.
Note: a) AND b) can BOTH be selected, when appropriate. A separate page for each a/b choice will display for you to specify the re-consent process. (Required)

-- IRB Modified Existing Documents Re-Consent --

Re-Consent Guidance from IRB Policy:

If the modifications are minor (see III.1.d.3. Expedited Review of Minor Changes in Previously Approved Research), including typographical errors or basic reformatting, re-consent is most likely not needed or re-consent may be accomplished by verbally informing subjects of the change with documentation in the medical record/study subject record that such notification took place.

If the modifications are more than minor and/or could affect the subject's willingness to continue participation, the IRB requires that research subjects be re-consented. It may be appropriate to provide the subject with an addendum to the original consent form that provides the new information, or to revise the full consent form. If an addendum is used, it must clearly state that the information in the original consent form is still current and valid, and that the information in the addendum is supplementary.

When a review includes new OR revised consent/assent/addendum form(s) OR the IRB has directed revisions to the consent/assent form/addendum form(s), the reviewer needs to determine whether already-enrolled subjects need to be re-consented with the new/revised document(s).

IRB approval letters will indicate whether or not re-consent is necessary AND the method that should be used for re-consent. This information will also be documented in the IRB record.
You indicated an EXISTING consent document(s) was a part of this review.

Please select the re-consent process for the modified, existing document(s) included in this review.

- **Re-consent is not needed, use new documents going forward.**
- **Re-consent IS needed of currently enrolled subjects.**
- **Re-consent of currently enrolled subjects via another method (specify other re-consent method)**

Note: Please add any comments/special instructions in the "specify other method" question below.
(Required)

SPECIFY OTHER RE-CONSENT METHOD (or comments/special instructions):

⇒Enter an unlimited amount of text.

-- IRB Added NEW Documents Re-Consent --

Re-Consent Guidance from IRB Policy:

If the modifications are minor (see III.1.d.3. Expedited Review of Minor Changes in Previously Approved Research), including typographical errors or basic reformatting, re-consent is most likely not needed or re-consent may be accomplished by verbally informing subjects of the change with documentation in the medical record/study subject record that such notification took place.

If the modifications are more than minor and/or could affect the subject's willingness to continue participation, the IRB requires that research subjects be re-consented. It may be appropriate to provide the subject with an addendum to the original consent form that provides the new information, or to revise the



IRB STANDARD OPERATING PROCEDURES

full consent form. If an addendum is used, it must clearly state that the information in the original consent form is still current and valid, and that the information in the addendum is supplementary.

When a review includes new OR revised consent/assent/addendum form(s) OR the IRB has directed revisions to the consent/assent form/addendum form(s), the reviewer needs to determine whether already-enrolled subjects need to be re-consented with the new/revised document(s).

IRB approval letters will indicate whether or not re-consent is necessary AND the method that should be used for re-consent. This information will also be documented in the IRB record.

You indicated a NEW consent document was a part of this review.

Please select the re-consent process for the new document(s) included in this review.

- **Re-consent is not needed, use new documents going forward.**
- **Re-consent IS needed of currently enrolled subjects.**
- **Re-consent of currently enrolled subjects via another method (specify other re-consent method)**

Note: Please add any comments/special instructions in the "specify other method" question below.
(Required)

SPECIFY OTHER RE-CONSENT METHOD (or comments/special instructions):

⇒Enter an unlimited amount of text.

-- IRB Action Expedited --

IRB ACTION Expedited Review (Check One)

⇒Select *one* of the following options from the list of radio buttons presented:

- APPROVED AS SUBMITTED
- APPROVE PENDING REQUIRED, SPECIFIC CHANGES (Requires minor revisions or there are minor questions to be resolved) - SPECIFY
- DEFER (Required major revisions or there are major questions to be resolved) - SPECIFY
- WARRANTS FULL BOARD REVIEW →→ FOR EXPEDITED REVIEW ONLY: (Modifications that do not represent a minor change to previously approved research, modifications that alter the risk-to-benefit analysis for the project, unanticipated problems involving risks to participants or others, potential serious or continuing non-compliance, or initial or continuing review that does not fit into a category of research approvable by an expedited procedure) - SPECIFY

SPECIFY RATIONALE (NOT required when IRB Action is APPROVE AS SUBMITTED):

⇒Enter an unlimited amount of text.

Optional Attachment: (e.g. for when you make Consent Form changes and the Consent Form was NOT considered part of the review, etc.)

⇒Attach 1 to 5 files of type "ICF w/IRB-Directed Changes" to this xForm.

-- IRB Action Modified NOT Expedited --

IRB ACTION Review (Check One)

⇒Select *one* of the following options from the list of radio buttons presented:



IRB STANDARD OPERATING PROCEDURES

- DEFER (Required major revisions or there are major questions to be resolved) - SPECIFY
- WARRANTS FULL BOARD REVIEW →→ FOR EXPEDITED REVIEW ONLY: (Modifications that do not represent a minor change to previously approved research, modifications that alter the risk-to-benefit analysis for the project, unanticipated problems involving risks to participants or others, potential serious or continuing non-compliance, or initial or continuing review that does not fit into a category of research approvable by an expedited procedure) - SPECIFY

SPECIFY RATIONALE:

⇒Enter an unlimited amount of text.

Optional Attachment: (e.g. for when you make Consent Form changes and the Consent Form was NOT considered part of the review, etc.)

⇒Attach 1 to 5 files of type "ICF w/IRB-Directed Changes" to this xForm.

-- IRB Reviewer Signature --

NAME & SIGNATURE OF REVIEWER (FOR ALL REVIEWS)

- **Did you complete any necessary addendum checklists for this review (i.e., expedited review criteria, vulnerable population checklist, etc.)?**
- **Did you indicate your recommended action & the rationale for it?**
- **If this is an expedited review submission that represents a possible unanticipated problem involving risks to participants or others OR possible serious or continuing non-compliance, did you inform the IRB Director and forward it to the chair and then full board for review, as BRANY IRB policy requires?**

Entering your IRBManager password and pressing approve on the following page signifies that you have fully read and completed the Reviewer Checklist for the item(s) specified.

Select the IRB Staff Member to send alert to when you submit this xForm:

The person you select will receive an email alerting them you have completed the Reviewer Checklist for this event so the xForm can be processed.

⇒Select *one* of the following options from the drop down list presented:

Michael Brown (00)	Casie Miller (35)
Raffaella Hart (05)	Ishita Modi (25)
Erika Jorquera (15)	Melissa Robilotto (45)
Aleena Kuriakose (20)	Michelle Rodriguez (40)
Lillian Losquadro (85)	Andrea Waldron (60)

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IRB STANDARD OPERATING PROCEDURES

Appendix 7 – BRANY IRB Standard Operating Procedures

Addendum Checklist – Consultant Review

Table with 2 columns: Field Name, Value. Fields include Principal Investigator, Sponsor Name & Protocol #, and BRANY IRB File #.

Instructions: On an as-needed basis, the BRANY IRB Chairperson, Members, will request review by or additional information from a consultant with specific knowledge or expertise. Please review the research project, complete the Reviewer Checklist and this checklist and indicate your response to the items that follow. The IRB may be request that you attend the IRB meeting for questions and clarification of issues. Consultants may not vote with BRANY IRB (45 CFR 46.107 and 21 CFR 56.107), and will not count toward establishing a quorum.

- 1) Do you have any conflict of interest or potential conflict of interest with this research? Please call the BRANY IRB office at 516-470-6900 with any questions. [] NO – Continue to item 2. [] YES – If so, please do not complete this review. Contact the BRANY IRB office immediately at 516-470-6900.

- 2) Has the IRB asked you to address a specific issue regarding this research? [] NO – Continue to item 3. [] YES – If so, please provide your response below (or attach separate sheet as necessary):

Multiple horizontal lines for providing a response to item 2.

- 3) Have you completed the REVIEWER CHECKLIST? [] NO – Please complete now. [] YES – If yes, please sign below to indicate completion of your consult review.

Consult Reviewer: Printed Name Signature Date



IRB STANDARD OPERATING PROCEDURES

Appendix 8 – BRANY IRB Standard Operating Procedures

Application for Continuing Approval [xForm # 11]

Continuing Approval Data Entry

-- User Access Form Screener --

For this xForm submission **to be valid**, a [BRANY System User Access Form](#) ***MUST*** be on file at BRANY for:

- the Principal Investigator of the study.
- the person entering xForms in *IRBManager*, i.e. you.

Please answer the following questions regarding [BRANY System User Access Form](#) status.

EACH person that creates, submits and/or authorizes a xForm in *IRBManager* is **required** to have a signed, completed [BRANY System User Access Form](#) on file with BRANY.

******If the [BRANY System User Access Form](#) is not on file at BRANY and not included with this submission, this xForm will be rejected******

Principal Investigator

Is the BRANY System User Access Form on file for the Principal Investigator listed above?

- A [BRANY System User Access Form](#) **MUST** be on file at BRANY for the **Principal Investigator** of the study.
- Click on the blue [BRANY System User Access Form](#) hyperlink for a copy of the user access form. Complete, sign and scan to an electronic document (e.g. PDF) so it can be attached to this xForm on one of the following pages.

⇒Select *one* of the following options from the drop down list presented:

- No - submitting with this xForm submission
- Yes - on file at BRANY

xForm Submitter (You)

Is the BRANY System User Access Form on file for you, the xForm submitter?

- A [BRANY System User Access Form](#) **MUST** be on file at BRANY for the **person entering xForms** in *IRBManager*, i.e. **you**.
- Click on the blue [BRANY System User Access Form](#) hyperlink for a copy of the user access form to attach a completed, sign form on another page.

⇒Select *one* of the following options from the drop down list presented:

- No - submitting with this xForm submission
- Yes - on file at BRANY

-- PI User Access Form Attachment --

Principal Investigator's BRANY Systems User Access Form

Attach Principal Investigator's signed, completed [BRANY Systems User Access Form](#)

PI's Completed, Signed and Dated User Access Form Attachment

- Click on the blue [BRANY System User Access Form](#) hyperlink for a copy of the user access form. Complete, sign and scan to an electronic document (e.g. PDF) so it can be attached to this xForm page.

⇒Attach a file of type "User Access Form BRANY Systems" to this xForm.



IRB STANDARD OPERATING PROCEDURES

-- Submitter User Access Form Attachment --

xForm Submitter/Your [BRANY Systems User Access Form](#)

Attach your signed, completed [BRANY Systems User Access Form](#)

Click on the blue [BRANY System User Access Form](#) hyperlink for a copy of the user access form.

Complete, sign and scan to an electronic document (e.g. PDF) so it can be attached to this xForm page.

⇒ Attach a file of type "User Access Form BRANY Systems" to this xForm.

-- Continuing Approval Types --

Continuing Review Form

For this Continuing Approval xForm, we have *COMBINED* the IRB *and* IBC review forms. The selections you make throughout the form will guide you to the appropriate questions for your study's Continuing Approval application.

Subject Status: Please make sure the total # of Enrolled subjects are accounted for:

#Enrolled = #Terminated Early + #Completed + #Presently Active + #In Follow-up Only

#Terminated = #Screen Failure + #Withdrawn Voluntarily + #Withdrawn by PI

#Enrolled = #Female + #Male

#Enrolled = sum for each race/ethnicity classification

INCOMPLETE OR LATE DOCUMENTS MAY RESULT IN

SUSPENSION OR TERMINATION OF YOUR RESEARCH PROJECT!

Applications for Continuing Review must be submitted no sooner than 30 (thirty) days prior to study expiration.

Continuing Approval Type. Please select ALL that apply (Note: Human Gene Transfer Research Projects **require** IBC continuing approval):

⇒ Check *one or more* of the following items from the list of check boxes presented:

- IBC - BRANY Institutional Biosafety Committee
- IRB - BRANY Institutional Review Board

Does the research involve Human Subjects?

⇒ Select either 'Yes' or 'No'

Does the research involve Human Gene Transfer?

⇒ Select either 'Yes' or 'No' (When **Yes**, you will be required to submit information to the IBC)

-- IRB Submission Requirements Checklist --

INSTRUCTIONS: Please complete all of the required items in this electronic xForm in order for your application to be considered. Any omissions will result in administrative suspension (during which no study activity may take place) until the completed application can be reviewed but the convened IRB.

The following items will be required for complete submissions of your continuing application:

- (a) Completed electronic xForm Application for Continuing Approval
- (b) Information regarding any Serious Adverse Events (SAEs) that have occurred at the investigational site
- (c) Most recent version of the Informed Consent form(s) approved by the IRB
- (d) Data Safety Monitoring Board Reports, when available



IRB STANDARD OPERATING PROCEDURES

- (e) Protocol Deviation reports, if any
- (f) Copies of any Sponsor Monitoring Reports
- (g) Copies of the last 2 consents signed by subjects in the research project
- (h) A summary of adverse events since the last IRB review
- (i) Copies of any relevant recent literature
- (j) Copies of interim findings
- (k) Copies of any relevant multi-center trial reports, if available.

****All multi-center research projects must also supply the separate, [Sponsor Supplement for Multi-center Research Projects](#)**** If your project is multi-center and the sponsor contact is in the IRBManager system, that contact person received an email with the form to complete. Please follow-up with the sponsor contact to ensure the form will be completed in time.

- (l) A current risk-potential benefit assessment based on study results.

****All multi-center research projects must also supply the separate, [Sponsor Supplement for Multi-center Research Projects](#)**** If your project is multi-center and the sponsor contact is in the IRBManager system, that contact person received an email with the form to complete. Please follow-up with the sponsor contact to ensure the form will be completed in time.

-- IBC Submission Requirements Checklist --

INSTRUCTIONS:

- Applications for Continuing Review must be submitted to BRANY IBC prior to expiration of IBC approval.
- Please complete all required questions on this electronic xForm: If an item is not applicable please indicate so by typing N/A.

The following items will be required for complete submissions of your continuing application:

- (a) Completed electronic xForm Application for Continuing Approval
- (b) Information regarding any Serious Adverse Events (SAEs) that have occurred at the investigational site
- (c) Most recent version of the Informed Consent form(s) approved by the IRB
- (d) Data Safety Monitoring Board Reports, when available
- (e) Copies of any Sponsor Monitoring Reports
- (f) Copies of any relevant recent literature
- (g) Copies of interim findings
- (h) All amendments attached, if applicable
- (i) Updated Safety precaution training, if applicable (All personnel handling the student agent MUST have documentation of valid safety precaution training)
- (j) Information regarding any emergencies, potential biohazard problems, spills, significant safety issues

-- IRB & IBC Submission Requirements Checklist --

The following items will be required for complete submissions of your continuing application:

- (a) Completed electronic xForm Application for Continuing Approval
- (b) Information regarding any Serious Adverse Events (SAEs) that have occurred at the investigational site
- (c) Most recent version of the Informed Consent form(s) approved by the IRB
- (d) Data Safety Monitoring Board Reports, when available



IRB STANDARD OPERATING PROCEDURES

- (e) Protocol Deviation reports, if any
- (f) Copies of any Sponsor Monitoring Reports
- (g) Copies of the last 2 consents signed by subjects in the research project
- (h) A summary of adverse events since the last IRB review
- (i) Copies of any relevant recent literature
- (j) Copies of interim findings
- (k) Copies of any relevant multi-center trial reports
- (l) A current risk-potential benefit assessment based on study results.

Also:

- (a) All amendments attached, if applicable
- (b) Updated Safety precaution training, if applicable (All personnel handling the student agent **MUST** have documentation of valid safety precaution training)
- (c) Information regarding any emergencies, potential biohazard problems, spills, significant safety issues

-- IRB Study Ongoing --

INSTRUCTIONS: Please complete all of the items in this form in order for your application to be considered. Any omissions will result in administrative suspension (during which no study activity may take place) until the completed application can be reviewed by the convened IRB.

Applications for Continuing Review must be submitted to BRANY IRB a maximum of 30 days prior to study expiration.

Is the study still ongoing (If you are STILL collecting data for this study, please select "*Yes - Closed for subject entry but open for follow-up OR for the collection of private identifiable information*")?

⇒Select *one* of the following options from the list of radio buttons presented:

- Yes - Actively Enrolling
- Yes - Closed for subject entry but open for follow-up OR for the collection of private identifiable information
- No - No study activity remains (no subject contact, no data queries, no data collection, no recruitment, no enrollment, sponsor close-out visit has already occurred)

If Is the Study Still Ongoing = No - No study activity remains (no subject contact, no data queries, no data collection, no recruitment, no enrollment, sponsor close-out visit has already occurred):

- Click Next then Submit to close this xForm.
- Please call the BRANY IRB and ask for the Continuing Review team if you have any questions: 516.470.6900

Study IS Closed:

If you have not already completed a 04-Study Status Change-Closed/Enrollment Closed xForm:

- Click Next then Submit to close this xForm.
- Click action "Start xForm" within this study page.
- Click on 04-Study Status Change-Closed/Enrollment Closed to complete the xForm to close the study.



IRB STANDARD OPERATING PROCEDURES

NOTE: 04-Study Status Change-Closed/Enrollment Closed xForm will terminate your IRB approval. Therefore, only do this if ALL YOUR STUDY ACTIVITY HAS BEEN COMPLETED. This means that you are:

- **no longer collecting data;**
- **no longer responding to data queries;**
- **no longer contacting subjects or following-up with them, AND;**
- **you have had a closeout visit from your study sponsor (if applicable).**

-- IBC Study Ongoing --

Is the study still ongoing (If you are STILL collecting data for this study, please select: "**Yes - Closed to new enrollment or inclusion of new test samples BUT open for continued collection of private identifiable information.**")?

⇒Select *one* of the following options from the list of radio buttons presented:

- Yes - Actively Enrolling (i.e. enrolling new subjects or including new test samples in the research).
- Yes - Closed to new enrollment or inclusion of new test samples BUT open for follow-up of subjects or testing of already collected samples.
- Yes - Closed to new enrollment or inclusion of new test samples BUT open for continued collection of private identifiable information
- No - Closed to Enrollment - No study activity remains (no subject contact, no data queries, no data collection, no recruitment, no enrollment, sponsor close-out visit has already occurred)

If Is the Study Still Ongoing = No - Closed to Enrollment - No study activity remains (no subject contact, no data queries, no data collection, no recruitment, no enrollment, sponsor close-out visit has already occurred):

- **Click Next then Submit to close this xForm.**
- **Please call the BRANY IRB and ask for the Continuing Review team if you have any questions: 516.470.6900**

Study IS Closed:

If you have not already completed a 04-Study Status Change-Closed/Enrollment Closed xForm:

- **Click Next then Submit to close this xForm.**
- **Click action "Start xForm" within this study page.**
- **Click on 04-Study Status Change-Closed/Enrollment Closed to complete the xForm to close the study.**

NOTE: 04-Study Status Change-Closed/Enrollment Closed xForm will terminate your IRB approval. Therefore, only do this if ALL YOUR STUDY ACTIVITY HAS BEEN COMPLETED. This means that you are:

- **no longer collecting data;**
- **no longer responding to data queries;**
- **no longer contacting subjects or following-up with them, AND;**
- **you have had a closeout visit from your study sponsor (if applicable).**

-- Translated Consents --

Translations - Informed Consent Documents

If you previously requested translations of the informed consent document(s), do you



IRB STANDARD OPERATING PROCEDURES

still require updated translations of the consent document(s)?

Selections:

Yes – Translations still required (go to [question A](#) to list each translation language)

No – Translations no longer required, foreign language subjects no longer participating in the study (Click [Next](#))

No – Translations no longer required, other reason (please enter other reason in [question B](#))

N/A – Not Applicable, Translations not previously requested (Click [Next](#)) (Required)

Select *one* of the following options from the drop down list presented:

‡Yes – Translations still required ‡No – Translations no longer required, foreign language subjects no longer participating in the study ‡No – Translations no longer required, other reason (please enter reason below as a note) ‡N/A – Not Applicable, Translations not previously requested

A. You indicated translations are still required. Please list the Translation Languages this study continues to require.

Enter an unlimited amount of text.

B. You indicated that translations are no longer required for another reason. Please enter the other reason why translations are no longer required.

Enter an unlimited amount of text.

-- IRB & IBC Subject Status --

Is the research study Gender specific/applies to ONE gender (i.e. does the study involve *only Male OR only Female* subjects)?

⇒Select either 'Yes' or 'No'

- Select **YES**: If the *ONLY* study subject eligible to participate can be of *one sex*: **ALL Male** or **ALL Female**. e.g. A gynecologic study would typically be an all Female study; A prostate study would typically be an all Male study.
- Select **NO**: If *ANY* gender can be a participant in this study.

Enter the **TOTAL #** of subjects Enrolled in this study (defined as those who signed consent) - enter a *number* ≥ 0

Note: The breakdown of the # of subjects enrolled must equal #Total Enrolled. (Required)

Enter a valid number. It must be ≥ 0 . It must be a whole number.

Terminated Early - enter a number ≥ 0

Enter total # of subjects who were terminated early. (You will be required to provide details for termination reason(s) in a later question.)

⇒Enter a valid number. It must be ≥ 0 . It must be a whole number.

Completed - enter a number ≥ 0

Enter # of subjects completed.

⇒Enter a valid number. It must be ≥ 0 . It must be a whole number.

Presently Active - enter a number ≥ 0

Enter # Subjects presently actively receiving the study intervention. If a non-interventional study (e.g., observation of routine care/behavior), list all subjects here.

⇒Enter a valid number. It must be ≥ 0 . It must be a whole number.

#In Follow-up Only - enter a number ≥ 0



IRB STANDARD OPERATING PROCEDURES

Enter # of subjects involved in follow-up procedures. If a non-interventional study (e.g., observation of routine care/behavior) list subjects **ABOVE** in "Presently Active" section.

⇒Enter a valid number. It must be ≥ 0 . It must be a whole number.

-- Data Collection Continuing --

All Patients are completed and not in follow-up HOWEVER, you are still collecting data and/or awaiting Close Out Site Visit.

Is Data Collection Continuing for the study as a whole?

⇒Select either 'Yes' or 'No'

- When **Yes**, you will be required to answer the remaining questions on the rest of this page.
- When **No**, you incorrectly entered 0 (zero) values for "**# Presently Active**" and "**# In Follow-up Only**"

OR

- You selected an **incorrect response** to "**Is the study still ongoing?**" in the beginning of this xForm. You need to do the following:
 - A. Click on the Back button to ensure the enrollment numbers you entered for "**# Presently Active**" and "**# In Follow-up Only**" are correct. If you modified either value, click Next and continue with the xForm.
 - B. If you did NOT correct either value for "**# Presently Active**" and "**# In Follow-up Only**" then:
 1. Click on Save for Later.
 2. Re-open the xForm you started (from your Dashboard, the study record or My Documents and Forms).
 3. Select the No response for "**Is the study still ongoing?**" question. Continue with the xForm.

If Data Collection is continuing, please specify ALL Data Collection that remains and/or you are currently completing on your study (select ALL that apply):

⇒Check *one or more* of the following items from the list of check boxes presented:

- Data Query
- Data Analysis
- Data Closeout
- Close of Site Visit (is scheduled and/or not occurred yet)
- OTHER (Please describe below)

Describe Other Data Collection Remaining for this Study ⇒Enter an unlimited amount of text.

If 0 (zero) subjects are presently Active and still requiring Follow-up and you are not still collecting data, DO NOT submit this form, unless you need your IRB approval to remain active because you are still collecting data and/or responding to data queries. Please complete and submit the 04-Study Status Change-Closed/Enrollment Closed xForm. When you press NEXT and then SUBMIT, the xForm will CLOSE

-- IBC & IRB Early Term Subject Details --

Subjects Terminated Early



IRB STANDARD OPERATING PROCEDURES

Show the breakdown of all subjects terminated early

Screen Failures - enter a *number* ≥ 0

Enter # of Screen Failures (of those who signed consent)

⇒Enter a valid number. It must be ≥ 0 . It must be a whole number.

Withdrawn Voluntarily - enter a *number* ≥ 0

Enter # Withdrawn Voluntarily.

You will be required to provide details for reasons in a later question.

⇒Enter a valid number. It must be ≥ 0 . It must be a whole number.

Withdrawn by Principal Investigator - enter a *number* ≥ 0

Enter # Withdrawn by Principal Investigator.

You will be required to provide details for reasons in a later question.

⇒Enter a valid number. It must be ≥ 0 . It must be a whole number.

Lost to Follow-up - enter a *number* ≥ 0

Enter # lost to follow-up.

⇒Enter a valid number. It must be ≥ 0 . It must be a whole number.

Deceased - enter a *number* ≥ 0 (Required)

Enter # of subjects who signed consent but have expired (are deceased).

Enter a valid number. It must be ≥ 0 . It must be a whole number.

Not Included in Research - enter a *number* ≥ 0

Enter # not included in research.

You will be required to provide details for reasons in a later question.

⇒Enter a valid number. It must be ≥ 0 . It must be a whole number.

-- Early Termination Reasons --

Early Termination Reasons

Describe reason for ALL Withdrawals/Terminations/Why Subject Not Included in Research:

⇒Enter an unlimited amount of text.

IRB Gender/Ethnic Classification (IRB)

-- IRB Gender/Ethnic Classification --

Is the research study *gender specific*, i.e. applies to ONE gender? (i.e. does the study involve *only* Male *OR* *only* Female subjects)

Choices:

YES-If the *ONLY* subjects eligible to participate can be of *ONE* sex: i.e. *ALL* Male or *ALL* Female.

e.g. A gynecologic study would typically be an all Female study; A prostate study would typically be an all Male study.

NO-If *ANY* gender can be a participant in this study *AND* the gender breakdown is *KNOWN*. (You will be required to specify # Male and # Female in follow-up questions.)

NO/Indeterminate-If *ANY* gender can be a participant in this study *BUT* the gender breakdown is *NOT* known, e.g. de-identified specimens, etc. (Required)

Select *one* of the following options from the list of radio buttons presented

Is the ethnic composition of subject enrollment known, i.e. do you know the ethnic breakdown of all the subjects who signed consent?



IRB STANDARD OPERATING PROCEDURES

Choices:

Yes-Ethnicity breakdown is KNOWN for total enrolled. (You will be required to specify ethnicity breakdown in follow-up questions.)

No-Ethnicity totals are NOT known, e.g. de-identified specimens, etc. (Required)

-- IRB Gender Classification --

#Female - enter a *number* >= 0

Enter # of female subjects entered in the study.

⇒Enter a valid number. It must be >= 0. It must be a whole number.

#Male - enter a *number* >= 0

Enter # of male subjects entered in the study.

⇒Enter a valid number. It must be a whole number.

-- IRB Ethnic Classification --

Please provide the race/ethnic classification of all subjects that signed consent for the study.

African-American ⇒Enter a valid number. It must be >= 0. It must be a whole number.

#**Caucasian** ⇒Enter a valid number. It must be >= 0. It must be a whole number.

#**Pacific Islander** ⇒Enter a valid number. It must be a whole number.

#**Native American/First Nations** ⇒Enter a valid number. It must be >= 0. It must be a whole number.

#**Middle Eastern** ⇒Enter a valid number. It must be >= 0. It must be a whole number.

#**Hispanic** ⇒Enter a valid number. It must be >= 0. It must be a whole number.

#**Asian** ⇒Enter a valid number. It must be >= 0. It must be a whole number.

#**Other** ⇒Enter a valid number. It must be >= 0. It must be a whole number.

Please specify Other ethnicity Description ⇒Enter an unlimited amount of text.

IBC Study Agent Administered

-- Study Agent --

Was the Study Agent was administered during this approval period?

⇒Select *one* of the following options from the list of radio buttons presented:

- Yes
- No

-- IBC Study Agent Administration --

Study Agent Administration

You are required to list information for EACH Subject who received at least one since last review, you MUST fill out this page in its entirety. If you inadvertently pressed **Repeat** and do have not any more Subject Study Agent Administration Doses to enter, select the "FINISHED ADDING SUBJECT STUDY AGENT ADMINISTRATION INFORMATION" action, then press **Next** to continue with the xForm.

⇒Select *one* of the following options from the list of radio buttons presented:

- ADDING Subject Who Received Dose(s)
- FINISHED ADDING SUBJECT STUDY AGENT ADMINISTRATION INFORMATION
- **Subject #** (Enter identifier for this subject): ⇒Enter one line of text.
- **Number of Dose(s) Received** (Enter number of dose(s) this subject received.)⇒Enter a valid number. It must be >= 0. It must be a whole number.



IRB STANDARD OPERATING PROCEDURES

-- IBC Study Agent Administration End --

Are you finished adding **Study Agent** doses received by subjects?

If **Yes**, press **Next** to continue completing this form. If **No**, press **Repeat** to process another Study Agent Dose.

-- Subjects Experience Benefits --

Subjects Experience Benefits at your Site

Have any subjects at your site benefited from participation in this study?

⇒Select either 'Yes' or 'No' (When **Yes**, you are required to explain the benefits in the following question.)

Subjects Benefit Description ⇒Enter an unlimited amount of text.

-- Subjects Experience Complaints --

Subjects Experience Complaints at your Site

Have there been any complaints from subjects at your site?

⇒Select either 'Yes' or 'No' (When **Yes**, you are required to explain the Subject Complaint in the next question.)

Subject Complaint description and how it was resolved ⇒Enter an unlimited amount of text.

-- Subjects Experience Adverse Events --

Adverse Events since Last Review

Please provide a summary of unexpected and associated Adverse Events that occurred since last review. Include the description of the adverse event, the relationship to the study agent, and whether the event was expected or unexpected. Description can be typed in below and/or attached in a separate document. If **NO Adverse Events occurred, please indicate in the space provided: "No Adverse Events have occurred since last review".**

Adverse Events Description

Describe and/or attach separate documents. ⇒Enter an unlimited amount of text.

Adverse Events Attachment ⇒Attach a file of type "Any" to this xForm.

-- Serious Adverse Events (SAEs) Experience --

Serious Adverse Event (SAE) Experience

At your site, have there been any Serious Adverse Events (SAEs)

- SAEs are defined as fatal or life threatening, permanently disabling or requiring hospitalization or prolongation of inpatient hospitalization or any other event the investigator considers significant.

⇒Select either 'Yes' or 'No'

If **YES, an SAE occurred, was it reported to the Sponsor yet?**

⇒Select either 'Yes' or 'No'

-- Serious Adverse Events --

SAE 1. Have you reported the SAE to the BRANY IRB yet?



IRB STANDARD OPERATING PROCEDURES

- You are required to submit xForm #16-Reportable Event to BRANY IRB *for each* Deviation/SAE.

⇒Select either 'Yes' or 'No'

SAE 1a. Completed Copy of SAE form - IF this study has completed paper SAE forms, prior to July 1, 2012, attach copies here. You may attach up to thirty (30) documents.

⇒Attach 1 to 30 files of type "SAE Form " to this xForm.

SAE 2. Were any events related to drug/device?

⇒Select either 'Yes' or 'No'

SAE 2a. Please describe event(s) and explain relationship to drug/device.

⇒Enter an unlimited amount of text.

SAE 3. Were any of the events related to the source of DNA or the host vector system?

⇒Select *one* of the following options from the list of radio buttons presented:

- Yes
- No
- N/A

-- Human Gene Transfer --

You indicated that events were related to the source of DNA or to the host vector system.

Have the events been reported to the BRANY Institutional Biosafety Committee (IBC)?

These events must be reported to the BRANY Institutional Biosafety Committee (IBC).

⇒Select either 'Yes' or 'No'

Please describe event and explain relationship to the source DNA or the host vector system.

⇒Enter an unlimited amount of text.

How many other sites are currently carrying out this research study?

⇒Enter a valid number. It must be ≥ 0 . It must be a whole number.

How many subjects enrolled at other research sites carrying out this research study?

⇒Enter a valid number. It must be ≥ 0 . It must be a whole number.

Have any significant safety issues been identified? ⇒Select either 'Yes' or 'No'

Significant Safety Issue Description ⇒Enter an unlimited amount of text.

-- IBC SAE(s) --

You are required to list information for EACH SAE which occurred since the last review, you MUST fill out this page in its entirety. If you inadvertently pressed **Repeat** and do not have any more Subject Study Agent Administration Doses to enter, select the "FINISHED ADDING SAE(s)" action, then press **Next** to continue with the xForm. For EVERY date a SAE occurred, you must list EACH subject as a separate entry.

Select Action:



IRB STANDARD OPERATING PROCEDURES

⇒Select *one* of the following options from the list of radio buttons presented:

- ADD another SAE
- FINISHED ADDING SAE(s)

Event Date ⇒Enter a valid date.

Subject# ⇒Enter one line of text.

Description ⇒Enter an unlimited amount of text.

Are you finished making SAE entries? If **Yes**, press **Next** to continue completing this form. If **No**, press **Repeat** to process another SAE.

-- BRANY Administered IBC --

1. Has the designated Biosafety Officer (BSO) for this project changed since the last IBC review?

When **YES**, you are required to supply the name of the new BSO in question 2. When **NO**, proceed to question 3.⇒Select either 'Yes' or 'No'

2. Full Name of New BSO ⇒Enter one line of text.

3. Have there been any changes to key personnel since the last IBC review (i.e. additions/removal of key study personnel)? ⇒Select either 'Yes' or 'No' (When **YES**, you will be required to provide additional information on another page.)

-- IBC Key Personnel Changes --

Key Personnel Changes - For EACH person you are submitting to ADD to the study, you MUST fill out this page in its entirety. If you are REMOVING an individual, you are required to indicate the name of the person to be removed. If you inadvertently pressed **Repeat** and do have not any more Key Personnel modifications to enter, select the "FINISHED MODIFYING KEY PERSONNEL" action, then press **Next** to continue with the xForm. NOTE: When **ADDING** key personnel to a study, you are required to respond to ALL questions (are they a research coordinator, attach COI, Training, and/or other documents, etc.). When **REMOVING** key personnel, you are only required to supply the name of the person being removed from the study.

• **If individual will handle the study agent, he/she must provide evidence of infection control training, training in appropriate safety precautions.**

• **Provide CVs for each key professional person (i.e. Principal Investigator, Sub-Investigator(s), Research Coordinator(s), Pharmacy or other non-Pharmacy personnel)**

⇒Select *one* of the following options from the list of radio buttons presented:

- Removal of study personnel
- Addition of study personnel
- FINISHED MODIFYING KEY STUDY PERSONNEL

Name ⇒Enter one line of text.

*****Remaining questions on this page, required when ADDING Key Personnel to the study ONLY*****

Role (e.g., PI, Sub-Investigator, Research Coordinator, Pharmacist, etc.) ⇒Enter one line of text.



IRB STANDARD OPERATING PROCEDURES

Will handle study agent? ⇒Select either 'Yes' or 'No'

Infection Control Training Attached ⇒Select either 'Yes' or 'No' (*If Yes, you will be required to attach copy in the following question.*)

Infection Control Training Attachment ⇒Attach a file of type "Any" to this xForm.

CV Attachment ⇒Attach a file of type "CV" to this xForm.

-- IBC Key Personnel Changes End --

Are you finished making Personnel Changes? If **Yes**, press **Next** to continue completing this form. If **No**, press **Repeat** to process another Key Study Personnel.

-- IBC Study Information --

Attach copies of documentation of all current and valid safety precaution training for all previously approved personnel handling the study agent. You may attach up to ten (10) separate documents.
⇒Attach 1 to 10 files of type "Site Correspondence" to this xForm.

How many OTHER sites are currently carrying out this research study? (*If greater than 0, you will be required to answer the following question about the other research sites.*)

⇒Enter a valid number. It must be ≥ 0 . It must be a whole number.

How many subjects/test samples are included at the other research sites carrying out this research study? ⇒Enter one line of text.

-- IBC Research Issues --

1. Have there been any emergencies, potential biohazard problems, spills, significant safety issues, contamination, sero-conversion, etc.? ⇒Select either 'Yes' or 'No'

1a. Describe Event Circumstances and the Response. ⇒Enter an unlimited amount of text.

1b. Enter date the event was reported to BRANY? ⇒Enter a valid date.

VECTOR CHANGES

2. Has there been any change to the vector used in this research? ⇒Select either 'Yes' or 'No'

2a. Describe the Vector Change. ⇒Enter an unlimited amount of text.

FACILITY CHANGES

3. Has there been any change to the facility used for this research? ⇒Select either 'Yes' or 'No'

3a. Describe the Facility Change. ⇒Enter an unlimited amount of text.

-- UPIRTSO Subject Experiences at Your Site --

Unanticipated Problems Involving Risk to Subjects or Others (UPIRTSO)

At your site, have there been any Unanticipated Problems involving risks to subjects or others (UPIRTSOs) (e.g. loss of a laptop containing confidential study information, loss of study drug)?

⇒Select *one* of the following options from the list of radio buttons presented:

- Yes
- No



IRB STANDARD OPERATING PROCEDURES

Unanticipated Problem involving risks to subjects or others (UPIRTSO) Description

Describe the Unanticipated Problem involving risks to subjects or others (UPIRTSO) here and/or attach separate document to explain. ⇒Enter an unlimited amount of text.

Unanticipated Problem involving risks to subjects or others (UPIRTSO) Description Attachment

⇒Attach a file of type "Any" to this xForm.

-- Attachments --

Relevant Recent Literature

Please provide the IRB with any relevant recent literature. List here or provide a summary and/or attach separate sheets as needed. *If "Not Applicable" please indicate that below.*

⇒Enter an unlimited amount of text.

Recent Literature Attachment(s) You may attach up to 10 (ten) separate documents.

⇒Attach 1 to 10 files of type "Literature" to this xForm.

Interim Findings Since Last IRB Review - Please summarize any interim findings since the last IRB review. *Explain here and/or attach separate sheets as needed. If "Not Applicable" please indicate that below.* ⇒Enter an unlimited amount of text.

Interim Findings Attachment - You may attach up to ten (10) documents.

⇒Attach 1 to 10 files of type "Any" to this xForm.

Data Safety Monitoring Board (DSMB) or Safety Monitoring Committee - Has the Sponsor established a Data Safety Monitoring Board (DSMB) or Safety Monitoring Committee? *If you are unsure, please confer with the sponsor representative prior to submitting this form.*

Please check your protocol for this information BEFORE answering this question.

If report is NOT available, you will be required to explain why the report is not available in the following question.

If report is available, you will be required to attach and other questions on another page.

⇒Select *one* of the following options from the list of radio buttons presented:

- YES - A copy of the most recent DSMB/safety monitoring committee report is available (you will be required to attach copy in another question).
- YES - The site contacted the Sponsor, and the report is currently unavailable
- NO
- N/A - Not Applicable

Explain why the Data Safety Monitoring Board (DSMB)/Safety Monitoring Committee report is NOT available.

Please provide as many details as possible in your explanation.

-- Data Safety Monitoring Board/Safety Monitor Detail --

Data Safety Monitoring Board (DSMB) or Safety Monitoring Committee - You indicated that the Sponsor established a Data Safety Monitoring Board (DSMB) or Safety Monitoring Committee AND the most recent committee report is available. Attach copy of most recent DSMB/safety monitoring committee report. ⇒Attach a file of type "Report" to this xForm.



IRB STANDARD OPERATING PROCEDURES

How often/When are they supposed to meet? ⇒Enter an unlimited amount of text.

Have they met at ALL the times stated above? ⇒Select either 'Yes' or 'No'

-- Local Research Context --

Evaluation of Local Research Context

1. What is the overall attitude toward the conduct of research in your community?

⇒Select *one* of the following options from the list of radio buttons presented:

- Neutral
- Positive
- Negative

2. Explain the community's attitude toward research. ⇒Enter an unlimited amount of text.

3. Are there any specific community attitudes relative to research (religious, ethical, ethnic, or economic) that the IRB should be aware of? *When YES, you will be required to explain in question 3a. When NO, proceed to question 4.* ⇒Select either 'Yes' or 'No'

3a. Explain the Specific Community Attitudes IRB Should Be Aware of. ⇒Enter an unlimited amount of text.

4. Are there any circumstances where certain subject populations in your community may feel coerced into participating in a research study? *When YES, you will be required to explain question 4a. When NO, proceed to question 5.* ⇒Select either 'Yes' or 'No'

4a. When YES, how have you approached enrollment of subjects from such populations to avoid coercion? ⇒Enter an unlimited amount of text.

5. Have there been any changes to laws governing medical research in your state, province, or country? ⇒Select *one* of the following options from the list of radio buttons presented:

- Yes
- No
- Unknown

-- Site Resources --

The investigator must ensure that adequate staffing and resources are available for each research project conducted so that the rights and welfare of research subjects will be protected. Staff should have sufficient time available to interact with subjects as needed.

1. How many studies does the PI currently supervise? ⇒Enter a valid number. It must be ≥ 0 . It must be a whole number.

2. Approximate number of active subjects? ⇒Enter a valid number. It must be ≥ 0 . It must be a whole number.

3. Are there any competing studies? *When YES, you will be required to answer question 3a. When NO, proceed to question 4.* ⇒Select either 'Yes' or 'No'



IRB STANDARD OPERATING PROCEDURES

3a. When **YES, there are competing studies, how will enrollment be determined?** ⇒Enter an unlimited amount of text.

4. How many studies does the Research Coordinator supervise? ⇒Enter a valid number. It must be >= 0. It must be a whole number.

5. Has there been any change in staffing since the last review of this project? When **YES**, you will be required to explain in question 5a. When **NO**, proceed to question 6.⇒Select either 'Yes' or 'No'

5a. Describe the Change In Study Staff Since Last Review ⇒Enter an unlimited amount of text.

6. Most Recent Monitoring Report Attachment (when available) ⇒Attach a file of type "Report " to this xForm.

7. Site Performance Comments ⇒Enter an unlimited amount of text.

-- PI Updated Documents --

PI: ADDITIONAL GOOD CLINICAL RESEARCH PRACTICE TRAINING

1. During this approval period, has the Principal Investigator completed any additional training in Good Clinical Research Practice?When **YES**, describe and/or attach correspondence confirming additional training: question 1a &/or 1b.When **NO**, proceed to question 2.
⇒Select either 'Yes' or 'No'

1a. Describe Additional Training in Good Clinical Practice - When **YES**, you are required to describe and/or attach correspondence confirming additional training. ⇒Enter an unlimited amount of text.

1b. Good Clinical Practice Training Confirmation Attachment(s) ⇒Attach 1 to 5 files of type "Human Sub. Prot. Training" to this xForm.

CONFLICT OF INTEREST

Please indicate whether there has been any change of status in Conflict of Interest, as indicated on the "Application or Review of a Research Project" submitted with the initial review of this clinical research project (see [BRANY IRB Conflict of Interest Disclosure](#) form). Conflict of Interest applies to you and all related parties. Click the hyperlink blue text to access a copy of the paper [BRANY IRB Conflict of Interest Disclosure](#) form.

2. Has there been a change of status in the Conflict of Interest as initially reported? When **YES**, in the next question you will be required to attach a copy of the [BRANY IRB Conflict of Interest Disclosure](#) form. If there are any **YES** responses on the [BRANY IRB COI Disclosure](#) form, a [BRANY IRB Conflict Report](#) form will also be required. When **NO**, click *Next* to continue. ⇒Select either 'Yes' or 'No'

2a. When **YES, attach [BRANY IRB Conflict of Interest Disclosure](#) form.** NOTE: If there are any **YES** responses on the [BRANY IRB Conflict of Interest Disclosure](#), then the PI *must* complete and attach a [BRANY IRB Conflict Report](#) form. ⇒Attach 1 to 5 files of type "Conflict Disclosure Statement" to this xForm.



IRB STANDARD OPERATING PROCEDURES

-- PI License and Protocol Design --

PI Current License(s)

You are **REQUIRED** to submit copies of the PI's license(s) at **EVERY** Continuing Approval Review.

Does the PI have a medical/clinical license?

YES – submitting non-expired license with this application

N/A – Does not apply for the PI (Required)

⇒ Select *one* of the following options from the drop down list presented:

YES – submitting non-expired license with this application

N/A – Does not apply for the PI

Attach copy(ies) of the Principal Investigator's unexpired, current license(s). (Required) ⇒ Attach a file of type "License" to this xForm.

PROTOCOL/STUDY DESIGN

Have all protocol/study design modifications been submitted and approved by the BRANY IRB?

*When either **NO** option is selected, you will be required to answer additional questions on another page.*

⇒ Select *one* of the following options from the list of radio buttons presented:

- YES - All modifications have been submitted and approved
- NO - Modifications have been submitted and under review
- NO - Submitting modifications with this form

-- Protocol/Study Design Submitted and Under Review --

You indicated that some protocol/study modifications have been submitted and are currently under review. Please enter identifying information for these modifications. ⇒ Enter an unlimited amount of text.

-- Protocol/Study Design Submitted With This Form --

You indicated that Protocol/Study Design Modifications are being submitted With This Form. Identify modifications being submitted. You will attach the documents in the next question.

⇒ Enter an unlimited amount of text.

Protocol/Study Design and Completed Request Form Attachments ⇒ Attach 1 to 10 files of type "Any" to this xForm.

-- Informed Consent Type --

Does this study require informed consent documents?

YES - you will be required to attach copies of the informed consent documents on



IRB STANDARD OPERATING PROCEDURES

another page

NO - you will required to supply additional information on another page (Required)

Select *one* of the following options from the list of radio buttons presented:

YES - study requires Consent(s)/Assent(s)/Addendum(s)

NO

-- Informed Consent Additional Study Information --

You indicated this study does not require informed consent documents.

Please select a choice from the following which correctly confirms the reason informed consent documents are not required:

Choices (select one):

- **Waiver of Informed Consent**
- **Waiver of Elements of Informed Consent**
- **Waiver of Documentation of Informed Consent**
- **In Vitro Diagnostic Device (IVDD)**
- **Exception from Informed Consent for Planned Emergency Research (EFIC)**

Please call the BRANY IRB Continuing Review team if you need assistance selecting the correct response. (Required)

Select *one* of the following options from the list of radio buttons presented:

Waiver of Informed Consent ‡Waiver of Elements of Informed Consent

Waiver of Documentation of Informed Consent ‡In Vitro Diagnostic Device (IVDD)

Exception from Informed Consent for Planned Emergency Research (EFIC)

-- Informed Consent Document Evaluation --

Informed Consent Documents - Please attach a copy of the *two (2) most recently signed* informed consent document(s) for this project. This is to show you are in compliance with the consent requirements of the study. If **NO** subjects have been enrolled, please **attach** a copy of the **most recently approved consent form(s)**. If a **Consent Waiver was approved** for this study, **attach proof of Consent Waiver approval (i.e. study's approval letter)**.

⇒Attach 1 to 10 files of type "CURRENT Consent In Use" to this xForm.

Have all consent modifications been submitted to the BRANY IRB? For *both* **NO** options, you will be required to supply additional information.

⇒Select *one* of the following options from the list of radio buttons presented:

- YES - All modifications have been submitted and approved
- NO - Modifications have been submitted and under review
- NO - Submitting modifications with this form

-- Informed Consent Document Under Review --



IRB STANDARD OPERATING PROCEDURES

You indicated that some consent form modifications have been submitted and are currently under review. Please enter identifying information for these modifications. ⇒Enter an unlimited amount of text.

-- Consent Modification Submitted With This Form --

You indicated that Consent Modifications are being Submitted With This Form - *Identify modifications being submitted. You will attach the documents in the next question.*
⇒Enter an unlimited amount of text.

Consent and Completed Request Form Attachments ⇒Attach 1 to 10 files of type "Any" to this xForm.

Multi-Center Trial Report

1A. Is this a Multi-Center Trial for which *YOU* are the *lead investigator*? (I.e., you are responsible for collecting data from all participating sites).

Definition: You and your site/organization are responsible for coordinating *all* other sites Multi-Center Trial Report

1A. Is this a Multi-Center Trial for which *YOU* are the *lead investigator*? (I.e., you are responsible for collecting data from all participating sites).

Definition: You and your site/organization are responsible for coordinating *all* other sites involved in the research?

When YES - our site is the lead investigator, the Multi-Center Trial report is attached, you are required to attach a copy of the Multi-Center Trial report in question 1B.

Otherwise, go to question 2. (Required)

Select *one* of the following options from the drop down list presented:

‡NOT a Multi-Center trial ‡YES - our site is NOT the lead investigator. ‡YES - our site is the lead investigator, the Multi-Center Trial report is attached

1B. Multi-Center Trial Report Attachment

You may attach up to 10 (ten) separate documents.

Attach 1 to 10 files of type "Any" to this xForm.

2. Sponsor Supplement

Effective March 1, 2014, the responsibility for ensuring the Sponsor Supplement form is provided to BRANY IRB will be transitioned *directly to the Researcher*, i.e. you will be **REQUIRED** to attain AND attach the Sponsor Supplement.

Please attach a copy of the completed Sponsor Supplement below.

Select:

Sponsor Supplement Attached (in question 2A)

Contacted Sponsor, Sponsor Supplement is not available (explain in question 2B) (Required)

Select *one* of the following options from the list of radio buttons presented:

‡Sponsor Supplement Attached (in question 2A) ‡Contacted Sponsor, Sponsor Supplement is not available (explain in question 2B)

2A. Sponsor Supplement - *Effective March 1, 2014*, the responsibility for ensuring the Sponsor Supplement form is provided to BRANY IRB will be transitioned *directly to the Researcher*, i.e. you will be **REQUIRED** to attain AND attach the Sponsor Supplement.

Please attach a copy of the completed Sponsor Supplement.

Attach 1 to 5 files of type "CR-Sponsor Supplement" to this xForm.



IRB STANDARD OPERATING PROCEDURES

2B. You indicated that you Contacted the Sponsor, and the Sponsor Supplement is not available. You are required to explain.

Sponsor Supplement - *Effective March 1, 2014*, the responsibility for ensuring the Sponsor Supplement form is provided to BRANY IRB will be transitioned *directly to the Researcher*, i.e. you will be **REQUIRED to attain **AND** attach the Sponsor Supplement. Enter an unlimited amount of text.**

-- Current Risk-Benefit Assessment --

Current Risk-Benefit Assessment

Based on study results thus far, please provide a current risk-potential benefit assessment. (*Required*)

Describe and/or attach a separate document.

Enter an unlimited amount of text.

Current Risk-Benefit Assessment Attachment

Attach 1 to 5 files of type "Site Correspondence" to this xForm.

-- Additional Instructions/Clarification/Comments --

Please feel free to provide and/or attach additional comments, documentation, and/or explanation of ANY information on this xForm submission. (*Optional*)

You may describe here and/or attach separate documents. ⇒Enter an unlimited amount of text.

Additional comments, documentation, and/or explanation Attachment(s)

⇒Attach 1 to 25 files of type "Any" to this xForm.

Applications for Continuing Review must be submitted no sooner than 30 (thirty) days prior to study expiration.

-- Reminder: Report SAE to Sponsor --

REMINDER: You are required to report Serious Adverse Event (SAE) to Sponsor IMMEDIATELY!

-- Reminder: Submit SAE Form to BRANY IRB --

REMINDER: You must submit a Serious Adverse Event (SAE) form to BRANY IRB

-- Reminder: Submit Report to IBC Immediately --

REMINDER: you are required to report Serious Adverse Event (SAE) to BRANY Institutional Biosafety Committee (IBC) IMMEDIATELY!

PI Submission Review Instructions (end)

ONLY THE PI IS REQUIRED TO SIGN THE xFORM! <--- NEW!!!

WHEN YOU CLICK THE SUBMIT BUTTON ON THE FOLLOWING PAGE:

- **The xForm will be ADDED to the PI'S My IRBManager Dashboard Home screen;**
- **An email alert is CREATED AND ADDED to the email queue to be sent.**



IRB STANDARD OPERATING PROCEDURES

PLEASE NOTE: *The Dashboard is MUCH more reliable to complete all xForms from than the alert email.*

Principal Investigator (PI) xForm Reviewing Instructions

Now that you have reviewed the information within this electronic xForm submission, please follow the appropriate instructions, a or b, below:

- a. Modifications required: alert your study coordinator that modifications are required on this xForm and click on the Close button to close the xForm. Once the modifications are complete, you will receive another email alert to review and authorize the updated xForm.*
- b. Complete/Submit to BRANY: if the content of this xForm is complete, click the Next button to display the "Form Signatures Stage". Enter your IRBManager password into the empty box on the row your name is listed, then click the Sign button to submit the xForm to BRANY.*

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IRB STANDARD OPERATING PROCEDURES

Appendix 9 – BRANY IRB Standard Operating Procedures

Checklist – Human Research

Determining Whether a Proposed Activity is Human Research According to DHHS or FDA Regulatory Definitions

Form with fields: Protocol Title, Submitted by, Brief Description (with instructions to append sheets and submit documents).

Submission of this Form is Optional.

This form is a guide to help investigators determine if an activity is human subject research and regulated by the Department of Health and Human Services (DHHS) and/ or Food and Drug Administration (FDA).

(1) An activity is “Human Research” according to DHHS regulations when ALL of the following are true:

- (a) The activity is a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge. [] TRUE [] FALSE

*Note: If the activity is NOT a systematic investigation designed to develop or contribute to generalizable knowledge, the activity does not meet the definition of research under the DHHS regulations. However, it may meet the definition of human subject research under the FDA definition.

- (b) The activity involves human participants because the data the investigator plans to collect is about living individuals. [] TRUE [] FALSE

- (c) The investigator obtains (i) data through intervention or interaction with the individual (e.g. Physical procedures performed on those individuals, Manipulation of those individuals, Manipulation of those individuals’ environments, Communication with those individuals, Interpersonal contact with those individuals); or (ii) identifiable private information. (e.g. the information is about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, or the individual has provided the information for specific purposes and can reasonably expect that the information will not be made public (for example, a medical record). [] TRUE [] FALSE

(2) An activity is “Human Research” according to FDA regulations when ANY of the following are true:

- (a) The activity involves an FDA regulated test article (use of a drug, other than the use of a marketed drug in the course of medical practice). The drug is either not approved by the FDA for marketing or it is not used in the course of medical practice. Note: For this policy “drug” means (i) an article recognized in the official United States Pharmacopoeia, official Homoeopathic Pharmacopoeia of the United States, or official National



IRB STANDARD OPERATING PROCEDURES

Formulary, or any supplement to any of them, (ii) an article intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in humans or other animals, (iii) an article (other than food) intended to affect the structure or any function of the body of humans or other animals, or (iv) an article intended for use as a component of any article specified in the above items.

TRUE FALSE

(b) The activity involves an FDA regulated medical device, other than the use of a marketed medical device in the course of medical practice. The device is either not approved by the FDA for marketing or it is not used in the course of medical practice.

Note: For this policy "medical device" means (i) Recognized in the official National Formulary, or the United States Pharmacopoeia, or any supplement to them, (ii) Intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in humans or other animals, or (iii) Intended to affect the structure or any function of the body of humans or other animals, and which does not achieve any of its primary intended purposes through chemical action within or on the body of humans or other animals and which is not dependent upon being metabolized for the achievement of any of its primary intended purposes.

TRUE FALSE

(c) The activity is otherwise subject to FDA regulations (i) Data from the activity will be submitted to, or held for inspection by, the FDA, or (ii) the activity involves one or more of the following FDA-regulated articles:

- Food or dietary supplement that bears a nutrient content or a health claim
- Food or color additive for human consumption
- Infant formula
- Biological product for human use
- Electronic product for human use
- Other article subject to the FD&C Act

TRUE FALSE

(d) The activity involves human participants because (i) the test article will be used on one or more humans, and/or (ii) the test article is a medical device, the medical device will be used on human specimens, the activity is being done to determine the safety or effectiveness of the device, and the data from the activity will be submitted to, or held for inspection by, the FDA.

TRUE FALSE

This activity is determined to be human research (meets either definition 1 or 2 above)

This activity is determined not to be human research (meets neither definition 1 nor 2 above)

IRB Chairperson's or Director's Name IRB Chairperson's or Director's Signature Date



IRB STANDARD OPERATING PROCEDURES

Appendix 10 – BRANY IRB Standard Operating Procedures

Sample IRB Approval Letter

To: \$piformattedname\$\$
From: \$\$username\$\$
CC: BRANY IRB File # \$\$ProtocolCode\$\$-\$\$SiteCode\$\$
\$\$GrantsManager\$\$, Grants Manager
FOR MSSM STUDIES: Liz Carroll, Assistant Director of Regulatory Affairs, MSSM PPHS
(liz.carroll@mssm.edu); Rosaria McEntee, Asst Director, Clinical Trials, Budget and Billing
Office (Rosaria.mcentee@mssm.edu); Moneesha Malloy, Grants Specialist
(moneesha.malloy@mssm.edu); Michael McAllister, Grants and Contracts Office
(michael.mcallister@mssm.edu)
FOR NSLIJ STUDIES: Hallie Kassan (hkassan@nshs.edu)
FOR HHC STUDIES: Christina Pili, HHC Research Administration; Imah Jones, HHC Research
Administration
Research Coordinator
Date: \$\$generationdate\$\$
Re: BRANY IRB Approval for \$\$SponsorName\$\$ Protocol \$\$SponsorProtocol\$\$

Protocol Title: \$\$ProtocolDescription\$\$

1. BRANY IRB Decision:
At the meeting of \$\$initialapproval\$\$, BRANY IRB approved the above referenced research
project, which was previously deferred at the meeting of _____ OR

, provided:

- a. Assent is sought, obtained, and documented from all minor subjects capable of giving
it.
i. Subjects ages 8-14 should document assent by signing a separate assent
form.
ii. Subjects 15-17 should document assent by signing an assent line on the main
informed consent form.
b. Permission is sought, obtained, and documented from one/both parents or legal
guardians, unless one parent is deceased, unknown, incompetent, or not reasonably
available, or when only one parent has the legal responsibility for the care and
custody of the child.

List provisions of approval here, if any (e.g., provided assent is obtained from all minors
capable of giving it).

**For Transfer Protocols: All subjects (who are active or in follow-up) are to be reconsented with
this BRANY IRB-approved consent form.

*This approval requires that all procedures and activities are performed in accordance with
relevant state law.



IRB STANDARD OPERATING PROCEDURES

2. Items Reviewed/Approved:

The BRANY IRB is in receipt of:

- \$\$SponsorName\$\$ Protocol \$\$SponsorProtocol\$\$, Version Date and/or Number
- Investigator's Drug Brochure Drug Name , Version Date and/or Edition Number
- FDA Form 1572 (dated version date)
- Subject Information and Informed Consent Form (Version version) with BRANY Informed Consent Feedback Tool appended (Check Question # 54 on the application and remove this reminder!)
 - **REMINDER: Check application and enter a translation event into IRBManager to indicate requested translations, if any. Then DELETE this reminder!**
- Assent Form (Version version)
- Additional Consent Form (Version version)
- Experimental Subject Bill of Rights **This bullet only remains for sites located in California.**
- Internet Advertisement (Version or "BRANY stamp dated")
- Public Service Announcement (Version or "BRANY stamp dated")
- Patient Diary/Questionnaire/Dosing Instructions (Version or "BRANY stamp dated")

The protocol, informed consent document(s), internet ad, public service announcement, and patient diary/questionnaire, etc... are now approved. Modifications are in accord with those suggested at the \$\$initialapproval\$\$ meeting **If project previously deferred, list other meetings at which it was considered here as well - use last meeting for approval date.** of the Biomedical Research Alliance of New York Institutional Review Board. Modifications to the informed consent document were incorporated as indicated in the enclosed redlined version(s).

This highlighted text stays in only if the study has a separate HIPAA form [required for California sites] - delete this section if HIPAA language is included in the consent form!! Any subject enrolled in a research study must sign the separate HIPAA compliant Authorization Form in addition to the informed consent.

- **To meet the requirements of HIPAA use the attached Authorization Form.**

This highlighted text stays in only if the study involves HIV testing!! Additionally, New York State Public Health Law mandates that subjects undergoing HIV testing in research studies must sign a separate consent form for HIV testing in addition to the main consent form. To meet this requirement, use the attached Consent for HIV Antibody Test. ****If this site is NOT in New York State, they must comply with their state laws - go see Raffaella!!****

- **FOR TEXAS SITES DOING HIV TESTING** Please note that you must obtain consent for HIV testing as required by relevant state law.

Please note: The following recruitment materials are approved:

- **LIST SPECIFIC ADVERTISEMENT ITEMS**
 - NOTE: This approval for **sponsor campaign materials** requires the missing phone number field to be completed with a valid phone number composed of numbers. If the phone number contains words, please submit for IRB review prior to use.
- **Doctor to Patient Letter (BRANY IRB Approved – Version A)**



IRB STANDARD OPERATING PROCEDURES

- NOTE: This approval requires that the **Doctor to Patient Letter** is distributed on site letterhead with contact information as indicated in your initial research application.

Please note: The following recruitment materials are *conditionally* approved:

- **LIST SPECIFIC ADVERTISEMENT ITEMS**

In order to receive final approval on the above mentioned items, please submit finalized version(s) with **IRB-directed changes** for review and approval.

Action Required: Before a final approval for the item(s) can be released, BRANY IRB must review them in final version(s) (i.e., recorded audio clip; recorded motion graphic video; print and/or web advertisements including any applicable final images, formatting, and URLs).

Please Note: BRANY IRB does not require submission of Study Tools intended for Study Staff, as these are an elaboration of information contained in the approved protocol.

Please note: "Advertisements" to the medical community need not be reviewed by the Institutional Review Board. This includes "Dear Colleague" letters and posters for nursing stations, unless it is likely that prospective subjects will see the advertisement. Such letters should be HIPAA compliant and not include a plan for collecting PHI. Rather, the letter should direct the colleague to have the potential subject contact the research investigator.

3. **Requirements for Translation of Informed Consent** (to be used when the IRB "recommends" a translation though the site did not request any!)

Item # 73 on the research application submitted by your site indicates that 20% of the population you anticipate enrolling at your site will be of **Hispanic** origin. Please note that in accordance with BRANY IRB policy, if this population includes individuals who are proficient in a language other than English, you *must* obtain translations of the consent form and other relevant translated subject materials (i.e., questionnaires or diaries) *prior to* enrolling such subjects. Please refer to BRANY IRB Standard Operating Procedures, Section IV.3.b, or contact BRANY IRB if you have any questions.

4. **Request for Waiver of Authorization to Release PHI for Research Purposes**

The convened BRANY IRB reviewed and approved your request for a waiver of the requirement to obtain authorization for release of protected health information (PHI). BRANY IRB has determined that this request satisfies the waiver criteria outlined in 45 CFR 164.512(i)2(ii).

The PHI requested will be retrieved from your private patient medical records, and has been identified to include all protected health identifiers except: account numbers, certificate/license numbers, vehicle identifiers, and serial numbers, including license plate numbers, device identifiers, and serial numbers, web URLs, internet protocol address numbers, biometric identifiers, including finger and voice prints, and full-face photographic images and any comparable images. **This highlighted text stays in only if the IRB approved a HIPAA Waiver for this project and the BLUE highlighting should be modified to be in accordance with what the site's HIPAA waiver request says...**

5. **Request for Waiver of Informed Consent**

BRANY IRB determined that your request for waiver of informed consent satisfies the waiver criteria set forth in 45 CFR 46.116(d).



IRB STANDARD OPERATING PROCEDURES

6. **Consent by a Legally Authorized Representative:**

Additionally, the IRB has approved this research project to include consent by a legally authorized representative. In the event surrogate consent becomes necessary, it is the responsibility of the Principal Investigator to ensure that consent is obtained from someone legally authorized under applicable law to consent on behalf of the prospective subject to the subject's participation in the research. If any questions arise regarding who may act as the legally authorized representative, Investigators are advised to consult with local counsel before enrolling a subject using surrogate consent. *This highlighted text stays in only if the IRB approved the project to include an LAR.*

OR, if the IRB has not approved an LAR for the project (and the PI requested it in the application):

The request to include consent by a legally authorized representative has not been approved because the IRB felt this research project did not meet its requirements for allowing this type of consent. According to BRANY IRB policy:

"...it is acceptable for a health care proxy (or other legally authorized representative) to sign the consent if:

- (a) *There is potential benefit over standard treatment; and*
- (b) *Standard treatment is not being withheld; and*
- (c) *There is no alternative standard treatment; and*
- (d) *Enrollment in the study is in the best interest of the patient; and*
- (e) *Participation in the research would not be contrary to the known wishes of the patient"*

In accordance with BRANY IRB policy and the regulations in order for the IRB to reconsider this request, you must submit a written explanation of how this project meets the above criteria.

7. **Study Personnel To Participate In This Project:**

The following study personnel have been approved to participate in this research project.

- i.
- ii.

The following study personnel have not been approved to participate in this research project because required documents have not been completed and/or submitted to the BRANY IRB, as detailed below.

- i. Insert Staff Name - Indicate what is missing or incomplete
- ii. Insert Staff Name - Indicate what is missing or incomplete

In order to receive approval for the above-mentioned study personnel to participate, the missing and/or completed required documents must be submitted to the IRB for review.

8. **Clinical Trial Agreement Execution:**

When applicable, this project may not commence without a fully executed Clinical Trial Agreement.



IRB STANDARD OPERATING PROCEDURES

9. **Review by Other Committees:**

Please note: Additional Health & Hospitals Corporation (HHC) central office approval is required for studies conducted at any of HHC facilities. Please obtain this approval from your local facility review committee, or go to <http://reason.nychhc.org/> and click on **PI and Reviewers only** to begin the process. Instructions are available for first time users. ***This stays here ONLY for HHC sites: Jacobi, Bellevue, Queens Hospital Center, Elmhurst, and North Central Bronx. There are about 80 sites that are components of HHC - if you're not sure if yours is one, please ask.***

This project requires review and approval by an **Institutional BioSafety Committee (IBC)** before it may begin. ***This stays here only for gene therapy or human DNA transfer studies ("11" in IRB file #).***

10. **IRB Approval Period/Expiration of IRB Approval:**

The IRB approval for this project will expire **ApprovalPeriod** months from the review date of **initialapproval**. **IRB approval expires EXPIRATIONDATE. TO ENSURE CONTINUING APPROVAL OF YOUR PROJECT, ALL CONTINUING REVIEW FORMS MUST BE SUBMITTED TO BRANY IRB ONE MONTH PRIOR TO THE EXPIRATION DATE.** If the status of the project changes, or if the project is completed prior to this date, you must notify the IRB (please use the Notification of Enrollment Closure or Study Termination form).

If you have any questions or require any additional information, please call me at **userphone** or send an email to me at **useremail**. Thank you.



IRB STANDARD OPERATING PROCEDURES

Appendix 11 – BRANY IRB Standard Operating Procedures

Research Application xForm

Initial Research Application Data Entry

Instructions

Below are key notes to help you to complete the electronic xForm version of BRANY's Initial Research Application.

PLEASE carefully read the questions within this electronic xForm. Incorrect responses will delay processing of your Research Application.

- **Error Messages:** appear at the TOP of the xForm page:
- **Red** when a required question is not answered.
- The "Required." label also appears above the answer for most required questions.
- **Yellow Highlight**, when you have broken a "rule" by not supplying additional information related to a choice you selected.
- **Add Note** is used to add additional comment(s) to any question, click the Add Note link available on most questions on each page of the xForm. Notes can be added to flag items to be addressed and/or add information to facilitate application completion and review.
- **ATTACHMENTS** are **REQUIRED** as you proceed through the xForm application. The xForm will not allow you to continue until you add **ALL** attachments where they are required. This is by design and to help ensure the BRANY IRB receives a fully complete research application. Please review the email you received listing the documents needed to complete the application so you can have them available in electronic form to attach as you complete the Initial Research Application xForm.
- **Member Organization** is used to facilitate xForm navigation so IRBManager will guide you to the appropriate questions for your organization. If there is more than one (1) Member Organization choice that applies to your site, please select the main performance site, i.e. the site that will be listed on the consent form.
- **IRB-Only studies** are **NOT BRANY Classic studies:** select **NO** for the BRANY Classic question
- If you are a BRANY Classic site, i.e. your site uses BRANY for ALL services: contracts, budgets and consent form revisions, you will not be required to re-attach protocol/drug/device/combination product documents that BRANY sent to you. You **WILL** be required to attach any updated protocol/drug/device/combination product documents received from the sponsor/CRO, AND documents that required site completion, such as but not limited to: 1572s, Statement of Investigator, BRANY IRB Conflict of Interest disclosures, consent waiver forms, etc.
- **BRANY IRB Conflict of Interest Disclosure (ATTACHMENTS REQUIRED):**
For the Principal Investigator, the BRANY IRB Conflict of Interest Disclosure form is integrated within this electronic xForm. For the primary research coordinator and all other key study personnel, you will be required to attach an electronic copy of a completed and signed **BRANY IRB Conflict of Interest Disclosure** form **AS you add each person to the application.** This is a requirement for ALL studies: a distinctive BRANY IRB Conflict of Interest Disclosure is required



IRB STANDARD OPERATING PROCEDURES

for each individual on each study they are affiliated with. (Please note, if any Yes responses are entered on the BRANY IRB Conflict of Interest Disclosure form, that individual will have to complete and sign a BRANY IRB Conflict Report form as well).

• **Human Subject Protection Training (ATTACHMENTS REQUIRED):**

For all key study personnel you add to the application, you will be required to attach non-expired copy(ies) of certificates of completion for Human Subject Protection Training As you add each person to the application unless BRANY has non-expired, valid Human Subject Protection Training certificates of completion on file for that individual.

• **Submitting the xForm:**

When you arrive at the Submission page, be sure to click on the Submit button after you enter your password to submit the xForm. When submitted, a message that begins with the following will be displayed:

Your form has been submitted. You may close this window.
xForm submitted to BRANY's IRBManager

If you press the Enter key, the xForm is saved NOT submitted. You will have to re-open the xForm (by going to My IRBManager Dashboard home screen OR My Documents & Forms), open the existing xForm then enter your password to submit the xForm. xForms MUST be submitted to proceed to the next stage in processing.

Study Identifier Information

Depending on the responses you select in the questions below and throughout the xForm, you will automatically be guided to the appropriate sections of the xForm that relate to the study identifying information/responses selected.

PLEASE carefully read the questions within this electronic xForm.

Incorrect responses will delay processing of your Research Application.

Member Health System Organization

1. Select the health system your facility is part of. If there is more than one (1) choice that applies to your site, please select the main performance site, i.e. the site that will be listed on the consent form. If your health system is NOT listed, please select NOT LISTED.

Choices:

- Beth Israel
- Gwinnett
- Montefiore
- Mount Sinai
- North Shore-Long Island Jewish Health System –NSLIJ
- NYC Health & Hospitals Corporation (e.g. Jacobi, Bellevue, etc.)
- New York University-NYU
- St. Luke's/Texas Heart Institute
- Western Connecticut Health Network-WCHN
- NOT LISTED-My health system/facility is NOT listed above



IRB STANDARD OPERATING PROCEDURES

Study Type

2. Select the appropriate study type for your research project from the following list:

- Combination Product (Drug/Device, Drug/Biologic, Device/Biologic,
- Drug/Device/Biologic, co-packaged test articles, 2 products separately packaged but labeled for use together)
- Drug/Biologic or New Use of Drug/Biologic
- Device
- Retrospective Chart Review
- Blood Draw
- Survey Study (e.g. questionnaire, etc.)
- Biological Specimen Research
- Data Collection during routine clinical care

When NONE OF THE ABOVE you will be required to explain why you selected NONE OF THE ABOVE in question 2a.

2a. Explain why you selected NONE OF THE ABOVE: ⇒Enter an unlimited amount of text.

3. Is this an Investigator Initiated study?

⇒Select either 'Yes' or 'No'

4. Does this research involve any form of Gene Transfer or Recombinant DNA?

⇒Select either 'Yes' or 'No'

5. Has this study (in its current or a modified form) been submitted to, disapproved, or terminated by another IRB prior to submission to BRANY IRB?

As specified in FDA's Frequently Asked Questions - Information Sheet - Guidance for Institutional Review Boards and Clinical Investigators:

“26. If an IRB disapproves a study submitted to it, and it is subsequently sent to another IRB for review, should the second IRB be told of the disapproval?

Yes. When an IRB disapproves a study, it must provide a written statement of the reasons for its decision to the investigator and the institution [21 CFR 56.109(e)]. If the study is submitted to a second IRB, a copy of this written statement should be included with the study documentation so that it can make an informed decision about the study. 21 CFR 56.109(a) requires an IRB to "... review ... all research activities [emphasis added]" The FDA regulations do not prohibit submission of a study to another IRB following disapproval. However, all pertinent information about the study should be provided to the second IRB.”

BRANY IRB considers suspension or termination of approval by another IRB to be analogous to the scenario referenced in the FDA's Frequently Asked Questions above, and expects information to be provided to BRANY IRB if the protocol you are submitting, in its current or a prior form, was disapproved, suspended, or terminated by another IRB.

⇒Select either 'Yes' or 'No'



IRB STANDARD OPERATING PROCEDURES

6. Does this project involve Additional Research such as:

- *Pharmacogenetic evaluation*
- *Pharmacodynamic evaluation*
- *Pharmacokinetic evaluation*
- *Exploratory biomarker evaluation*
- *Pharmacoeconomic evaluation*
- *Other additional research or sub-study?*

Involve Additional Research? ⇒Select either 'Yes' or 'No'

Data Safety Monitoring Provisions

7. ALL clinical trials require safety monitoring, but not necessarily by a formal committee. Describe the provisions for safety monitoring of this project:

- *NONE - study is not a clinical trial or a study that requires safety monitoring (e.g. chart review)*
- *Formal data monitoring committee has been established*
- *Formal data monitoring committee has NOT been established*

8. Is this a Multi-Center research project? ⇒Select either 'Yes' or 'No'

A multi-center research project is from the Sponsor/CRO's point of view:

- **Study is conducted over multiple institutions across the country (i.e. subjects are from multiple institutions NOT sites within ONE institution).**
- **Listed within the protocol document.**
- **Typically, multi-center is listed in the study title.**

If you are unsure, please contact BRANY at 516.470.6900

9. Are you requesting a waiver of consent for this study? ⇒Select either 'Yes' or 'No'

Does this research involve radioactive drugs/radiologic devices and/or otherwise expose subjects to radiation? ⇒Select either 'Yes' or 'No' (When YES, you will be required to answer additional questions on another page.)

10. Is this a BRANY Classic research study? ⇒Select either 'Yes' or 'No'

BRANY Classic = You contract/pay BRANY for the FULL BRANY Classic package: assistance with your budget, contract, regulatory and consent documents. Please note there is an additional fee for this BRANY service. You are only a BRANY Classic if you purchased all the services of BRANY.

If this is an IRB-Only study (you do not pay BRANY for ALL services), you must select NO to this question.

If you are unsure, please contact the BRANY associate who sent you the email to start this xForm and have your BRANY IRB # and the email available: 516.470.6900.

BRANY Classic Contact

IF THIS IS AN IRB ONLY STUDY: DO NOT COMPLETE THIS PAGE!

Click the Back button and change the response to the "Is this a BRANY Classic research study?" question to No, to complete this Research Application xForm.



IRB STANDARD OPERATING PROCEDURES

If you are unsure, please contact the BRANY associate who sent you the email to start this xForm and have your BRANY IRB # and the email available: 516.470.6900.
BRANY Grants/Business Development Regulatory Department Contact

Please select the item which includes the name/names of the BRANY Grants/Business Development associate(s) with whom you work with regularly to complete Research Applications at BRANY.

Tracy or Coleen should be the BRANY associate who sent you the email which included the BRANY# (BRANY IRB#) and instructions to start this electronic xForm Research Application.

If you are unsure, please call your BRANY Relationship Manager and/or Regulatory/Grants/BD associate:
Coleen DeSouza 516.470.6908
Tracy Feliciano - 516.470.6973
Jill Filipelli - 516.470.6911
Eileen Summers - 516.470.6933

Radiation Exposure

Is the exposure to the subjects greater than s/he would have received if NOT involved in the study?
E.g. Study participation requires two additional CT scans.

⇒Select either 'Yes' or 'No'

- When YES: you will be required to describe additional procedures.
- When YES: you will be required to attach approval from your institution's radiation safety committee or appropriate approval documentation from the radiation safety review process (e.g., email, letter, other).
- When YES: you will be required to describe additional procedures.

⇒Enter an unlimited amount of text.

⇒Attach 1 to 5 files of type "Radiation safety review docs" to this xForm.

NSLIJ Cancer Review Req'd

For North Shore-Long Island Jewish Health System-NSLIJ only!

Did this study require review by the Cancer Services Research Review Committee?

⇒Select either 'Yes' or 'No'

- When YES: you are required to attach a copy of the approval correspondence (MUST be attached to application!)
- When YES: you are required to attach a copy of the approval correspondence (MUST be attached to application!)

⇒Attach 1 to 5 files of type "Site Correspondence" to this xForm.

Protocol Documents

NOTE: Drug/Device/Investigator Brochures, Informed Consents will be required to be attached later in the application, when required for your study type. Advertisements and Recruitment items will be requested, if applicable and available to you now, later in the application.



IRB STANDARD OPERATING PROCEDURES

1. A Project Summary is **required** with your application, unless your site is using the BRANY Regulatory Department for contract and budget negotiations. Please select the appropriate choice below.

⇒Select one of the following options from the list of radio buttons presented:

- BRANY Classic (BRANY will assist with your IRB submission & Project Summary)
- Project Summary Attached (default value)

⇒Attach 1 to 5 files of type "Project Summary" to this xForm.

2. Protocol Document Status. Please select the appropriate response.

NOTE: The Protocol Document must contain adequate information so the IRB can conduct an analysis of the risks and potential benefits, such as:

- The scientific or scholarly rationale.
- The procedures to be performed.
- A description of the procedures being performed already for diagnostic or treatment purposes.
- The risks and potential benefits of the research to participants.

⇒Select one of the following options from the list of radio buttons presented:

- Protocol Document attached: Initial, Updated or Additional
- BRANY Classic (Copy on file and supplied to research site by BRANY)
- Protocol Supplied with PRE-Application, no updates available at this time

⇒Attach 1 to 20 files of type "Any" to this xForm.

3. Subject Materials, if available (Items the subject will be given to use during the study, e.g. diaries, instruction packets, questionnaires, tote bags, etc.)

⇒Attach 1 to 20 files of type "Subject Materials" to this xForm.

IF NOT LISTED ABOVE

4. Other Protocol Documents you have must be submitted with this application. If you enter a description here you will be required to attach at least one (1) document below.

⇒Enter an unlimited amount of text.

⇒Attach 1 to 10 files of type "Application Materials" to this xForm.

Study Sponsor Information

1. Will this study be registered on www.clinicaltrials.gov?

⇒Select either 'Yes' or 'No'

2. Source of Funding (check all that apply):

⇒Check one or more of the following items from the list of check boxes presented:

- Drug or Medical Device Company
- Not-for-profit sponsor
- Federal Government (When "Federal Government" is selected, you will be required to explain in question 3.)



IRB STANDARD OPERATING PROCEDURES

- *Other (Explain below)*

3. Name of Federal Agency funding research:

⇒Enter one line of text.

4. Source of Funding "Other" - Please provide explanation:

⇒Enter an unlimited amount of text.

Federal Wide Assurance (FWA)

5. Is this study being conducted under a FWA?

⇒Select either 'Yes' or 'No' (When YES, you will be required to answer questions on another page.)

6. Does your institution have a policy for Human Subject Protections Training Requirements?

⇒Select one of the following options from the drop down list presented:

- YES – attaching current institutional training requirements policy with application
- YES – current institutional training requirements on file at BRANY
- NO

Federally Funded Research and Research Conducted Under a Federal Wide Assurance (FWA)

1. FWA Number: ⇒Enter one line of text.

2. NIH Human Participant Protections Learning - Attach copies of the NIH Completion

Certificates for ALL key personnel on your study. You may attach up to twenty five (25) separate documents. All key personnel must complete the "Protecting Human Research Participants" online training offered by the NIH Office of Extramural Research at this link:

<http://phrp.nihtraining.com/users/login.php> ⇒Attach 1 to 25 files of type "Human Sub. Prot. Training" to this xForm.

3. Is the NIH Office of Extramural Research's "Protecting Human Research Participants" online training the required research training for your institution/facility? When YES, we will not require you to attach additional Human Participant Protections certificates when you supply contact information for key personnel you wish to participate in this study. You will only be required to attach the NIH certificates on this page for ALL key personnel. ⇒Select either 'Yes' or 'No'

4. Will BRANY IRB be the only reviewing IRB for all research sites conducting this study? When YES, you will be required to attach a copy of the **complete Grant** or other funding application in **question 4a.** ⇒Select either 'Yes' or 'No'

4a. When YES, copy of complete Grant or other funding application attachment. ⇒Attach 1 to 10 files of type "Non-BRANY IRB Documents" to this xForm.

5. In order for your submission to be processed. BRANY IRB must be designated as a reviewing IRB on your FWA. If this is not the case, or if a previous Authorization Agreement with the BRANY IRB was study specific, please submit an Authorization Agreement to be made available for review by OHRP upon request. See [Authorization Agreement](#) for a sample Institutional Review Board (IRB)/Authorization Attach a copy of the Authorization Agreement with the BRANY IRB, if required. BRANY IRB will provide you with a fully-executed version once your submission is received. ⇒Attach 1 to 5 files of type "IRB Authorization Agreement" to this xForm.



IRB STANDARD OPERATING PROCEDURES

Institutional Policy in Human Subject Protection (CITI, NIH, etc.) Requirements

Please provide a description of your institutional policy for Training in Human Subject Protections You can describe and/or attach a separate document. ⇒Enter an unlimited amount of text.

Attach a description of your institutional policy for Training in Human Subject Protections You can describe and/or attach a separate document. ⇒Attach 1 to 5 files of type "Site Correspondence" to this xForm.

Sponsor/CRO Study Contacts

Who will serve as the sponsor contact(s) for BRANY IRB? (Select one (1) or both - BRANY will contact the designated contact(s) directly with questions related to the BRANY IRB review for this study.)

- Sponsor Contact
- CRO Contact

Sponsor Contact Information

S1. Sponsor Contact Full Name: ⇒Enter one line of text.

S2. Sponsor Contact Email: ⇒Enter a valid e-mail address.

S3. Sponsor Contact Full Address (please include street, suite, city, state/province/country, ZIP/postal code) ⇒Enter an unlimited amount of text.

S4. Sponsor Contact Phone: ⇒Enter one line of text.

S5. Sponsor Contact Fax: ⇒Enter one line of text.

ANY Changes to the contact information listed above MUST be reported promptly to BRANY IRB.

CRO Contact Information

CRO1. Contact Organization: ⇒Enter one line of text.

CRO2. Contact Full Name: ⇒Enter one line of text.

CRO3. Contact Email: ⇒Enter a valid e-mail address.

CRO4. Contact Full Address (please include street, suite, city, state/province/country, ZIP/postal code) ⇒Enter an unlimited amount of text.

CRO5. Contact Phone: ⇒Enter one line of text.

CRO6. Contact Fax: ⇒Enter one line of text.

ANY Changes to the contact information listed above MUST be reported promptly to BRANY IRB.

Consent Form Contact for BRANY IRB

Who is the Party Responsible for Consent Form Review/Approval on the Sponsor's Behalf? If the individual responsible for Consent Form Review/Approval on the Sponsor's Behalf is the SAME Sponsor/CRO contact you already entered contact information for in this xForm, you will not be required to enter their contact information again. If the individual responsible for Consent Form Review/Approval on the Sponsor's Behalf is NOT the same as the Sponsor/CRO contact you already entered into this xForm, select **Other** so you can supply this individual's contact information.

⇒Select one of the following options from the list of radio buttons presented:

- Sponsor Contact (entered previously in this Research Application)
- CRO Contact (entered previously in this Research Application)
- Other Contact for Consent Changes



IRB STANDARD OPERATING PROCEDURES

Consent Contact Information

- C1. Consent Contact Full Name:** ⇒Enter one line of text.
C2. Consent Contact Email: ⇒Enter a valid e-mail address.
C3. Consent Contact Full Address (please include street, suite, city, state/province/country, ZIP/postal code) ⇒Enter an unlimited amount of text.
C4. Consent Contact Phone: ⇒Enter one line of text.
C5. Consent Contact Fax: ⇒Enter one line of text.

ANY Changes to the contact information listed above MUST be reported promptly to BRANY IRB.

COMBINATION Product Study

Combination Product: Drug/Device, Drug/Biologic, Device/Biologic, Drug/Device/Biologic, co-packaged test articles, 2 products separately packaged but labeled for use together. NOTE: Informed Consents will be required to be attached later in the application, when required for your study type. Advertisements and Recruitment items will be requested, if applicable and available to you now, later in the application.

1. Describe the Combination Product components (e.g., drug with device, device with biologic, drug with biologic, etc.). ⇒Enter an unlimited amount of text.
2. Provide either the IND or IDE number. ⇒Enter one line of text.
3. Documentation of the IND or IDE number is provided as follows (check ALL that apply):
Choices:
 - IND or IDE number appears within the protocol or investigator brochure - answer question 3A.
 - FDA correspondence confirming the assigned IND or IDE number for this investigation (attach documentation below) - answer question 4/4A
 - Sponsor correspondence confirming the assigned IND or IDE number for this investigation (attach documentation below) - answer question 4/4A
 - IND/IDE Not Available (provide explanation and/or attach documentation below) - questions 3B and/or 4/4A
- 3A. Specify IND/IDE Location in Protocol/Investigator Brochure:
 - List Document(s) IND/IDE is located AND
 - Page Number/Section within the specified document(s)

E.g.: Protocol page Appendix A section A.13 and Investigator Brochure Drug AB1x Section 12.3. ⇒Enter one line of text.
- 3B. If an IND/IDE number is not available, explain why one was not obtained and/or provide correspondence indicating why the investigation is exempt from the IND/IDE requirements in question 4/4A. ⇒Enter an unlimited amount of text.
4. IND/IDE Document Status. Please select the appropriate response. ⇒Select one of the following options from the drop down list presented:
 - IND/IDE Documents attached
 - BRANY Classic (Copy on file and supplied to research site by BRANY)
- 4A. IND or IDE Letter/Documentation Attachment(s) ⇒Attach 1 to 10 files of type "FDA Letter (IND or IDE)" to this xForm.

COMBINATION Product Study-II



IRB STANDARD OPERATING PROCEDURES

5. **1572/Statement of Investigator Document Status. Please select the appropriate response.**
⇒Select one of the following options from the list of radio buttons presented:
 - 1572/Statement of Investigator Documents attached
 - BRANY Classic (Copy on file and supplied to research site by BRANY)
- 5A. **1572 or Statement of Investigator Attachment - The Statement of the Investigator is a required document for ALL device studies unless exempt from the IDE requirements under 21 CFR 812.2(c) (e.g. 510k correspondence).** ⇒Attach 1 to 5 files of type "Any" to this xForm.
6. **Combination Product Related Documents Status. Please select the appropriate response.**
⇒Select one of the following options from the list of radio buttons presented:
 - Combination Product Documents attached
 - BRANY Classic (Copy on file and supplied to research site by BRANY)
- 6A. **Combination Product Related Documents - Attach documents related to the Combination Product: e.g. Investigator/Device Brochure, Drug/Device Instructions for Use, Package Inserts, etc.** ⇒Attach 1 to 20 files of type "Combination Product Docs" to this xForm.

Investigational DRUG Study

NOTE: Informed Consents will be required to be attached later in the application, when required for your study type. Advertisements and Recruitment items will be requested, if applicable and available, later in the application.

FDA Form 1572

1. **1572 Status. Please select the appropriate response.** ⇒Select one of the following options from the list of radio buttons presented:
 - 1572 attached
 - BRANY Classic (Copy on file at BRANY)
- 1a. **Attach completed, signed and dated 1572** ⇒Attach 1 to 5 files of type "1572/IDE" to this xForm.
2. **IND Number** ⇒Enter one line of text.
3. **Documentation of the IND Number is provided as follows (check ALL that apply):**
Choices:
 - IND appears within the protocol or investigator brochure (specify location below) - Question 4
 - FDA correspondence confirming the assigned IND number for this investigation (attach documentation below) - Question 5A/5B
 - Sponsor correspondence confirming the assigned IND number for this investigation (attach documentation below) - Question 5A/5B
 - IND Not Available (provide explanation AND attach documentation below) - Question 6
4. **Specify IND Location in Protocol/Investigator Brochure:**
 - List Document(s) IND is located AND
 - Page Number/Section within the specified document(s)**E.g: Protocol page Appendix A section A.13 and Investigator Brochure Drug AB1x Section 12.3.** ⇒Enter one line of text.
- 5A. **IND Document Status. Please select the appropriate response.** ⇒Select one of the following options from the list of radio buttons presented:
 - IND Documents attached
 - BRANY Classic (Copy on file and supplied to research site by BRANY)
- 5B. **IND Documentation/Letter Attachment(s)** ⇒Attach 1 to 5 files of type "FDA Letter (IND or IDE)" to this xForm.



IRB STANDARD OPERATING PROCEDURES

6. Explain why IND was NOT obtained. ⇒Enter an unlimited amount of text.

Investigational DRUG Study-II

Investigator Brochure

7. Investigator Brochure Status. Please select the appropriate response. ⇒Select one of the following options from the list of radio buttons presented:

- Investigator Brochure attached
- BRANY Classic (Copy on file and supplied to research site by BRANY)

Investigator Brochure (IB) Attachments

Please attach Investigator Brochure (IB), IB Signature page, IB Summary of Changes, etc.
⇒Attach 1 to 10 files of type "Any" to this xForm.

If available, please provide the following:

Drug Package Inserts or Other Documents relating to the study agent, if available.

⇒Attach 1 to 10 files of type "Drug Package Insert" to this xForm.

IF NOT LISTED ABOVE:

Other Drug Documents you have to submit with this application.

If you enter a description here you will be required to attach at least one (1) document below.

⇒Enter an unlimited amount of text.

Drug Other Documents Attachments.

If you attach a document here, you will be required to enter a description above.

⇒Attach 1 to 10 files of type "Application Materials" to this xForm.

Investigational Device Study

NOTE: Informed Consents will be required to be attached later in the application, when required for your study type. Advertisements and Recruitment items will be requested, if applicable and available to you now, later in the application.

Is this an "In Vitro Diagnostic Device Study Using Leftover Human Specimens that are Not Individually Identifiable"?

⇒Select either 'Yes' or 'No'

The Research Sponsor classifies this device as a (select one):

Please see FDA definition at 21 CFR 812.3(m)

⇒Select one of the following options from the list of radio buttons presented:

- Significant Risk device (SR)
- Non-Significant Risk device (NSR)

Device Letter

For ALL device studies, provide one (1) of the following documents:



IRB STANDARD OPERATING PROCEDURES

- *FDA letter granting an investigational device exemption for the proposed use*
- *Letter from the sponsor stating that the study is a Non-Significant Risk device study*
- *Letter explaining why the investigation is exempt from the IDE requirements under 21 CFR 812.2(c) (e.g. 510k correspondence)*

Device Letter Status. Select the appropriate response.

⇒*Select one of the following options from the list of radio buttons presented:*

- *Device Letter Attached*
- *BRANY Classic (Copy on file and supplied to research site by BRANY)*

Device Letter: Attach the document selected in previous question

⇒*Attach 1 to 5 files of type "Letter" to this xForm.*

Statement of the Investigator

Statement of the Investigator Status. Select the appropriate response.

⇒*Select one of the following options from the list of radio buttons presented:*

- *Statement of the Investigator attached*
- *BRANY Classic (Copy on file and supplied to research site by BRANY)*

Statement of the Investigator (attachment signed and dated copy):

The Statement of the Investigator is a required document for ALL device studies unless exempt from the IDE requirements under 21 CFR 812.2(c)

(e.g. 510k correspondence).

⇒*Attach 1 to 5 files of type "Statement of the Investigator" to this xForm.*

Device Instructions for Use/User Guide

Device Instructions for Use/User Guide Status. Select the appropriate response.

⇒*Select one of the following options from the list of radio buttons presented:*

- *Device Instructions for Use/User Guide attached*
- *BRANY Classic (Copy on file and supplied to research site by BRANY)*

Device Instructions for Use/User Guide Attachment

⇒*Attach 1 to 10 files of type "Device Instructions for Use" to this xForm.*

IF NOT LISTED ABOVE:

Other Device Documents you have to submit with this application.

If you enter a description here you will be required to attach at least one (1) document below.

Enter an unlimited amount of text.

Device Other Documents Attachments.

⇒*Attach 1 to 10 files of type "Application Materials" to this xForm.*

Gene Transfer or Recombinant DNA

Has the study been submitted to the RAC (Recombinant DNA Advisory Committee)? *When YES, you will be required to attach a copy of the RAC Correspondence in the following question.*

⇒*Select either 'Yes' or 'No'*



IRB STANDARD OPERATING PROCEDURES

RAC Attachment

⇒Attach 1 to 5 files of type "Any" to this xForm.

Has there been institutional biosafety committee (IBC) review for any sites involved? When Yes - attach IBC recommendations affecting the protocol and/or consent form, you will be required to attach IBC recommendations affecting the protocol and/or consent form.

⇒Select one of the following options from the list of radio buttons presented:

- Yes - attach IBC recommendations affecting the protocol and/or consent form
- No - IBC review with my institution's existing (non-BRANY administered) IBC is scheduled
- No - My site has an IBC administered by BRANY and would like to initiate IBC review
- No - My site would like more information about BRANY's IBC services

IBC Recommendations affecting the Protocol and/or Consent form attachment

⇒Attach 1 to 5 files of type "Any" to this xForm.

Submitted to Another IRB Prior to BRANY IRB

Attach IRB Decision, disapproval and/or termination letter and/or other relevant correspondence:

⇒Attach a file of type "Letter" to this xForm.

Are you requesting a Transfer of IRB Oversight? When YES, you will be required to attach a BRANY Transfer of IRB Oversight form.

⇒Select either 'Yes' or 'No'

BRANY Transfer of Oversight form ⇒Attach a file of type "Any" to this xForm.

Additional Research

1. Is your site participating in the additional research? If you select NO, scroll to the top or bottom of this page and click NEXT. When YES, your site is participating in the Additional Research you are required to continue responding to the remaining questions on this xForm page.

⇒Select either 'Yes' or 'No'

2. Where is the Additional Research described?

- Main Protocol (List page/section below)
- Separate Document (Attach below)
- Other (Explain below)

3. Page/Section of Protocol Additional Research is described: ⇒Enter one line of text.

4. Additional Research Document Status. Please select the appropriate response.

⇒Select one of the following options from the list of radio buttons presented:

- Additional Research Documents attached
- BRANY Classic (Copy on file and supplied to research site by BRANY)

5. Additional Research Description Attachment ⇒Attach a file of type "Protocol" to this xForm.

6. Other Explanation where Additional Research is described: ⇒Enter an unlimited amount of text.

Additional Research II

7. Is the Additional Research optional for subjects? ⇒Select either 'Yes' or 'No'

8. How will subjects indicate consent for the Additional Research?

- Additional Consent and HIPAA forms (attach below)
- Within the Main Consent and HIPAA forms
- Other (explain below)



IRB STANDARD OPERATING PROCEDURES

9. Additional Consent Document Status. Please select the appropriate response.

⇒Select one of the following options from the list of radio buttons presented:

- Additional Consent Documents attached
- BRANY Classic (Copies of Additional Consent and HIPAA forms on file and supplied to research site by BRANY)

10. Additional Consent for Additional Research attachment:

⇒Attach 1 to 10 files of type "ICF/Assent/Adden Submitted" to this xForm.

11. Other Explain: How will subjects indicate consent for the Additional Research?

⇒Enter an unlimited amount of text.

Multi-Center Research Project

Are you the lead PI? (Definition: You and your site/organization are responsible for coordinating all other sites involved in the research?)

⇒Select either 'Yes' or 'No'

If YES - BRANY IRB expects that the lead PI/organization be responsible to obtain & manage the information obtained from the multi-center research that might be relevant to participant protections, including but not limited to:

- Unanticipated problems involving risks to participants or others
- Interim results
- Protocol modifications

Please provide a detailed plan for managing the above information. Describe here and/or attach additional documents. ⇒Enter an unlimited amount of text.

Multi-Center Plan Attachment

⇒Attach 1 to 5 files of type "Any" to this xForm.

Data Safety Monitoring Committee Established

Specify protocol pages/section describing the Data Monitoring Plan and/or attach document explaining the Data Monitoring Plan. ⇒Enter an unlimited amount of text.

Data Monitoring Plan attachment ⇒Attach a file of type "Any" to this xForm.

Data Safety Monitoring Committee NOT Established

You indicated that a data safety monitoring committee has not been established for this research. Please describe what mechanism is in place for safety monitoring below. ⇒Enter an unlimited amount of text.

HIV Testing

Does this study involve HIV testing (either by the protocol or allowed by protocol at investigator's discretion)? When YES, you will be required to check off the Acknowledged box below.

⇒Select either 'Yes' or 'No'

Study Involves HIV Testing:

Please acknowledge by checking the Acknowledged box, that it is the Principal Investigator's responsibility to ensure compliance with state/local regulations/laws related to HIV testing.



IRB STANDARD OPERATING PROCEDURES

⇒Check one or more of the following items from the list of check boxes presented:

- Acknowledged

B. Principal Investigator Information

Principal Investigator (PI) Contact Information

⇒The name and contact information of the Investigator for this protocol will be displayed.

1. **Is the PI Contact Information displayed above, correct as shown?** *Select NO, if any contact information items are incorrect or missing: name, full address, telephone, etc., then you will be required to enter the missing/incorrect information on the following page. Select YES: if all contact information displayed is correct.*

⇒Select one of the following options from the list of radio buttons presented:

- Yes
- NO - Missing/Incorrect PI Contact Information

Principal Investigator (PI) Conflict of Interest Disclosure

For the Principal Investigator, the BRANY Conflict of Interest Disclosure form is integrated within this electronic xForm.

- If you, the study PI, are completing this application, at the end of the application, you will complete the Conflict of Interest Disclosure questions.
- If someone OTHER than the PI is completing this application, an email will be sent to the PI for them to both view the content of this application and complete the Conflict of Interest

Disclosure questions.

2. **Is the PI's current, non-expired CV on file at BRANY?** For a CV to be current, it needs to include the following:

- show affiliation with current facility where the research is occurring; and
- signed and dated by the PI: date must be less than two (2) years old.

⇒Select one of the following options from the drop down list presented:

- NO – attaching current, non-expired CV with application
- YES – current, non-expired CV on file at BRANY

3. **Is the PI's current, non-expired, Human Subject Protections Training (CITI, NIH, etc.) completion certification on file at BRANY?**

⇒Select one of the following options from the drop down list presented:

- NO – attaching current, non-expired copies of training completion certification with application
- YES – current, non-expired training completion certification on file at BRANY

4. **For the PI, the BRANY Systems User Access Form is:**

⇒Select one of the following options from the drop down list presented:

- NO – attaching current, signed copy with application
- YES – current, signed copy on file at BRANY

5. **Will the PI Obtain Consent from Subjects?** ⇒Select either 'Yes' or 'No'

Modify Principal Investigator Contact Information

You indicated that some/all of the Principal Investigator Contact Information was missing and/or incorrect. Please supply the complete, correct information for the missing and/or incorrect contact information.



IRB STANDARD OPERATING PROCEDURES

⇒The name and contact information of the Investigator for this protocol will be displayed.

PI Full Name ⇒Enter one line of text.

Email ⇒Enter a valid e-mail address.

Full Address (please include street, suite, city, state/province/country, ZIP/postal code) ⇒Enter an unlimited amount of text.

Phone (Please include Area Code, include Country Code, if applicable.)⇒Enter one line of text.

FAX (Please include Area Code, include Country Code, if applicable.)⇒Enter one line of text.

Principal Investigator's (PI's) Current Curriculum Vitae (CV)

Attach a copy of the PI's current, non-expired, signed and dated CV, dated within the last two (2) years. ⇒Attach 1 to 10 files of type "CV" to this xForm.

PI Evidence of Training in Human Subject Protection

⇒Attach 1 to 5 files of type "Human Sub. Prot. Training" to this xForm.

BRANY System User Access Form

PI Completed, Signed and Dated BRANY System User Access Form

⇒Attach a file of type "User Access Form BRANY Systems" to this xForm.

Principal Investigator (PI) Qualifications

1. Has the Principal Investigator ever received ANY of the following:

Form FDA 483
FDA Warning Letter
OHRP Warning Letter
NIDPOE Letter

Please check all that apply unless this information has previously been reported to the BRANY IRB. Contact the IRB Director at 516-470-6909 if you have any questions.

1a. Attachment(s) selected, required unless N/A. ⇒Attach 1 to 10 files of type "Letter" to this xForm.

2. Does the PI have a medical/clinical license? When YES - submitting non-expired license with this application is selected, you will be required to supply the PI's NON-EXPIRED medical license information on another page.

⇒Select one of the following options from the drop down list presented:

- YES – submitting non-expired license with this application
- YES – current, unexpired license on file at BRANY
- N/A – Not Applicable

3. Does this study involve narcotics or controlled substances?

When YES you will be required to supply DEA information on another page. NOTE: If you are a researcher in Massachusetts you will be required to supply information about your Application for Massachusetts Controlled Substances Registration to Use Controlled Substances and Investigational New Drugs in Research in Accordance with the Controlled Substances Act, M.G.L. Chapter 94C.

⇒Select one of the following options from the drop down list presented:

- YES
- N/A – Not Applicable



IRB STANDARD OPERATING PROCEDURES

4. **Research Conducted in State of Massachusetts - Will this Investigator's research study involve drugs and/or controlled substances in the state of Massachusetts? When YES, you will be required to supply the Massachusetts Researcher Registration# in question 4a below.**

When NO, click Next. (See the [Application](#) for Massachusetts Controlled Substances Registration to Use Controlled Substances and Investigational New Drugs in Research in Accordance with the Controlled Substances Act, M.G.L. Chapter 94C from the Commonwealth of Massachusetts, Department of Public Health, Drug Control Program. Contact the Massachusetts department of public health at (617) 983-6712 or <http://www.mass.gov/dph/> to obtain information about registering to dispense investigational drugs.)

You must obtain the appropriate registration before conducting research in the state of Massachusetts.

⇒Select either 'Yes' or 'No'

- 4a. **Massachusetts Researcher Registration # - You must obtain the appropriate registration before conducting research in the state of Massachusetts.**

⇒Enter one line of text.

Principal Investigator (PI) Licensing Information

You are required to complete at least one (1) set of license questions AND attach a copy of each of the PI's medical/clinical licenses at the bottom of this xForm page. You may enter information for up to three (3) licenses for the PI.

Attach a copy of the PI's CURRENT, NON-EXPIRED LICENSE

1. **PI Clinical/Medical License**

1a. **License#** ⇒Enter one line of text.

1b. **State:** ⇒Select a state from the list.

1c. **Expiration Date:** ⇒Enter a valid date.

2. **PI Clinical/Medical License**

2a. **License#:** ⇒Enter one line of text.

2b. **State:** ⇒Select a state from the list.

2c. **Expiration Date:** ⇒Enter a valid date.

3. **PI Clinical/Medical License**

3a. **License#:** ⇒Enter one line of text.

3b. **State:** ⇒Select a state from the list.

3c. **Expiration Date:** ⇒Enter a valid date.

PI Medical/Clinical License Attachment(s)

Current, non-expired Medical/Clinical license(s) (if expiration is upcoming, submit an updated copy as soon as it is available)

⇒Attach 1 to 10 files of type "License" to this xForm.

DEA Information

Dispensing of Controlled Substances or Narcotics

1. **Brand Name** ⇒Enter one line of text.

2. **Generic Name** ⇒Enter one line of text.

3. **Controlled Substance Classification:**



IRB STANDARD OPERATING PROCEDURES

⇒Select one of the following options from the list of radio buttons presented:

- Class I
- Class II
- Class III
- Class IV
- Class V

3. **Does this study involve narcotics or controlled substances? When YES – submitting non-expired DEA license with this application, you will be required to supply DEA information on another page. NOTE: If you are a researcher in Massachusetts you will be required to supply information about your Application for Massachusetts Controlled Substances Registration to Use Controlled Substances and Investigational New Drugs in Research in Accordance with the Controlled Substances Act, M.G.L. Chapter 94C.**

⇒Select one of the following options from the drop down list presented:

- YES – submitting non-expired DEA license with this application
- YES – current, unexpired DEA license on file at BRANY

4. **Attach copy of the CURRENT, NON-EXPIRED DEA license for the PI (if expiration is upcoming, submit an updated copy as soon as it is available). If a pharmacy is dispensing the Controlled Substance or Narcotic, attach a copy of the Pharma.**

⇒Attach 1 to 10 files of type "License" to this xForm.

Investigator Resources

The Investigator must ensure that adequate staffing and resources are available for each research project conducted, so that the rights and welfare of research subjects will be protected. Staff should have sufficient time to interact with subjects as needed.

How many of the following does the PI currently supervise? Answer a - f.

- a. **Open Research Studies:** Enter zero (0) if not applicable. ⇒Enter a valid number. It must be ≥ 0 . It must be a whole number.
- b. **Locations:** Enter zero (0) if not applicable. ⇒Enter a valid number. It must be ≥ 0 . It must be a whole number.
- c. **Physician Sub-Investigators:** Enter zero (0) if not applicable. ⇒Enter a valid number. It must be ≥ 0 . It must be a whole number.
- d. **Research Staff:** Enter zero (0) if not applicable. ⇒Enter a valid number. It must be ≥ 0 . It must be a whole number.
- e. **Approximate # of active subjects:** Enter zero (0) if not applicable. ⇒Enter a valid number. It must be ≥ 0 . It must be a whole number.
- f. **Approximate # of subjects to be enrolled in THIS study at your site(s):** ⇒Enter a valid number. It must be ≥ 1 . It must be a whole number.

C. Research Staff Information

Primary Study Coordinator Contact Information

⇒The name and contact information of the primary Coordinator for this protocol will be displayed.



IRB STANDARD OPERATING PROCEDURES

- 1. Is Primary Research Coordinator Contact Information displayed above, correct as shown?**
Select NO, if any contact information items are incorrect or missing: name, full address, telephone, etc., then you will be required to enter the missing/incorrect information on the following page. Select YES: if all contact information displayed is correct.
⇒Select one of the following options from the list of radio buttons presented:
 - Yes
 - NO - Missing/Incorrect Coordinator Contact Information
- 2. Is the Primary Coordinator's current, non-expired, Human Subject Protections Training (CITI, NIH, etc.) completion certification on file at BRANY?**
⇒Select one of the following options from the drop down list presented:
 - NO – attaching current, non-expired copies of training completion certification with application
 - YES – current, non-expired training completion certification on file at BRANY
- 3. For the Primary Study Coordinator, the BRANY Systems User Access Form is:**
⇒Select one of the following options from the drop down list presented:
 - NO – attaching current, signed copy with application
 - YES – current, signed copy on file at BRANY
- 4. Will the Primary Research Coordinator Obtain Consent from Subjects?**
⇒Select either 'Yes' or 'No'
- 5. Primary Research Coordinator - BRANY IRB Conflict Disclosure Statement**
BRANY IRB Conflict of Interest forms are required for each study you work on.

BRANY Classic: If you are a BRANY CLASSIC study and have already sent a completed, signed BRANY IRB Conflict of Interest Disclosure form to BRANY, please change the response below. If you have not sent the form to BRANY you will be required to attach it on the following page.
NOTE: As always, until a BRANY IRB Conflict of Interest form is received from you, you will not be approved and CANNOT work with study subjects

All others: Click Next.

Please note: The Principal Investigator's Conflict Disclosure Statement is integrated into this electronic xForm.

⇒Select one of the following options from the list of radio buttons presented:

- BRANY IRB COI attached (including COI Report form when required)
- BRANY Classic (Copy on file/sent to BRANY)

Modify Primary Study Coordinator Contact Info

You indicated that some/all of the Coordinator Contact Information was missing and/or incorrect. Please supply the complete, correct information for the missing and/or incorrect contact information.

⇒The name and contact information of the primary Coordinator for this protocol will be displayed.

Full Name: *⇒Enter one line of text.*

Email: *⇒Enter a valid e-mail address.*

Full Address (please include street, suite, city, state/province/country, ZIP/postal code) *⇒Enter an unlimited amount of text.*

Phone: *Please include Area Code, include Country Code, if applicable. ⇒Enter one line of text.*



IRB STANDARD OPERATING PROCEDURES

FAX: Please include Area Code, include Country Code, if applicable. ⇒Enter one line of text.

Primary Research Coordinator Evidence of Training in Human Subject Protection

⇒Attach 1 to 5 files of type "Human Sub. Prot. Training" to this xForm.

Primary Study Coordinator User Access Form

BRANY System User Access Form

Primary Research Coordinator Completed, Signed and Dated BRANY System User Access Form

⇒Attach a file of type "User Access Form BRANY Systems" to this xForm.

Primary Study Coordinator Conflict Disclosure

Primary Research Coordinator's BRANY IRB Conflict Disclosure Statement

Please note: The Principal Investigator's Conflict Disclosure Statement is integrated into this electronic xForm.

Optional: to add additional comment(s) to any question, click **Add Note**

BRANY IRB Conflict Disclosure Statement

BRANY IRB's form for declaring conflicts of interest, NOT the sponsor's financial disclosure form

Click on the blue link to access a blank copy of the [BRANY IRB Conflict Disclosure Statement](#)

⇒Attach a file of type "Conflict Disclosure Statement" to this xForm.

BRANY IRB Conflict Report Form

BRANY IRB's form for reporting details about declared conflicts of interest NOT the sponsor's financial disclosure form. NOTE: Conflict Report Form is required to be completed and attached ONLY if you answered YES to any question on Form BRANY IRB Conflict Disclosure Statement.

Click on the blue link to access a blank copy of the [BRANY IRB Conflict Report Form](#)

⇒Attach a file of type "Conflict Report Form" to this xForm.

Regulatory Personnel Addition

Do you have a Regulatory Coordinator to add to the study? A regulatory coordinator DOES NOT interact with subjects in any way.

⇒Select either 'Yes' or 'No'

Regulatory Coordinator

R1. Full Name ⇒Enter one line of text.

R2. Email ⇒Enter a valid e-mail address.

R3. Full Address (please include street, suite, city, state/province/country, ZIP/postal code) ⇒Enter an unlimited amount of text.

R4. Phone ⇒Enter one line of text.

R5. Fax ⇒Enter one line of text.

R6. Does this person require access to the IRBManager database (i.e., do they need to process and/or view submissions to the IRB)? When YES, you will be required to include additional information including attaching a completed, signed and dated IRBManager User Access Form for this individual.

⇒Select either 'Yes' or 'No'



IRB STANDARD OPERATING PROCEDURES

Regulatory Needs IRBManager Access

For the regulatory coordinator, the BRANY Systems User Access Form is:

⇒Select one of the following options from the drop down list presented:

- NO – attaching unexpired copy with application
- YES – current, unexpired copy on file at BRANY

Completed, Signed and Dated BRANY System User Access Form

⇒Attach 1 to 5 files of type "User Access Form BRANY Systems" to this xForm.

Key Personnel Addition

Do you have additional Key Study personnel to add to the study?

When YES, you will be sent to additional questions to supply information for each individual that you need to add to the study. You will also be required to attach ALL required documents for each individual AS you add them to the study.

If you DO NOT have all the signed, completed BRANY IRB Conflict of Interest forms and non-expired Human Protections Training Certificate(s) of Completion for each individual, you may either:

- a. Add ONLY the individuals you have all the required documents for OR*
- b. Add study personnel later.*

Please Note:

- 1. If you have previously submitted non-expired Human Protections Training Certificate(s) of Completion for an individual, you can select that option in the question.**
- 2. EACH study requires its own distinct, signed, completed BRANY IRB Conflict of Interest form for each individual. This document will ALWAYS be required when adding a person to a study: during the application process AND during the duration of the research project.**

Select YES to add additional key study personnel.

⇒Select either 'Yes' or 'No'

Key Personnel Information

For each key study personnel, complete this entire page and indicate if they will be obtaining consent. You will be required to attach copies of certificates of completion for ALL Human Subjects Protection and a copy of the BRANY Conflict Disclosure Statement for this study.

Definition: Key Personnel - Individuals who are responsible for the design and conduct of a study.

Another Key Personnel to Add? Continue Adding Key Personnel?

⇒Select one of the following options from the drop down list presented:

- Yes
- DONE-Continue to next section of the xForm Research Application

KP1. Full Name: ⇒Enter one line of text.

KP2. Research Role: ⇒Select one of the following options from the drop down list presented:



IRB STANDARD OPERATING PROCEDURES

- *Sub-Investigator*
- *Coordinator*
- *CC Recipient*
- *Faculty Advisor*
- *Research Assistant*
- *Regulatory Coordinator*
- *Other/Not Listed (explain)*

KP2a. Other/Not Listed Explanation: ⇒Enter an unlimited amount of text.

KP3. Obtain Consent from Subjects? ⇒Select either 'Yes' or 'No'

KP4. BRANY IRB Conflict Disclosure Statement

- **BRANY Classic:** If you are a BRANY CLASSIC study and have already sent a completed, signed BRANY IRB Conflict of Interest Disclosure form to BRANY, please change the response below. If you have not sent the form to BRANY you will be required to attach it on the following page.
- **NOTE:** As always, until a BRANY IRB Conflict of Interest form is received from you, you will not be approved and CANNOT work with study subjects

⇒Select one of the following options from the drop down list presented:

- *BRANY IRB COI attached (including COI Report form when required)*
- *BRANY Classic (Copy on file/sent to BRANY)*

KP4a. BRANY IRB Conflict Disclosure Statement

⇒Attach 1 to 15 files of type "Conflict Disclosure Statement" to this xForm.

KP4b. BRANY IRB Conflict Report Form

⇒Attach 1 to 15 files of type "Conflict Report Form" to this xForm.

KP5. Human Subjects Protection Training (CITI, NIH, etc.)

For current individual:

⇒Select one of the following options from the drop down list presented:

- *NO – attaching unexpired copy with application*
- *YES – current, unexpired copy on file at BRANY*

KP5a. Human Subjects Protection Training (CITI, NIH, etc.) - Attachments

⇒Attach 1 to 50 files of type "Human Sub. Prot. Training" to this xForm.

KP6. Does this person require access to the IRBManager database (i.e., do they need to process and/or view submissions to the IRB)?

⇒Select either 'Yes' or 'No'

IRBManager Database Access Information

Email: ⇒Enter a valid e-mail address.

Phone: ⇒Enter one line of text.

For current individual, the BRANY Systems User Access Form is:

⇒Select one of the following options from the drop down list presented:

- *NO – attaching current, signed copy with application*
- *YES – current, signed copy on file at BRANY*

Completed, Signed and Dated BRANY System User Access Form

⇒Attach 1 to 15 files of type "User Access Form BRANY Systems" to this xForm.

Additional Key Personnel to Add to the Study?

Do you have additional Key Study Personnel to add to the study?

- When YES, press Repeat to enter **ANOTHER** Key Study Personnel to the study.



IRB STANDARD OPERATING PROCEDURES

- When NO, press Next to continue with the next section of this xForm.

Research Site Location(s)

Any change to the site contact information (e.g. phone number(s), address, etc.) must be reported promptly to BRANY IRB. *Note: Only Include sites at which subjects will be seen.*

1. **Institution/Organization Name** ⇒Enter one line of text.
2. **What type of Facility is this site?**
⇒Select one of the following options from the drop down list presented:
 - Medical Office
 - Psychiatric Institution
 - Research Clinic
 - Hospital
 - Nursing Home
 - Dialysis Center
 - University
 - Laboratory
 - Surgery Center
 - Other (specify)
- 2A. **Other Facility Type** ⇒Enter one line of text.
3. **Telephone** - Please include Area Code, include Country Code, if applicable. ⇒Enter one line of text.
4. **Emergency (24 Hour) Phone** - Please include Area Code, include Country Code, if applicable. If the study **DOES NOT INCLUDE** subjects, enter "N/A" for Not Applicable⇒Enter one line of text.
5. **Full Physical Address (please include street, suite, city, state/province/country, ZIP/postal code)**
NOTE: Address MUST MATCH Box 3 of submitted form FDA 1572, when form FDA 1572 required. ⇒Enter an unlimited amount of text.
6. **Should the phone and address of the site listed above, appear on the Informed Consent?**
Choices:
 - Yes
 - No - requested consent waiver/documentation of consent waiver
 - No - specify a different phone and address for consent form
 - No - use the phone/address for site #1

Informed Consent Address - Below, please enter the phone and address to appear on the informed consent:

- **Phone** - Please include Area Code, include Country Code, if applicable. ⇒Enter one line of text.
- **Consent Form Full Address (please include street, suite, city, state/province/country, ZIP/postal code)** ⇒Enter an unlimited amount of text.

Responsible Institutional Individual

This individual will:

Provide information about the appropriate institutional/organizational liaison in charge of research in order to facilitate reporting in the event of unanticipated problems involving risks to subjects or others, serious and/or continuing non-compliance, or other reportable issues (e.g., research director, institutional official, vice president for research, CEO).

⇒Select one of the following options from the list of radio buttons presented:

- PI (Principal Investigator)



IRB STANDARD OPERATING PROCEDURES

- *Another Institutional Individual (specify)*

Institutional/Organizational Liaison

Provide information about the appropriate institutional/organizational liaison in charge of research in order to facilitate reporting in the event of unanticipated problems involving risks to subjects or others, serious and/or continuing non-compliance, or other reportable issues (e.g., research director, institutional official, vice president for research, CEO)

Optional: to add additional comment(s) to any question, click **Add Note**

IL1. Name ⇒Enter one line of text.

IL2. Title ⇒Enter one line of text.

IL3. Phone Please include Area Code, include Country Code, if applicable. ⇒Enter one line of text.

IL4. Email ⇒Enter a valid e-mail address.

IL5. Fax ⇒Enter one line of text.

IL6. Full Address (please include street, suite, city, state/province/country, ZIP/postal code) ⇒Enter an unlimited amount of text.

BRANY IRB Authorization Agreement

BRANY IRB requires a written IRB Authorization Agreement from the site before any submissions can be reviewed. Failure to provide an indemnification agreement may result in a delay of IRB review. If this is the Main Research Site/Research Location #1, you are required to attach a copy of the completed and signed IRB Authorization Agreement OR specify the date IRB Authorization was signed by your organization. If you are adding an additional research site and the IRB Authorization Agreement for the Main Site/Research Location #1 covers the current site you are adding to the research application, you are not required to re-attach or re-enter the date.

⇒Select one of the following options from the list of radio buttons presented:

- Completed and signed IRB Authorization Agreement submitted with this application. This must be signed by a signatory official from your site (individual with authority to sign contracts).
- Already filed IRB Authorization Agreement with BRANY IRB (specify date IRB Authorization was signed by your organization).
- Main Site/Research Location #1's IRB Authorization Agreement covers this current research site location.

Signed BRANY Authorization Agreement ⇒Attach 1 to 15 files of type "IRB Authorization Agreement" to this xForm.

Date IRB Authorization signed by your organization: ⇒Enter a valid date.

Additional Site-Required Reviews for BRANY IRB-Approved Research

1. Does this Investigator have an obligation to submit this project to another committee, or to obtain other organizational/institutional approval for conducting this study at this research site location (Example: Radiation Safety, Protocol Review Committee, GCRC, CTSA, Pharmacy, hospital/department approval, etc.)? When YES, it is the Principal Investigator's obligation to ensure other required approvals are in place **BEFORE initiating BRANY IRB approved research. If **available**, please attach copies of approval documentation in **question 1B**. ⇒Select either 'Yes' or 'No'**

1A. When YES, it is the Principal Investigator's obligation to ensure other required approvals are in place **BEFORE initiating BRANY IRB approved research. If available, please attach copies of the required approvals above.**

⇒Check one or more of the following items from the list of check boxes presented:



IRB STANDARD OPERATING PROCEDURES

- *When Yes, you are required to check this box as your acknowledgement of this responsibility.*

1B. Other Committee Approval Attachments, if available

⇒Attach 1 to 50 files of type "Site Correspondence" to this xForm.

2. Does this investigator have an obligation to submit this study to another IRB or obtain other organizational/institutional approval for conducting this study at this research site location?

⇒Select either 'Yes' or 'No'

If YES, you are required to provide documentation from the other IRB authorizing review by BRANY IRB in the following question. Contact the BRANY IRB for further instructions (516-470-6900 or rhart@brany.com).

2A. Other IRB Approval Attachments, if available ⇒Attach 1 to 50 files of type "Any" to this xForm.

2B. When YES, you are required to provide documentation from the other IRB authorizing review by BRANY IRB in the following question. If available, please attach copies of the required approvals above.

⇒Check one or more of the following items from the list of check boxes presented:

- *When Yes, you are required to check this box as your acknowledgement of this responsibility.*

Emergency Situations - The Investigator should ensure a plan is in place to have trained staff available to provide coverage in emergency situations.

1. Describe Emergency Equipment available at this site (select ALL that apply):

- *Crash Cart*
- *Access to 911*
- *Emergency Medications*
- *CPR Trained Staff*
- *Other (Explain)*
- *N/A (Explain)*

1a. Other Emergency Equipment at Site ⇒Enter an unlimited amount of text.

1b. N/A – Explain Why Emergency Equipment is Not Applicable/Not Available. ⇒Enter an unlimited amount of text.

2. Are Research Personnel available to subjects 24 hours a day? ⇒Select either 'Yes' or 'No'

2a. When NO - explain how subject can contact research personnel ⇒Enter an unlimited amount of text.

3. Describe any additional resources available to subjects:

- *Counseling Services*
- *Certified Medical Interpreters*
- *Other (specify)*
- *NONE*

3a. Other Subject Resources

⇒Enter an unlimited amount of text.

Additional Site Locations

Will there be another Research Site Location? ⇒Select either 'Yes' or 'No'

- **If YES, press Repeat to add ANOTHER research site location.**



IRB STANDARD OPERATING PROCEDURES

- If NO, press Next to continue with the next section of this xForm.

F. Site-Specific Study Procedure Information

Study Drug Dispensation

Who will dispense the study drug? (check all that apply):

- Credentialed and/or licensed professional in accordance with my state's law
- Pharmacist
- Study personnel (in accordance with my state's law)
- Combination product with no drug dispensation involved
- Other (specify below)
- **Other Drug Dispenser:** ⇒Enter one line of text.

Where will the study drug be stored? ⇒Enter an unlimited amount of text.

Optional - As needed, please provide other details explaining the study drug dispensation plan: Describe here and/or attach a separate document below. ⇒Enter an unlimited amount of text.

Optional Document - As needed, please provide other details explaining the study drug dispensation plan ⇒Attach a file of type "Site Correspondence" to this xForm.

G. Request Waiver/Alteration of Informed Consent

-- Request for Waiver or Alteration of Informed Consent --

Select the Informed Consent Waiver type you are requesting, NONE if not applicable:

Choices:

- NONE-NOT requesting Waiver of Informed Consent
- Request for **WAIVER OF INFORMED CONSENT - NO FORM OF CONSENT** (oral, written, or other) will be obtained from subjects
- Request for **WAIVER OF DOCUMENTATION** of Informed Consent - consent will be obtained from subjects but a **CONSENT FORM WILL NOT BE SIGNED**
- Request for **WAIVER OF ELEMENTS** of Informed Consent - if there is a consent form/process planned but you are **REQUESTING TO NOT INCLUDE SOME** required elements of informed consent – per 45CFR46.116 and 21CFR50.25.
- **In Vitro Diagnostic Device (IVDD) Studies Using Leftover Human Specimens research-does not require consent/consent waiver**

Select **ONE CHOICE** that applies to your research. If you feel that more than one choice may apply, please contact the BRANY IRB team at 516.470.6900 for guidance.

NOTE: Research that falls within the guidelines of FDA's guidance document, entitled Guidance on Informed Consent for In Vitro Diagnostic Device (IVDD) Studies Using Leftover Human Specimens that are Not Individually Identifiable, does not require consent. As such, this request for a consent waiver is not required for IVDD research. The consent process questions will be skipped. (Required)

IVDD research-does not require consent



IRB STANDARD OPERATING PROCEDURES

Select *one* of the following options from the list of radio buttons presented

-- Choice 1a: Subject to FDA Regulation --

Choice 1: Request for Waiver of Informed Consent: NO FORM OF CONSENT (oral, written, or other) will be obtained from subjects. The IRB may waive the requirement to obtain informed consent if one of the two following sets of criteria in part B is met.

A) Is this research subject to FDA regulation?

Selections:

- **YES** - A waiver of consent IS NOT allowed. This section of the xForm will be SKIPPED! This study is *NOT ELIGIBLE* for a waiver of informed consent.
- **No** - You will be required to answer questions on another page.

NOTE: Research that falls within the guidelines of FDA's guidance document, entitled **Guidance on Informed Consent for In Vitro Diagnostic Device Studies Using Leftover Human Specimens** that are **Not Individually Identifiable**, does not require consent. As such, this request for a consent waiver is not required for IVDD research. (Required)

Select *one* of the following options from the list of radio buttons presented

-- Choice 1b: Request for Waiver of Informed Consent --

B) Check the box next to the criteria you believe should be applied to this research:

Selection A: (1) The research or demonstration project is to be conducted by or subject to the approval of state or local government officials and is designed to study, evaluate, or otherwise examine: (i) public benefit or service programs; (ii) procedures for obtaining benefits or services under those programs; (iii) possible changes in or alternatives to those programs or procedures; or (iv) possible changes in methods or levels of payment for benefits or services under those programs; AND (2) The research could not practicably be carried out without the waiver or alteration.

----- OR -----

Selection B: (1) The research involves no more than minimal risk to the subjects; (2) The waiver or alteration will not adversely affect the rights and welfare of the subjects; (3) The research could not practicably be carried out without the waiver or alteration; and (4) Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

(Required) Select *one* of the following options from the list of radio buttons presented

C) Provided explanations/justifications for the choice you selected

(Required) (Required) Enter an unlimited amount of text.

D) Will you be providing a written description of information to subject?

When YES: you will be required to attach the description in the following question. (Required)
Select either 'Yes' or 'No'

You selected YES in question D.

Please attach a copy of the written description of information you will be providing the subject.
Attach 1 to 5 files of type "Application Materials" to this xForm.

-- Not Eligible/Skipping: Request for Waiver of Informed Consent --

Not Eligible *Skipping* Request for Waiver of Informed Consent Section



IRB STANDARD OPERATING PROCEDURES

You indicated this research IS subject to FDA regulation therefore, this study is *NOT ELIGIBLE* for a waiver of informed consent and this section of the xForm is being skipped.

If this is incorrect, please click on the Previous button and correctly modify the questions.

Otherwise, click Next to continue.

-- Choice 2: Request for Waiver of Documentation --

Choice 2: Request for Waiver of Documentation of Informed Consent: consent will be obtained from subjects but a CONSENT FORM WILL NOT BE SIGNED

The IRB may waive documentation of informed consent for some or all of the subjects if one of the following conditions is met.

A) Select one (1) of the following:

i. The research is NOT subject to FDA regulation and the only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality.

ii. The research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside the research context.

(Required) Select *one* of the following options from the list of radio buttons presented

REQUIRED when i. is selected:

A1) Will each subject be asked if he/she wants documentation linking him/her with the research? (The subject's wishes would govern). Select either 'Yes' or 'No'

B) PROVIDE EXPLANATIONS/JUSTIFICATIONS for choices in question A above. (Required) Enter an unlimited amount of text.

-- Choice 3: Request for Waiver of Elements of Informed Consent --

Choice 3: Request for Waiver of Elements of Informed Consent: Request for WAIVER OF ELEMENTS of Informed Consent

- if there is a consent form/process planned but you are REQUESTING TO NO INCLUDE SOME required elements of informed consent – per 45CFR46.116 and 21CFR50.25.

If it can be justified, the IRB may approve a consent procedure which does not include or which alters some of the required elements of informed consent.

Which Elements of Informed Consent do you wish for the IRB to waive, and why?

Please be sure to list EACH element and the specific reason(s) why.

(Required) Enter an unlimited amount of text.

H. Recruiting and Enrolling Process

Subject Recruitment

A. How do you intend to recruit research subjects (check all that apply):

Choices:

- *My Private Patient Population/Database*



IRB STANDARD OPERATING PROCEDURES

- *Research Database Obtained from a 3rd Party*
 - *Physician Referrals*
 - *Clinical Patient Population at my Institution (in accordance with applicable law and my institutional policies on protection of patient confidentiality)*
 - *Flyers*
 - *Advertising - answer C below when selected*
 - *Other (specify)*
- B. Other:** ⇒Enter an unlimited amount of text.
- C. Have you attached Advertising/Flyers/Recruitment material for review?**
Required when Flyers and/or Advertising selected in Question A above.
When YES you will be required to list and attach all Flyers/Advertising materials.
⇒Select one of the following options from the drop down list presented:
- YES
 - NO-not submitting Flyers and/or Advertising/Recruitment Materials at this time.
 - BRANY Classic (Copy on file and supplied to research site by BRANY)

Advertising/Recruitment Materials To Be Reviewed

Describe all Advertisement/Recruitment materials you are submitting for review with this application and attach copies of each item below. ⇒Enter an unlimited amount of text.

Attach Advertisement/Recruitment materials you are submitting for review ⇒Attach 1 to 30 files of type "Advertising/Recruitment" to this xForm.

Subject Participation

1. Will you be accessing records for patients other than your own for recruitment purposes (i.e. patients for whom you do not have the usual duty of care)? *When YES, You will need to complete separate, applicable forms, which may include:*
 - *Request for Waiver or Alteration to Release Protected Health Information (PHI) for Research Purposes [HIPAA Waiver] -> Go to: BRANY IRB Forms*
 - *Data Use Agreement (Optional - required only if you are requesting access to a limited data set of Protected Health Information) -> Go to: BRANY IRB Forms*⇒Select either 'Yes' or 'No'
- 1a. Request for Waiver and/or Alteration to Release Protected Health Information and/or Data Use Agreement form - Click on the blue hyperlink to access a blank copy of that form:
 - HIPAA Waiver Request Form
 - HIPAA Waiver Reference Page
 - Data Use Agreement Form⇒Attach 1 to 3 files of type "Any" to this xForm.

Subject Eligibility

2. How will you determine if a potential subject is eligible (i.e. meets the inclusion/exclusion criteria) for participation in research? (e.g., screening examination, review medical record/history) ⇒Enter an unlimited amount of text.
3. Are you involved in any research projects that may involve the same subject population as this study? ⇒Select either 'Yes' or 'No'
- 3a. If YES, how will you select which study the subjects are offered participation in? *NOTE: The investigator should not influence which project the potential subject participates in.
⇒Enter an unlimited amount of text.



IRB STANDARD OPERATING PROCEDURES

Subject Complaints

4. What procedure will be provided for participants to ask questions and voice concerns or complaints to the investigator?

- *Not applicable - requested consent waiver/documentation of consent waiver*
- *Informed consent will include contact information for the research team (*see BRANY IRB's sample informed consent for language requirements)*
- *No consent form will be used, explain how subjects will be instructed to contact the investigator for this purpose (explain below)*
- *Other Procedure(s) (explain below)*

4a. Subject Complaint Procedure(s) Explanation: ⇒Enter an unlimited amount of text.

Subject Compensation

Please provide subject payment information. The informed consent will be modified to reflect this information, if it's not already included in the document:

- *Subjects will NOT be paid/Not Applicable*
- *Subjects will present receipts and be reimbursed for travel and or parking*
- *Subjects will be paid per completed visit*

Subject Presents Receipts

Subjects Present Receipts - Subjects will present receipt and be reimbursed for travel and/or parking as follows.

Payment method (cash, credit, etc) and Payment Dates/Timing will be required on the following page. ⇒Enter an unlimited amount of text.

Subjects Paid Per Completed Visit

Payment method (cash, credit, etc) and Payment Dates/Timing will be required on the following page.

- 1. Amount Paid Per Completed Visit** ⇒Enter one line of text.
- 2. # of Visits in the Study:** ⇒Enter one line of text.
- 3. Any Visits Not Paid** ⇒Enter one line of text.
- 4. Total Payment: Please ensure the figures add up**
TOTAL PAYMENT is (#of Visits in Study minus #of Visits Not Paid) **multiplied by** Amount Paid Per Completed Visit. ⇒Enter one line of text.
Additional Comments: ⇒Enter an unlimited amount of text.

Subject Payout Information/Method of Payment

In what form can the subject expect to receive payment? Please indicate ALL methods of payment: cash, check, other (specify).

⇒Check one or more of the following items from the list of check boxes presented:

- *Cash*
- *Check*
- *Other (specify) ⇒Enter an unlimited amount of text.*



IRB STANDARD OPERATING PROCEDURES

When can the subject expect to receive payment? (Cannot be contingent upon completion of the study)

Please indicate WHEN subjects will be paid: e.g. each visit, at the 5, 17, and 28th visits, etc.

⇒Enter an unlimited amount of text.

Additional Comments: *⇒Enter an unlimited amount of text.*

Demographics of Anticipated Subject Population

Approximate the ethnic makeup of the population to be recruited (If demographics DOES NOT APPLY to this study, then click in the check box in the following question: "Unknown because study involves de-identified data/specimens". Please note: this option is only available to specific study types.) *NOTE: If you anticipate enrolling subjects with limited English proficiency ("LEP") (e.g. the investigator's practice is in an area with a known population of foreign-language speaking persons the investigator must obtain an informed consent form translated into the language(s) of the anticipated LEP population, with such translation being approved by BRANY IRB.

Unknown Demographics - Valid for SPECIFIC study types ONLY if demographic data is unavailable. Please call the BRANY IRB at 516.470.6900 if you have questions.

⇒Check one or more of the following items from the list of check boxes presented:

- *Unknown because study involves de-identified data/specimens*

Approximate Demographics of Anticipated Subject Population

% African American - Enter zero (0) if you do not anticipate including this population in the study.

⇒Enter a valid number. It must be ≥ 0 . It must be a whole number.

% Asian - Enter zero (0) if you do not anticipate including this population in the study.

⇒Enter a valid number. It must be ≥ 0 . It must be a whole number.

% Pacific Islander - Enter zero (0) if you do not anticipate including this population in the study.

⇒Enter a valid number. It must be ≥ 0 . It must be a whole number.

% Middle Eastern - Enter zero (0) if you do not anticipate including this population in the study.

⇒Enter a valid number. It must be ≥ 0 . It must be a whole number.

% Caucasian - Enter zero (0) if you do not anticipate including this population in the study.

⇒Enter a valid number. It must be ≥ 0 . It must be a whole number.

% Hispanic - Enter zero (0) if you do not anticipate including this population in the study.

⇒Enter a valid number. It must be ≥ 0 . It must be a whole number.

% Native American/First Nations - Enter zero (0) if you do not anticipate including this population in the study.

⇒Enter a valid number. It must be ≥ 0 . It must be a whole number.

% Other (specify below) - Enter zero (0) if you do not anticipate including this population in the study.

⇒Enter a valid number. It must be ≥ 0 . It must be a whole number.

Other Population(s) Description: *⇒Enter an unlimited amount of text.*



IRB STANDARD OPERATING PROCEDURES

Protections Against Undue Influence

Subjects recruited must be free of any outside influences while deciding whether to participate. Even in the absence of overt coercive or inducing statements, an element of coercion may be introduced because of the relationship between the potential subject and the investigator. Describe the steps taken to minimize the possibility of coercion or undue influence (check all that apply).

Choices:

- *Not applicable*
- *Subjects will be given information during the informed consent process without the bias or emphasis on potential risks or benefits*
- *Subjects will be reassured that they will receive no penalty if they decide not to participate*
- *Other steps (explain) ⇒ Enter an unlimited amount of text.*

I. Informed Consent Process

-- General Informed Consent Documents --

Informed Consent Documents -- Select one of the following for the consent document(s):

- **BRANY Classic (BRANY will assist with your IRB submission & ICF revisions)**
- **Additional PI (I confirmed study previously approved by BRANY IRB & consent on file at BRANY)**
- **ICF Preparation Services Requested with the PRE-Application Submitted (only available IF PRE-Application submitted for this study)**
- **ICF Attached (research site responsible for ALL modifications – attach ICF in BRANY format below; template ICF cannot be accepted) (Required)**

Select one of the following options from the drop down list presented:

Attach Informed Consent &/OR Assent document(s). You may attached up to twenty (20) separate documents

Consent Document Address - Please specify the address of the facility/site to appear in the Consent Form Document(s)

Please include:

Site name

Street, Suite/Floor

City, State/Province/Country, ZIP/Postal code

(Required) Enter an unlimited amount of text.

24 hour Phone Number of the facility/site to appear in the Consent Form Document(s) – Please include Area Code, include Country Code, if applicable. (Required) Enter one line of text.

Phone Number of the facility/site to appear in the Consent Form Document(s) - Please include Area Code, include Country Code, if applicable. (Required) Enter one line of text.

General Informed Consent Process

Consent Process

1. **Where will the consent process take place? ⇒ Enter an unlimited amount of text.**
2. **What opportunity will be afforded to the prospective subject (or the subject's legally authorized representative) to consider whether or not to participate? (check all that apply)**

Choices:



IRB STANDARD OPERATING PROCEDURES

- *Schedule screening visits that allow for adequate discussion of the research and alternatives*
- *Review informed consent form in detail with potential subject*
- *Provide opportunity for subject to digest information and come back with questions at a later time*
- *Mail consent document in advance of visit to allow extra time for review*
- *Other (please specify) - respond to question 3A.*
- *N/A (only if consent waiver is requested)*

2A. Other: ⇒Enter an unlimited amount of text.

3. How will it be determined that the subject (or the subject's legally authorized representative) understands what has been explained?

Choices:

- *N/A (only if consent waiver is requested)*
- *Have a conversation with the subject to assess understanding and document this conversation in the subject's research record (NOTE: asking the subject if s/he understands in the form of yes/no questions is not sufficient)*
- *Use the BRANY IRB Informed Consent Feedback Tool (available at www.branyirb.com)*
- *Other Method (describe) - respond to question 4A*
- *A Combination of the Methods (describe) - respond to question 4B*

3A. Other Method description: ⇒Enter an unlimited amount of text.

3B. Please describe the combination of methods you will use (e.g., if more than one, explain how research staff will determine which to use). ⇒Enter an unlimited amount of text.

4. Attach a copy of any relevant documentation templates or other tools you might use to make this assessment. ⇒Attach 1 to 10 files of type "Subject Materials" to this xForm.

FOR LONG TERM STUDIES (subject participation is greater than 1 year)

5. How will you determine the ongoing consent of subjects?

Choices:

- *Telephone contact - discussion reviewing informed consent details and reminding subject of their right to withdraw at any time*
- *Documented at scheduled visit - discussion reviewing informed consent details and reminding subject of their right to withdraw at any time*
- *Repeat the informed consent process (documented by obtaining a newly signed consent form)*
- *N/A - This application does not apply to a long term study OR consent waiver have been requested*

Certificate of Confidentiality

Does this research involve the collection of highly sensitive information about individually identifiable subjects?

Choices:

- *Information relating to sexual attitudes, preferences, or practices;*
- *Information relating to the use of alcohol, drugs or other addictive products;*
- *Information pertaining to illegal conduct;*
- *Information that if released could reasonably be damaging to an individuals' financial standing, employability, or reputation within the community;*
- *Information that would normally be recorded in a patient's medical record, and the disclosure of which could reasonably lead to social stigmatization or discrimination (e.g., HIV);*
- *Information pertaining to an individual's psychological well being or mental health;*



IRB STANDARD OPERATING PROCEDURES

- *Genetic Information (if the results will be made available to the site and/or subject).*
- *NOT APPLICABLE – This research does not involve the collection of highly sensitive information about individually identifiable subjects.*

For such sensitive research, the IRB may at its discretion require that the investigator obtain a Certificate of Confidentiality from the DHHS (federal funding is not a prerequisite). For studies not funded by DHHS the sponsor/investigator can request a Certificate of Confidentiality from FDA if there is an Investigational New Drug Application (IND) or an Investigational Drug Exemption (IDE). The purpose of the Certificate of Confidentiality is to protect against involuntary release of sensitive information about individual subjects for use in Federal, state, or local civil, criminal, administrative, legislative, or other legal proceedings.

Click -> [Certificates of Confidentiality](#) for additional information from the [NIH website](#).

Population Screening Questions

1. **Indicate the anticipated population of subjects to be included in the research (check all that apply):**

⇒*Check one or more of the following items from the list of check boxes presented:*

- *Male*
- *Female*

2. **Have members of minority groups been included in the study population whenever possible and scientifically desirable? ⇒*Select either 'Yes' or 'No'***

2a. **When NO, please explain: ⇒*Enter an unlimited amount of text.***

For each of the following questions, a Yes response will bring you to additional questions regarding the proposed subject population.

3. **Do you anticipate that you will recruit/enroll individuals from any of the following "vulnerable" populations listed, at your site?**

- **Vulnerable Populations: Mentally Ill, Institutionalized, Incompetent adults, Hospitalized, Poor/uninsured, Prisoners, Mentally Disabled, Chronic Condition, Pregnant women, Those in emergent care settings, Nursing home residents, Terminally ill, Limited or non-readers, Children/children who are wards, Emancipated Minors, Students of the PI/study staff, Students to be recruited in their educational settings (e.g. in class or at school), Employees of the research site, PI or Sponsor, etc.**

Vulnerable Populations ⇒*Select either 'Yes' or 'No'*

4. **Subjects Who Become (or Whose Partners Become) Pregnant**

Many protocols, especially those involving investigational agents, include plans for collecting data from female subjects who may become pregnant or partners of male subjects who may become pregnant. Please check your protocol carefully, as the IRB must make special determinations for the potential involvement of pregnant women in the data collection for this research.

Is there a plan for collection of data from Subjects/Partners Who Become Pregnant during this research study? (Required) ⇒*Select either 'Yes' or 'No'*

5. **Languages and Translations - Do you anticipate enrolling subjects whose primary language is not English? Translations** ⇒*Select either 'Yes' or 'No'*

6. **Will you include Adult Individuals who may lack capacity to consent or who require consent by a surrogate (legally authorized representative - LAR) in this study at your site? (Required)**

⇒*Select either 'Yes' or 'No'*

7. **Do you plan to include Incapacitated (Mental or Physical) patients in this study at your site? Incapacitated (Mental or Physical)** ⇒*Select either 'Yes' or 'No'*



IRB STANDARD OPERATING PROCEDURES

- 8. Do you plan to include Children in this study at your site? ⇒Select either 'Yes' or 'No'
- 9. Do you plan to include Pregnant Subjects in this study at your site? (Required)
⇒Select either 'Yes' or 'No'
- 10. Do you plan to include Women in Labor in this study at your site? ⇒Select either 'Yes' or 'No'
- 11. Do you plan to include Surgical Patients in this study at your site? ⇒Select either 'Yes' or 'No'
- 12. Do you plan to include Psychiatric Patients in this study at your site? ⇒Select either 'Yes' or 'No'

Subjects/Partners Who Become Pregnant

Provide the page or section number of the protocol that describes the provisions for collecting data from subjects/partners who may become pregnant during research participation. (Required)
⇒ Enter an unlimited amount of text.

Please indicate if you:

⇒Select *one* of the following options from the drop down list presented:

-
- Attached a separate consent form for subjects/partners who become pregnant with main consent form, or
- Will submit a separate consent form for subjects/partner who become pregnant in the event an applicable pregnancy occurs at your site.

For the research to be approvable you **MUST** confirm all three (3) of the following 1-3:

1) No inducements, monetary or otherwise, will be offered to terminate a pregnancy. (Required)

⇒Select either 'Yes' or 'No'

2) Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy. (Required)

⇒Select either 'Yes' or 'No'

3) Individuals engaged in the research will have no part in determining the viability of a neonate. (Required)

⇒Select either 'Yes' or 'No'

Vulnerable Populations

A. You indicated that you will recruit/enroll individuals from "vulnerable" populations at you site. Please select all that apply:

- | | |
|----------------------|-----------------------------------|
| • Mentally Ill | • Those in emergent care settings |
| • Institutionalized | • Nursing home residents |
| • Incompetent adults | • Terminally ill |
| • Hospitalized | • Limited or non-readers |
| • Poor/uninsured | • Children |
| • Prisoners | • Children who are wards |
| • Mentally Disabled | • Emancipated Minors |
| • Chronic Condition | • Students of the PI/study staff |
| • Pregnant women | |



IRB STANDARD OPERATING PROCEDURES

- *Students to be recruited in their educational settings (e.g. in class or at school)*
 - *Employees of the research site, PI or Sponsor*
 - *Others Vulnerable to Coercion (specify) - respond to question 3B.*
- B. Specify the Other "vulnerable" populations you will recruit/enroll.** ⇒Enter an unlimited amount of text.
- C. What is the justification for including each "vulnerable" category of subjects indicated above?**
⇒Enter an unlimited amount of text.
- D. Are the safeguards afforded to all subjects in the protocol sufficient to protect the "vulnerable" subjects indicated above?**
⇒Select either 'Yes' or 'No'
- E. If YES - What are the safeguards?** ⇒Enter an unlimited amount of text.
- F. If NO, what are the safeguards in the protocol, and what additional safeguards are needed?**
⇒Enter an unlimited amount of text.

Languages and Translations

- A. For which language(s) will you require translation?** ⇒Enter an unlimited amount of text.
- B. Who will provide translations?** ⇒Select one of the following options from the drop down list presented:
- *BRANY IRB Vendor*
 - *Sponsor/CRO*
- C. Describe the plan for conducting the consent discussion and ongoing communication with non-English speaking subjects:**
Choices:
- *Staff member fluent in foreign language*
 - *Use a certified medical interpreter*
 - *Other (specify)*
- D. Other (specify):** ⇒Enter an unlimited amount of text.

Adult Individuals May Lack Capability to Consent

- A. Who will decide whether an individual subject is competent to consent?** ⇒Enter an unlimited amount of text.
- B. How will this assessment be made?**
⇒Enter an unlimited amount of text.
- C. Will you obtain assent from adult participants who may lack capacity to consent?**
⇒Select either 'Yes' or 'No'
- D. No - Why not?** ⇒Enter an unlimited amount of text.
- E. Yes - What is the plan for obtaining the assent?**
- *assent form - must be submitted for IRB review*
 - *documented assent discussion*
 - *other (explain) - answer 5F*
- F. Other (explain):** ⇒Enter an unlimited amount of text.

Adult Individuals Who Require Surrogate Consent - consent by a Legally Authorized Representation (LAR)

- A. Does this study meet all of the following criteria?**
Need all 5 (five) for IRB to consider approval:



IRB STANDARD OPERATING PROCEDURES

- *There is a potential benefit over standard treatment*
- *Standard treatment is not being withheld*
- *There is no alternative standard treatment*
- *Enrollment in the study is in the best interest of the patient*
- *Participation in the research would not be contrary to the known wishes of the patient*

If the study DOES NOT meet ALL five (5) of the criteria listed, you will be required to Comment/supply further justification to the BRANY IRB in the following question.

B. Comments/Further Justification: ⇒Enter an unlimited amount of text.

Incapacitated Patients (Mentally or Physically)

A. By checking this box, you are stating the PI acknowledges this responsibility: ⇒Check one or more of the following items from the list of check boxes presented:

- *The PI is responsible to ensure appropriate legal consultation is obtained to determine who is an appropriate authorized representative for incapacitated (mental or physical) patients.*

Children

A. Ages of children involved in the research: ⇒Enter one line of text.

B. Are any of the children wards? ⇒Select either 'Yes' or 'No'

C. Children are Wards: has an advocate has been appointed?

When YES: answer question D.

When NO: answer question E.

⇒Select either 'Yes' or 'No'

D. Yes Advocate Appointed. Supply the Advocate's Name and Contact Information:

⇒Enter an unlimited amount of text.

E. No Advocate Appointed for Children who are wards: Why not?

⇒Enter an unlimited amount of text.

F. By checking this box, you are stating the PI acknowledges this responsibility:

⇒Check one or more of the following items from the list of check boxes presented:

- *Confirm that provisions will be made to solicit the consent of at least one parent or legal guardian (Note: BRANY IRB may, at its discretion, require permission of both parents).*

G. Obtain assent from: ⇒Select one of the following options from the list of radio buttons presented:

- *All children*
- *Some children*
- *Not obtaining assent*

H. Which children will assent be obtained from? ⇒Enter an unlimited amount of text.

I. How will assent be documented?

⇒Check one or more of the following items from the list of check boxes presented:

- *assent form*
- *not obtaining assent*
- *other (specify)*

J. Other (specify): ⇒Enter an unlimited amount of text.

K. What provisions will be made for soliciting the assent of the children? (check all that apply)

⇒Check one or more of the following items from the list of check boxes presented:

- *interview child without the parents*
- *interview child with the parents*
- *interview child with an impartial witness present (*required by BRANY)*
- *other (explain)*

L. Other (explain): ⇒Enter an unlimited amount of text.



IRB STANDARD OPERATING PROCEDURES

M. Will this research include any pregnancy testing for female minors of childbearing potential?

⇒Select either 'Yes' or 'No'

N. If YES - will parents/guardians be informed of positive pregnancy test results at your site?

Please select the answer that is in accordance with your state law.

⇒Select either 'Yes' or 'No'

-- Pregnant Subjects --

Pregnant Subjects

For the research to be approvable you *MUST* confirm all three (3) of the following 1-3:

1) No inducements, monetary or otherwise, will be offered to terminate a pregnancy. (Required)

⇒Select either 'Yes' or 'No'

2) Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy. (Required)

⇒Select either 'Yes' or 'No'

3) Individuals engaged in the research will have no part in determining the viability of a neonate. (Required)

⇒Select either 'Yes' or 'No'

Women in Labor

A. Check all that apply:

⇒Check one or more of the following items from the list of check boxes presented:

- *Pregnant women in labor will be approached for her informed consent*
- *Efforts will be made to obtain informed consent during a prenatal visit, if possible.*

B. Other consent issues/safeguards: *⇒Enter an unlimited amount of text.*

C. By checking this, you are stating the PI acknowledges this responsibility:

⇒Check one or more of the following items from the list of check boxes presented:

‡If the woman will be in active labor, consent will also be asked of a second person, typically her husband, father of the baby or woman's mother, or close relative accompanying her.

Surgical Patients

A. Check all that apply:

⇒Check one or more of the following items from the list of check boxes presented:

- *Efforts will be made to obtain written informed consent during pre-surgical testing visits, if possible*
- *Consent will be obtained on the day of surgery, but prior to sedation*

B. Other consent issues/safeguards: *⇒Enter an unlimited amount of text.*

Psychiatric Patients

A. Check all that apply:

⇒Check one or more of the following items from the list of check boxes presented:

- *If the patient is hospitalized during enrollment, I agree to contact the subject's primary psychiatrist or other attending physician before recruiting the subject*
- *I agree to tell patients that a research coordinator or other investigator in connection with the research will approach them*
- *I agree to have a third party independent of the study assess the subject's capacity to consent to participate prior to enrolling subjects with psychiatric illness affecting competency in the study (*required by BRANY)*



IRB STANDARD OPERATING PROCEDURES

J. Privacy and Confidentiality

Confidentiality Precautions - study data protection/security

1. What precautions will be used to maintain the confidentiality of identifiable health information

Choices:

- Paper based records will be kept in a secured location & only accessible to personnel involved in study
- Computer based files will only be made available to personnel in the study through the use of access privileges & passwords
- Prior access to any study-related information, personnel will be required to sign statements agreeing to protect the security and confidentiality of identifiable health information.
- Whenever feasible, identifiers will be removed from study-related information.
- Other precaution(s) (specify)

1a. Other precaution(s): *⇒Enter an unlimited amount of text.*

2. How will information about research participants be obtained? (check all that apply)

- Surveys
- Questionnaires
- Interview
- Direct Observation
- Performance of tests & procedures
- Other (specify)

2a. Other Way Information Obtained: *⇒Enter an unlimited amount of text.*

Participant Privacy Provisions = subject protection

1a. What provisions are in place to protect privacy interests of participants?

The IRB will assess the methods used to identify potential research subjects or to gather information about subjects in order to ensure that the privacy of individuals is not invaded.

Describe the methods in place to protect the privacy of participants (e.g. private interviews, use of barriers when subject is required to disrobe, private room for performing research interventions, consideration of whether teen subjects should be interviewed without parents when sensitive subject matter is involved):

Describe and/or attach description in questions 1a and/or 1b.

⇒Enter an unlimited amount of text.

1b. Protect Privacy Provisions Attachment *⇒Attach 1 to 5 files of type "Site Correspondence" to this xForm.*

2. Please enter number of years after close of study research data will be stored by the investigator? *A minimum of 3 years after close or as specified by the sponsor, whichever is longer. Please enter a whole number of years data will be stored.*

⇒Enter a valid number. It must be ≥ 3 . It must be a whole number.

3. HIPAA Training (check all that apply):

I have training in the fundamental requirements imposed by the privacy rule (HIPAA).

I will not enroll any subjects without first having them sign a research consent/authorization form that is compliant with the privacy rule (HIPAA)



IRB STANDARD OPERATING PROCEDURES

I will ensure that all patients and/or research subjects receive a privacy notice.

3a. If you left any of the 3 HIPAA boxes (in the preceding question) unchecked, you are required to explain why here: ⇒Enter an unlimited amount of text.

K. Local Research Context Evaluation

The IRB is responsible for understanding the community in which research occurs. Questions in this section are intended to provide a description of the community from which you will recruit your research subjects.

Describe your research setting and study site(s): (check all that apply)

⇒Check one or more of the following items from the list of check boxes presented:

- *Suburban;*
- *Urban (city);*
- *Rural;*
- *Hospital;*
- *Nursing Home;*
- *University;*
- *Clinic;*
- *Research Facility;*
- *Private Practice;*
- *Other (describe)*

Other research setting/site: ⇒Enter an unlimited amount of text.

Review statements below and select ALL that apply to your site:

You will be required to explain your choice(s).

⇒Check one or more of the following items from the list of check boxes presented:

- *Federally Funded Research is conducted at your site(s)*
- *Negative overall attitude towards conduct of research in you community*
- *Positive overall attitude towards conduct of research in you community*
- *Neutral overall attitude towards conduct of research in you community*
- *Specific community attitudes exist relative to research (religious, ethical, ethnic, or economic) that the IRB should be aware of*
- *Recent media focus on research in the community*
- *Certain circumstances exist where certain subject populations in your community may feel coerced into participating in a research study (e.g. poor and/or uninsured)*

Explain the choice(s) you made in the previous question: ⇒Enter an unlimited amount of text.

Hospital Questions

What is the name of the nearest hospital or medical center? ⇒Enter one line of text.

Approximately how many miles away (Round response to the nearest mile.)?

⇒Enter a valid number. It must be ≥ 0 . It must be a whole number.

Regulators

1. Does this organization/institution have an institutional review board/ethics committee?

⇒Select one of the following options from the list of radio buttons presented:



IRB STANDARD OPERATING PROCEDURES

- *Yes*
 - *No*
 - *Unknown*
2. Confirm that you are aware of applicable federal, state and local regulations/laws governing human subject research (e.g. 21CFR312, 21CFR812, 21CFR50, 54, 56, 45CFR46, state department of health regulations) ⇒*Select either 'Yes' or 'No'*
3. Are you aware of any changes to such regulations/laws in the past year?
⇒*Select one of the following options from the list of radio buttons presented:*
- *Yes*
 - *No*
 - *Unknown*

L. Billing Information

Billing Information: Party Responsible for BRANY Fees

Choices:

- **BRANY's Regulatory Department is assisting with this project's IRB submission & start up and will provide the BRANY IRB with appropriate billing information - BRANY Classics (ALL), Montefiore, Mount Sinai, NYC HHC, and Western Connecticut Health Network only!**
- **Payment HAS BEEN MAILED to BRANY via Check.
Payment to BRANY via Credit Card (Visa or MasterCard - contact BRANY IRB to process payment)**
- **Bill to Individual - Select Billing Contact in another page.**

If you are paying by check, the xForm will ask for check number and amount BEFORE asking about billing contact information. If you select Bill to Individual you will select the billing contact on another page and enter their contact information.

Check Payment

- **Check Has Been Sent To BRANY IRB**
- **Check Number:** ⇒*Enter one line of text.*
- **Check Amount:** ⇒*Enter a valid number. It must be ≥ 0.01 .*

Who is responsible for paying BRANY IRB Fees? Please select from the choices below.

If your study's billing contact is an individual OTHER than your study's:

- **Principal Investigator,**
- **Sponsor Contact (contact information entered earlier in this xForm),**
- **CRO Contact (contact information entered earlier in this xForm),**
- **Consent Form Contact (contact information entered earlier in this xForm),**
Select Other Contact.

When Other Contact is selected, you are required to complete the remaining questions on this page.

Billing Contact Information

BC1. Full Name: ⇒*Enter one line of text.*



IRB STANDARD OPERATING PROCEDURES

BC2. Title ⇒Enter one line of text.

BC3. Organization ⇒Enter one line of text.

BC4. Email ⇒Enter a valid e-mail address.

BC5. Phone ⇒Enter one line of text.

BC6. Fax ⇒Enter one line of text.

BC7. Full Address (please include street, suite, city, state/province/country, ZIP/postal code)
⇒Enter an unlimited amount of text.

M. Compensation for Injury

-- Compensation for Injury-Montefiore --

Compensation for Injury-IRB Only Studies - Montefiore

For IRB Only studies, BRANY IRB will require the PI to confirm that any language addressing Compensation for Injury for this study is consistent between the consent form and the study contract set forth between the study sponsor and research site.

Please select the appropriate choice for this study:

- a. *YOU MAY ONLY CHECK THIS OPTION IF YOU HAVE OBTAINED APPROVAL FROM THE OFFICE OF CLINICAL TRIALS*: Yes, the compensation for injury language in the consent form is consistent with that set forth in the study contract.**
- b. Contract is still under review. (NOTE: BRANY IRB will submit the proposed consent language to the Montefiore OCT and await reconciliation.)**
- c. No compensation for injury available. (NOTE: This can only be applicable in limited circumstances, like minimal risk studies such as chart reviews, etc.)**
- d. There is no sponsor or contract for this study.**

For selection a or b, you are required to supply language from the informed consent document relating to compensation for research related injury in the following question.

Your application will continue to be pre-screened by the BRANY IRB team so that it will be ready for the PI's conflict of interest disclosure and signature. It will be submitted to the next available BRANY IRB meeting after the Montefiore OCT provides confirmation that the consent language and contract are consistent. (Required)

Select one of the following options from the list of radio buttons presented:

When a or b: Please copy and paste the language from the informed consent document relating to compensation for research related injury here. Enter an unlimited amount of text.

-- Compensation for Injury --

Compensation for Injury-IRB Only Studies

For IRB Only studies, BRANY IRB will require the PI to confirm that any language addressing Compensation for Injury for this study is consistent between the consent form and the study contract set forth between the study sponsor and research site.

Please select the appropriate choice for this study: (Required)

Select one of the following options from the list of radio buttons presented:

Yes, the compensation for injury language in the consent form is consistent with that set forth in the study contract. ‡I am utilizing BRANY's contract negotiation services.



IRB STANDARD OPERATING PROCEDURES

There is no compensation for injury available.

Conflict of Interest: PI Entered Application

Conflict of Interest Disclosure Statement

PI Conflict of Interest Disclosure Statement - ANY change to the responses must be promptly reported to BRANY IRB.

Definitions:

Financial Interest: Anything of monetary value from a financially interested company, including but not limited to: officer's/director's fees; consulting fees; compensation for service on an Advisory Board (including scientific advisory boards); honoraria for Lectures/Teaching; gifts; other emoluments or "in kind" compensation such as travel and entertainment from a financially interested company (including those from a third party if the original source is a financially interested party), for any services not directly related to the reasonable costs of conducting the research as specified in the research agreement; equity interest of any kind and in any amount in a non-publicly or publicly traded Financially Interested Company (e.g. stocks, stock options, convertible notes, other ownership interests), including those for which the value cannot be determined through reference to publicly available prices, those for which the value may be affected by the outcome of the research, and those which represent a 5% or more interest in any one single entity; an intellectual property related to the proposed research, license fees, technology transfers, and/or current and future royalties from patents and copyrights; board or executive relationships related to the research (regardless of compensation); paid/reimbursed travel (meaning the occurrence and value of any paid/sponsored (i.e., sponsored travel is that which is paid on behalf of the Investigator and not reimbursed to the Investigator so that the exact monetary value may not be readily available), and/or reimbursed travel, whether in connection with an outside position or for consulting, lecturing, or service on a scientific advisory board, data safety monitoring board, steering committee for a clinical trial, executive committee for a clinical trial, or other committee for an outside entity, or for any other purpose including the purpose of the trip, the identity of the sponsor/organizer, the destination and the duration).

The term "Financial Interest" does not include:

- *Salary or other remuneration received from the institution/organization*
- *Grant support for salaries from the institution/organization*
- *Holdings in mutual funds or 401K/403B retirement funds;*
- *De minimus gifts whose aggregate value does not exceed \$100 per annum.*

Financially Interested Company: An entity whose financial interests could reasonably appear to be affected by the conduct or outcome of a research project. The term "entity" means any corporation, limited liability company, partnership, limited partnership, limited liability partnership, joint venture, business trust, or other business organization, and any not-for-profit organization, charity or foundation.

Related Party: Spouse, domestic partner & dependent children, siblings, parents, or equivalents by marriage, or other individuals residing in the household.

Significant Financial Interest: A Financial Interest that is over \$5,000, or is less than \$5,000, and also involves a non-financial role in a Financially Interested Company, or is less than \$5,000, and the value cannot be determined through reference to publicly available prices, if the value will be affected by the



IRB STANDARD OPERATING PROCEDURES

outcome of the research, or the value represents 5% or more interest in any one single entity, and is determined by the COIC to be related to the research.

Performed Any Work

- a. Within the last 12 months, have you or, to the best of your knowledge, has any related party **performed any work** (not directly related to the costs of conducting research) for a Financially Interested Company?
⇒Select either 'Yes' or 'No'

Received Compensation

- b. Within the last 12 months, have you or, to the best of your knowledge, has any related party **received compensation** (not directly related to the costs of conducting research) from a Financially Interested Company? Please answer Yes for paid/reimbursed travel (see definitions).
⇒Select either 'Yes' or 'No'

Board or Executive Relationship

- c. Do you or, to the best of your knowledge, does any related party maintain any **board or executive relationship** related to the research, regardless of compensation?
⇒Select either 'Yes' or 'No'

Anticipate Performing Any Work and/or Receiving Any Compensation

- d. Within the next 12 months, will you or, to the best of your knowledge, does any related party **anticipate performing any work and/or receiving any compensation** (not directly related to the costs of conducting research) from a Financially Interested Company? Please answer Yes for paid/reimbursed travel (see definitions).
⇒Select either 'Yes' or 'No'

Ownership: Stock, Stock Options or any other forms of Ownership

- e. Do you or, to the best of your knowledge, do any of your related parties **own stock, stock options or other forms of ownership** in a Financially Interested Company?
⇒Select either 'Yes' or 'No'

Intellectual Property

- f. Do you, or to the best of your knowledge, do any of your related parties have any **intellectual property rights** (e.g. named as inventor in an issued patent or patent application, license fees, technology transfer, current or future royalties from patents and copyrights)?
⇒Select either 'Yes' or 'No'

Department/Institution/Organization Have Financial Interest

- g. Does your **department/institution/organization** have a **financial interest** in the agent under investigation or in a company that could benefit from the study findings, or receive significant financial support from such a company?
⇒Select either 'Yes' or 'No'

Voluntarily Disclose Anything Else



IRB STANDARD OPERATING PROCEDURES

h. Do you want to voluntarily disclose anything else? ⇒Select either 'Yes' or 'No'

For any YES answer above, you will be required to respond to the corresponding questions of the Conflict Report Form, on the next xForm page(s).

Conflict Report - Individual Information

Full Name of Individual/Entity for whom interest is being reported: ⇒Enter one line of text.

Individual's relationship to You: ⇒Select one of the following options from the list of radio buttons presented:

- Self (Principal Investigator)
- Related party (spouse, domestic partner, dependent children, siblings, parents, equivalents by marriage or other individuals residing in the household)
- Other (specify)

To whom is the party related? ⇒Enter one line of text.

Other (specify): ⇒Enter one line of text.

Work Performed

a) Work performed within the last 12 months not directly related to the costs of conducting research (check ALL that apply):

Consultant/Advisor ⇒Select either 'Yes' or 'No'

Consultant/Advisor Sponsor/Entity name: ⇒Enter one line of text.

Employee ⇒Select either 'Yes' or 'No'

Employer Sponsor/Entity name: ⇒Enter one line of text.

Independent Contractor ⇒Select either 'Yes' or 'No'

Independent Contractor Sponsor/Entity name: ⇒Enter one line of text.

Officer/Director ⇒Select either 'Yes' or 'No'

Officer/Director Sponsor/Entity name: ⇒Enter one line of text.

Fiduciary Role ⇒Select either 'Yes' or 'No'

Fiduciary Role Sponsor/Entity name: ⇒Enter one line of text.

Other (specify) ⇒Select either 'Yes' or 'No'

Other (specify): ⇒Enter one line of text.

Other Sponsor/Entity name: ⇒Enter one line of text.

Compensation Received 1 of 3

b) Compensation received within the last 12 months not directly related to the costs of conducting research (check ALL that apply):

For each type of compensation you select, you will be required to enter the value and the sponsor/entity name (e.g., If you select Consulting Fees you will be required to enter the value received and the sponsor/entity name who you receive this compensation from.).

Consulting Fees ⇒Select either 'Yes' or 'No'

Consulting Fees Value \$ ⇒Enter one line of text.

Consulting Fees Sponsor/Entity name: ⇒Enter one line of text.

Honoraria (lectures, papers, teaching) ⇒Select either 'Yes' or 'No'

Honoraria Value \$ ⇒Enter one line of text.

Honoraria Sponsor/Entity name: ⇒Enter one line of text.

Salaries: ⇒Select either 'Yes' or 'No'

Salaries Value \$ ⇒Enter one line of text.

Salaries Sponsor/Entity name: ⇒Enter one line of text.



IRB STANDARD OPERATING PROCEDURES

Compensation Received 2 of 3

- B) Compensation received within the last 12 months not directly related to the costs of conducting research (check ALL that apply):**

For each type of compensation you select, you will be required to enter the value and the sponsor/entity name (e.g., If you select Officer's/Directors Fees you will be required to enter the value received and the sponsor/entity name who you receive this compensation from.).

Officer's / Director's fees ⇒Select either 'Yes' or 'No'

Officer's / Director's Fees Value \$ ⇒Enter one line of text.

Officer's / Director's fees Sponsor/Entity name: ⇒Enter one line of text.

Gifts / Gratuities (>\$100) ⇒Select either 'Yes' or 'No'

Gifts / Gratuities (>\$100) Value \$ ⇒Enter one line of text.

Gifts / Gratuities (>\$100) Sponsor/entity name: ⇒Enter one line of text.

Compensation for Service on Advisory Board ⇒Select either 'Yes' or 'No'

Compensation for Service on Advisory Board value \$ ⇒Enter one line of text.

Compensation for Service on Advisory Board Sponsor/Entity name: ⇒Enter one line of text.

Compensation Received 3 of 3

- b) Compensation received within the last 12 months not directly related to the costs of conducting research (check ALL that apply):**

For each type of compensation you select, you will be required to enter the value and the sponsor/entity name (e.g., If you select Royalty payments you will be required to enter the value received and the sponsor/entity name who you receive this compensation from.).

Royalty Payments ⇒Select either 'Yes' or 'No'

Royalty Payments value \$ ⇒Enter one line of text.

Royalty Payments Sponsor/Entity name: ⇒Enter one line of text.

Paid/Reimbursed Travel ⇒Select either 'Yes' or 'No'

Paid/Reimbursed Travel Value \$ ⇒Enter one line of text.

Name of entity providing paid/reimbursed travel: ⇒Enter one line of text. **Other**

Compensation ⇒Select either 'Yes' or 'No'

Other Compensation type (specify): ⇒Enter one line of text.

Other Compensation value \$ ⇒Enter one line of text.

Other Compensation Sponsor/Entity name: ⇒Enter one line of text.

Board or Executive Relationship

- c) Board or executive relationship related to research, regardless of compensation (check ALL that apply):**

For each type you select, you will be required to enter the value and the sponsor/entity name (e.g., If you select Board Member, you will be required to enter the value received and the sponsor/entity name who you receive this compensation from.).

Board Member ⇒Select either 'Yes' or 'No'

Board Member value \$ ⇒Enter one line of text.

Board Member Sponsor/Entity name: ⇒Enter one line of text.

Director ⇒Select either 'Yes' or 'No'

Director value \$ ⇒Enter one line of text.

Director Sponsor/Entity name: ⇒Enter one line of text.



IRB STANDARD OPERATING PROCEDURES

- Trustee** ⇒Select either 'Yes' or 'No'
Trustee value \$ ⇒Enter one line of text.
Trustee Sponsor/Entity name: ⇒Enter one line of text.
Other Relationship ⇒Select either 'Yes' or 'No'
Other Relationship (specify) ⇒Enter one line of text.
Other Relationship value \$ ⇒Enter one line of text.
Other Relationship Sponsor/Entity name: ⇒Enter one line of text.

Anticipated Work and/or Receipt of Compensation

- d) **Anticipated work and/or receipt of compensation (within the NEXT 12 months) not directly related to the costs of conducting research (specify any anticipated paid/reimbursed travel here).**

- Sponsor/Entity name:** ⇒Select either 'Yes' or 'No'
In what capacity? ⇒Enter one line of text.
Anticipated Compensation in Next Year value \$ ⇒Enter one line of text.

Publicly Traded Companies

- e) **Stock, stock options and other forms of ownership: Please respond to the following for each entity, including those for which the value cannot be determined through reference to publicly available prices, those for which the value may be affected by the outcome of the research, and those which represent a 5% or more interest in any one (1) single entity.**

- Publicly Traded Stock** ⇒Select either 'Yes' or 'No'
Publicly Traded Stock # of Shares ⇒Enter one line of text.
Publicly Traded Stock Entity name: ⇒Enter one line of text.
Publicly Traded Stock Options ⇒Select either 'Yes' or 'No'
Publicly Traded Stock Options # of Shares ⇒Enter one line of text.
Publicly Traded Stock Options Entity name: ⇒Enter one line of text.
Publicly Traded Other ⇒Select either 'Yes' or 'No'
Publicly Traded Other (specify) ⇒Enter one line of text.
Publicly Traded Stock Options Other # of Shares ⇒Enter one line of text.
Publicly Traded Stock Options Entity name: ⇒Enter one line of text.

Non-Publicly Traded Companies

- e) **Stock, stock options and other forms of ownership: Please respond to the following for each entity, including those for which the value cannot be determined through reference to publicly available prices, those for which the value may be affected by the outcome of the research, and those which represent a 5% or more interest in any one (1) single entity.**

- Non-Publicly Traded Stock** ⇒Select either 'Yes' or 'No'
Non-Publicly Traded Stock value \$ ⇒Enter one line of text.
Non-Publicly Traded Stock % Share ⇒Enter one line of text.
Non-Publicly Traded Stock Entity name: ⇒Enter one line of text.
Non-Publicly Traded Stock Options ⇒Select either 'Yes' or 'No'
Non-Publicly Traded Stock Options value \$ ⇒Enter one line of text.
Non-Publicly Traded Stock Options % Share ⇒Enter one line of text.
Non-Publicly Traded Stock Options Entity name: ⇒Enter one line of text.
Non-Publicly Traded Other Ownership ⇒Select either 'Yes' or 'No'
Non-Publicly Traded Other Ownership Description ⇒Enter one line of text.



IRB STANDARD OPERATING PROCEDURES

Non-Publicly Traded Other Ownership value \$ ⇒Enter one line of text.

Non-Publicly Traded Other Ownership % Share ⇒Enter one line of text.

Non-Publicly Traded Other Ownership Entity name: ⇒Enter one line of text.

Intellectual Property Related to the Proposed Research

f) Intellectual Property Related to the Proposed Research: e.g. named as an inventor in an issued patent or patent application, license fees, technology transfers, current or future royalties from patents and copyrights.

Intellectual Property Right ⇒Select either 'Yes' or 'No'

Intellectual Property Right Description ⇒Enter an unlimited amount of text.

Intellectual Property Right value (if known) \$

If value is NOT known, enter N/A. ⇒Enter one line of text.

Department/Institution/Organization's Financial Interest

g) Is there Department/Institution/organizational Financial Interest in the agent under investigation or in a company that could benefit from the study findings, or receipt of significant financial support from such a company?

⇒Enter an unlimited amount of text.

Describe the financial interest or support (include amount/\$ value if applicable):

If value is NOT known or applicable, enter N/A. ⇒Enter one line of text.

Voluntary Disclosure

h) Voluntary Disclosure: describe ⇒Enter an unlimited amount of text.

Conflict Report – Comments

i) Comments (optional): ⇒Enter an unlimited amount of text.

Any change to the preceding responses must be promptly reported to BRANY IRB.

ATTESTATION - Conflict Report

I certify that I have read the BRANY policy regarding Financial Conflict of Interest in Research (available in the current BRANY IRB Standard Operating Procedures). I hereby attest that with respect to the aforementioned clinical research project/application that the above information is accurate and complete, and that I will report any new significant financial interests within 30 days of acquisition or discovery.

⇒Check one or more of the following items from the list of check boxes presented:

Check box to confirm Conflict Report attestation specified above

Principal Investigator's Statement of Compliance

The proposed investigation involves the use of human subjects. I am submitting this form with a description of my project, prepared in accordance with organizational/institutional policy for the protection of human subjects participating in the research. I understand BRANY IRB's policy concerning research involving human subjects and:

- I will not engage in any research involving human subjects without obtaining prior IRB approval;
- I agree that the BRANY IRB approved consent form must be the only consent form used in this study and must be used for every patient prior to enrollment;
- I agree to report to BRANY IRB any unanticipated effects on subject that become apparent during the course or as a result of experimentation and the actions taken as a result; all serious



IRB STANDARD OPERATING PROCEDURES

adverse events must be reported to the IRB within 5 days, unless otherwise agreed to by IRB administration;

- I agree to cooperate with members of BRANY IRB charged with the continuing review of this project and agree to submit continuing review applications in a timely fashion;
- I agree to obtain prior approval from BRANY IRB before amending or altering the scope of the project or implementing changed to the approved protocol or consent form;
- I agree to maintain documentation of consent forms and continuing review applications;
- I agree that all advertising must be approved by the IRB prior to submission to any agencies and before posting;
- I agree to notify BRANY IRB of study termination and/or change in the status of the study;
- I agree to maintain records for a minimum of 3 years after closure, or as specified by the sponsor of the research, whichever is longer;
- I will ensure that research subjects are given referrals for needed health care during the research or for follow-up after the research.
- I have received and am familiar with the BRANY IRB Standard Operating Procedures/Research Manual.

I further understand that:

- Failure to comply with any of the above, with the BRANY IRB's Standard Operating Procedures, or with any applicable regulations may result in immediate closure of this study, which is reportable to my organization/institution, FDA and/or OHRP.
- This research project will be subject to routine audits by BRANY QA department, and at the discretion of the BRANY Institutional Official, the results of such audits may be shared with the appropriate Department Chairpersons, the Organization/Institutional Official and/or Sponsor.

NOTE: Investigators are referred to the BRANY IRB's Standard Operating Procedures for a complete statement of institutional policy and procedures regarding research and human subjects.

⇒Check one or more of the following items from the list of check boxes presented:

- *Check box to attest you agree to the Principal Investigator's Statement of Compliance*

Research Application Stages

You have completed Research Application Data Entry Stage. xForm Stages:

1. Data Entry (by the site initiating the research application AFTER receiving email from BRANY the study is set-up in IRBManager).
2. PI Notify and Signature (including the PI's BRANY Conflict of Interest questions and PI Statement of Compliance attestation). The PI will receive an Email alert and this xForm will be listed in their My IRBManager Dashboard "There are # xForms awaiting your attention."
3. BRANY Processing (BRANY Classic Regulatory Processing and/or Alert IRB) - BRANY reviews content and rejects/sends back to site if information incorrect and/or missing)
4. Event is added to IRBManager for processing and future IRB Meeting date when the research application contents are complete.

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IRB STANDARD OPERATING PROCEDURES

Appendix 12 – BRANY IRB Standard Operating Procedures

CIRB Sponsor Request for IRB Review Form

- Changes may not be initiated without prior IRB approval except when necessary to eliminate immediate hazards to subjects.
• This form is NOT for reporting Adverse Events, Deviations, or study closure.
• INCOMPLETE submissions will result in delayed processing.
• If you have any questions, please contact BRANY IRB staff.

- Advertisement(s) – All ads must be submitted in their final format.
• Clinical trial Web site
• Print advertisement
• Flyer
• Internet ad
• Press Release – Specify intended audience: _____

- Protocol Amendment(s)/Update(s) to the Investigator’s Brochure
• Version/Date: _____
• Attach a detailed summary of changes (*required*)
• Attached is revised consent version:

- Consent form revision (without amendment to protocol/investigator’s brochure)
• Version/Date: _____
• What is the rationale/justification for this revision? _____
• Attach a detailed summary of changes (*required*)
• Attach file in Word-compatible format with tracked/highlighted changes

- Translation
• Translation type (e.g., consent form, subject diary, advertisement, etc.):
• Attach a certificate of accuracy (*required*)

Unanticipated Problem Involving Risks to Participants or Others

- Attach documentation supporting the event is unexpected, related to the research, and suggests that subjects/others are at a greater risk than was previously known or recognized? (e.g., involves harm to one or more subjects/others, or placed one or more subjects/others at increased risk of harm) (*required*)

- A report of modifications initiated without prior IRB approval to eliminate immediate hazards to the patient. Please provide supporting documentation and indicate whether this report was consistent with assuring patient welfare.

- Other: _____

Printed Name and Signature of Submitter

Date

Please complete and return to the BRANY IRB Office: 1981 Marcus Ave., Ste. 210, Lake Success, NY 11042, or fax # 516-470-6903, or email to info@brany.com.

Version: 08.06.13



IRB STANDARD OPERATING PROCEDURES

Appendix 13 – BRANY IRB Standard Operating Procedures

Reportable Event Form [xForm #16]

Reportable Event Data Entry

-- User Access Form Screener --

BRANY System User Access Form

For xForm submissions to be valid, a copy of the signed, dated, completed (including attestation box checked off that you read the included BRANY compliance with 21 CFR Part 11) BRANY System User Access Form **MUST** be on file at BRANY for:

- the Principal Investigator of the study.
- the person adding a xForm into *IRBManager*, i.e. you.

EACH person that creates, submits and/or authorizes a xForm in *IRBManager* is **required** to have a signed, completed (including attestation box checked off that you read the included BRANY compliance with 21 CFR Part 11) copy of the BRANY System User Access Form on file with BRANY.

If the BRANY System User Access Form is *NOT* on file at BRANY and *NOT* included with this submission, this xForm **WILL BE REJECTED****

Principal Investigator - BRANY System User Access Form Status

Is a signed, dated, completed (attestation box checked off that you read BRANY policy included with the form) copy of a BRANY System User Access Form on file for the **PRINCIPAL INVESTIGATOR** listed above?

⇒Select *one* of the following options from the drop down list presented:

- No - submitting with this xForm submission
- Yes - on file at BRANY

xForm Submitter (You) - BRANY System User Access Form Status

Is a signed, dated, completed (attestation box checked off that you read BRANY policy included with the form) copy of a BRANY System User Access Form on file for **YOU**, the **xForm submitter**?

⇒Select *one* of the following options from the drop down list presented:

- No - submitting with this xForm submission
- Yes - on file at BRANY

-- PI User Access Form Attachment --

Principal Investigator's BRANY Systems User Access Form

Attach Principal Investigator's signed, dated, completed (attestation box checked off that you read BRANY policy included with the form) BRANY Systems User Access Form. Click on the blue BRANY System User Access Form hyperlink for a copy of the user access form. Complete, sign and scan to an electronic document (e.g. PDF) so it can be attached to this xForm page.

⇒Attach a file of type "User Access Form BRANY Systems" to this xForm.

-- Submitter User Access Form Attachment --

xForm Submitter/Your BRANY Systems User Access Form



IRB STANDARD OPERATING PROCEDURES

Attach **YOUR** signed, dated, completed (attestation box checked off that you read BRANY policy included with the form) [BRANY Systems User Access Form](#). Click on the blue [BRANY System User Access Form](#) hyperlink for a copy of the user access form. Complete, sign and scan to an electronic document (e.g. PDF) so it can be attached to this xForm page.

⇒ Attach a file of type "User Access Form BRANY Systems" to this xForm.

-- Event Submission Type --

Please read **ALL** The Definitions **BEFORE** Selecting the Event Type

The following guidance documents are available on the BRANY IRB Forms and Downloads page:

- *Information Sheet for Researchers - Reportable Events*
- *Information Sheet for Researchers - Unanticipated Problems*

“Protocol Exception”

A deviation that has been submitted to the IRB for review, and has been approved by the IRB prior to initiation.

"Serious Adverse Events (SAEs)" include, but are not limited to events, that are:

- (a) Fatal;
- (b) Life threatening or potentially life threatening;
- (c) Result in permanent disability;
- (d) A congenital anomaly;
- (e) Require inpatient hospitalization or prolongation of hospitalization stay;
- (f) Any additional adverse events, which the Investigator considers significant;
- (g) Any unanticipated device effects.

“Protocol Deviation”

Any temporary alteration/modification to the IRB-approved protocol. The protocol may include the detailed protocol, protocol summary, consent form, recruitment materials, questionnaires, and any other information relating to the research study. Deviations can be major or minor.

“Major Protocol Deviation”

A deviation that affects subject safety, rights, welfare, or data integrity. Examples of major protocol deviations include (but are not limited to):

- *Failure to obtain informed consent (i.e., no documentation of informed consent, consent obtained after study procedures were initiated)*
- *Enrolling subject who does not meet inclusion/exclusion criteria*
- *Use of study procedures not approved by the IRB*
- *Failure to report serious adverse events to the IRB and/or sponsor (per applicable requirements)*
- *Failure of subject to show up for a study appointment that results in missing treatment*



IRB STANDARD OPERATING PROCEDURES

- *Failure to perform a required study procedure or lab test that could affect subject safety or integrity of study data (e.g., procedure or lab test results needed to determine eligibility for the research)*
- *Error in dispensing or dosing of drug/study medication, whether committed by subject or study team*
- *Error involving use of device*
- *Study visit conducted outside of required timeframe, only if it affects subject safety*
- *Failure to follow safety monitoring plan*
- *Enrollment of subjects after IRB-approval of study expired*

“Minor Protocol Deviation”

A deviation that does not affect subject safety, rights, welfare, or data integrity. Examples of minor protocol deviations include (but are not limited to):

- *Missing original signed and dated consent form (only photocopy available)*
- *Inappropriate documentation of informed consent, including:*
 - *Copy not given to the person signing the consent form*
 - *Someone other than the subjects dated the consent form*
 - *Expired consent used, but the version letter is identical to the currently approved consent form.*
- *Deviations from the approved study procedure that do not affect subject safety or data integrity*
- *Study procedure conducted out of sequence*
- *Omitting an approved portion of the protocol*
- *Failure to perform a required lab test*
- *Missing lab results*
- *Study visit conducted outside of required timeframe*
- *Failure of subject to return study medication*

“Unanticipated Problems Involving Risks to Participants or Others”

Any event that:

(1) is unexpected

(2) suggests that participants or others are at greater risk than was previously known or recognized, and

(3) is related to the research procedures

Definitions:

- **Unexpected:** An event is “unexpected” when its specificity and severity are not accurately reflected in the informed consent document or other information available (e.g., protocol, investigator’s brochure)
- **Related to the research procedures:** An event is “related to the research procedures” if in the opinion of the principal investigator, it was more likely than not to be caused by the research procedures or if it is more likely that not that the event affects the rights and welfare of current participants.

“Unanticipated Adverse Device Effect (UADE)” - any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

What type of event are you reporting, per definitions on this page - Please select ALL that apply:

The following guidance documents are available on the BRANY IRB Forms and Downloads page:



IRB STANDARD OPERATING PROCEDURES

- **Information Sheet for Researchers - Reportable Events**
- **Information Sheet for Researchers - Unanticipated Problems**

Notes:

- Minor deviations should NOT be reported to the BRANY IRB with this xForm (see definition below).
- You cannot select both "Deviation" choices nor both "Unanticipated..." choices.
- You can combine "Deviation" with either of the two "Unanticipated..." choices.
- You can combine Serious Adverse Event with either of the two "Unanticipated..." choices.
- Protocol Exception nor NONE OF THE ABOVE cannot be selected with any other choices.

If you have any questions whether an event is reportable to the BRANY IRB and/or which event type to select, please contact Svetlana Abramova (516.470.6929).

(Required) (List Box/At least 1 selection)

Major Deviation

Minor Deviation

Serious Adverse Event

Protocol Exception

Unanticipated Problem Involving Risks to Subjects or Others

Unanticipated Adverse Device Effect

NONE OF THE ABOVE

-- Event Description --

Reportable Event - For reporting problems, deaths and injuries that require prompt reporting to the IRB.

- **Event Date** ⇒ Enter a valid date.
- **Subject Initials/Code#** ⇒ Enter one line of text.
- **Subject Age** ⇒ Enter a valid number. It must be ≥ 0 . It must be ≤ 200 . It must be a whole number.
- **Select Years or Months or Days for Subject Age:** ⇒ Select *one* of the following options from the drop down list presented:
 - Years
 - Months
 - Days
- **Location Event Occurred** ⇒ Select *one* of the following options from the drop down list presented:
 - Internally (at your site)
 - Externally (at another site conducting the study)

-- Detailed Event Description --



IRB STANDARD OPERATING PROCEDURES

- **Please provide a full description of the activities leading to the problem, and the type and nature of the problem. *You are required to describe below and/or in a separate, attached document.***
⇒Enter an unlimited amount of text.
- **Event Description Attachment**
⇒Attach a file of type "Site Correspondence" to this xForm.

-- Actions Taken --

- **Describe the actions taken in response to the problem, including measures (corrective actions) taken to ensure that similar problems do not occur in the future. *You are required to describe below and/or in a separate, attached document.***
⇒Enter an unlimited amount of text.
- **Actions Taken Description Attachment**
⇒Attach a file of type "Site Correspondence" to this xForm.

-- Current Subject Status in Relation to Reported Event --

Current Status of the Subject in Relation to the Reported Event:

For example:

- **Is the subject still in the study?**
- **Has the subject experienced any adverse events or other problems in relation to the reported event?**

You are required to describe below and/or in a separate, attached document.

⇒Enter an unlimited amount of text.

Current Status of the Subject Description Attachment

⇒Attach a file of type "Site Correspondence" to this xForm.

-- Event Deviation --

- **Is this event a Deviation from the IRB approved protocol, IRB policy, the IRB's requirements for this study, or regulatory requirements?**
⇒Select either 'Yes' or 'No'

-- Event Unexpected --

- **Event Unexpected?** Was the reported event *unexpected* in terms of *nature, severity, or frequency* given the research procedures that are described in the protocol related documents such as the protocol, investigator's brochure, and informed consent document?
⇒Select either 'Yes' or 'No'
- **When **Yes**, has the event occurred in any other subjects (How many subjects? How many times? etc.)? When **No**, explain where the event is described in study documents (Specify the document title, section/pages, etc.).**
⇒Enter an unlimited amount of text.

-- Subjects at Greater Risk --

- **Subjects at Greater Risk?** *Does this reported event suggest that subjects/others are at a greater risk than was previously known or recognized?* (e.g., involves harm to one or more subjects/others, or placed one or more subjects/others at increased risk of harm)



IRB STANDARD OPERATING PROCEDURES

- When **Yes**, you will be required to explain in the following question.
 - When **No**, press **Next** to continue.
- ⇒Select either 'Yes' or 'No'

- When **Yes**, explain why subjects are at greater risk. ⇒Enter an unlimited amount of text.

-- Event Related to Research --

- **Was this event related or probably Related to the Research?** An event is "*related to the research procedures*" if, *in the opinion of the PI*:
 - the event was more likely than not to be caused by the research procedures; **OR**
 - it is more likely than not that the event affects the rights and welfare of current participants.

NOTE

- **All protocol deviations should be designated as related to the research.**
- **All medication and/or dosing errors/deviations should also be designated as related to the research.**

When **Yes**, you will be required to answer the remaining questions on this page. When **No**, press **Next** to continue.

⇒Select either 'Yes' or 'No'

- When **Yes**, explain why event is **Related to Research**. ⇒Enter an unlimited amount of text.
- When **Yes**, indicate the *degree of relationship to the research*.
⇒Select *one* of the following options from the drop down list presented:
 - Definitely
 - Probably
 - Possibly

-- Adverse Device Effect --

- **Unanticipated Adverse Device Effect?** Does this event involve an *unanticipated adverse device effect*? When **Yes**, you will be required to explain below. When **No**, press **Next** to continue.
⇒Select either 'Yes' or 'No'
- When **Yes**, explain the *unanticipated adverse device effect*.
⇒Enter an unlimited amount of text.

-- Study Data Integrity --

- **Did this event affect the integrity of the study data?** When **Yes**, you will be required to explain in the following question. When **No**, press **Next** to continue.
⇒Select either 'Yes' or 'No'
- When **Yes**, explain affect on Integrity of the Study Data.
⇒Enter an unlimited amount of text.

-- Is This Event A Serious Adverse Event? --

- **Is this event a Serious Adverse Event - **Serious Adverse Events (SAEs)** include, but are not limited to events, that are:**
 - (a) **Fatal;**
 - (b) **Life threatening or potentially life threatening;**
 - (c) **Result in permanent disability;**
 - (d) **A congenital anomaly;**



IRB STANDARD OPERATING PROCEDURES

- (e) **Require inpatient hospitalization or prolongation of hospitalization stay;**
- (f) **Any additional adverse events, which the Investigator considers significant;**
- (g) **Any unanticipated device effects.**

When **Yes**, you will be required to answer additional questions on another page.

⇒Select either 'Yes' or 'No'

-- Serious Adverse Event Details --

- **Report Type**
⇒Select *one* of the following options from the drop down list presented:
 - Initial
 - Follow-up (Supply Follow-Up#)
 - Other (Explain)
- **If Follow-Up is selected, you are required to supply the Follow-Up#** ⇒Enter one line of text.
- **If Other Report Type is selected, you are required to explain "Other"** ⇒Enter an unlimited amount of text.
- **Seriousness:**
⇒Select *one* of the following options from the list of radio buttons presented:
 - Fatal
 - Immediately Life Threatening
 - Required/prolonged hospitalization
 - Congenital Anomaly
 - Permanent Disability
 - Important medical event requiring intervention to prevent the outcomes listed in this question.
- **Outcome:**
⇒Select *one* of the following options from the list of radio buttons presented:
 - Fatal
 - Resolved
 - Resolved with sequelae
 - Not Resolved
 - Unknown

-- Modifications Needed --

- **Are Modifications Needed?** - Does the Consent Form *or* the Research Project need to be modified? When **Yes**, you will be required to describe proposed changes below and/or in a separate, attached document. When **No**, press **Next** to continue.
⇒Select either 'Yes' or 'No'
- **When Yes, describe proposed changes below and/or in a separate, attached document.**
⇒Enter an unlimited amount of text.
- **Proposed changes description attachment** ⇒Attach 1 to 5 files of type "Site Correspondence" to this xForm.
- **Does Not Require Report to BRANY**

-- Site Verify --

We need you to verify the following...

You selected the following responses regarding this Reportable Event:



IRB STANDARD OPERATING PROCEDURES

- Is this event a Deviation from the IRB approved protocol/policy/regulations/requirements? = **NO**
- Is the Event Unexpected? = **NO**
- Are Subjects at Greater Risk? = **NO**
- Was this event related or probably Related to the Research? = **NO**
- Is this event a Serious Adverse Event? = **NO**

Is this correct?

⇒Select either 'Yes' or 'No'

-- Yes - Correct --

You said the responses to the following questions in this xForm submission are correct:

- Is this event a Deviation from the IRB approved protocol? = **NO**
- Is the Event Unexpected? = **NO**
- Are Subjects at Greater Risk? = **NO**
- Was this event related or probably Related to the Research? = **NO**
- Is this event a Serious Adverse Event? = **NO**

You are **not required** to report an event of this nature to the BRANY IRB.

This xForm will be *closed as complete* **AFTER** your PI authorizes/signs the xForm.

-- No - Need to Modify --

You said **at least one (1)** of the **responses** to the following questions is **incorrect**:

- Is this event a Deviation from the IRB approved protocol? = **NO**
- Is the Event Unexpected? = **NO**
- Are Subjects at Greater Risk? = **NO**
- Was this event related or probably Related to the Research? = **NO**
- Is this event a Serious Adverse Event? = **NO**

You need to *modify* the question(s) on this xForm that have the incorrect response by:

1. Click **Save for Later**;
2. Re-open the xForm (via study's **xForms(#)** *OR* My *IRBManager* Dashboard **unsubmitted xForms**);
3. Re-read **EACH** question carefully;
4. Modify question(s) where needed.

-- Verify Minor Deviation Verify --

You indicated that you want to report a **Minor Protocol deviation** (see definitions below).

Is this correct? (Required)

⇒Select either 'Yes' or 'No'

“Protocol Deviation”

Any temporary alteration/modification to the IRB-approved protocol. The protocol may include the detailed protocol, protocol summary, consent form, recruitment materials, questionnaires, and any other information relating to the research study. Deviations can be major or minor.

“Major Protocol Deviation”



IRB STANDARD OPERATING PROCEDURES

A deviation that affects subject safety, rights, welfare, or data integrity. Examples of major protocol deviations include (but are not limited to):

- *Failure to obtain informed consent (i.e., no documentation of informed consent, consent obtained after study procedures were initiated)*
- *Enrolling subject who does not meet inclusion/exclusion criteria*
- *Use of study procedures not approved by the IRB*
- *Failure to report serious adverse events to the IRB and/or sponsor (per applicable requirements)*
- *Failure of subject to show up for a study appointment that results in missing treatment*
- *Failure to perform a required study procedure or lab test that could affect subject safety or integrity of study data (e.g., procedure or lab test results needed to determine eligibility for the research)*
- *Error in dispensing or dosing of drug/study medication, whether committed by subject or study team*
- *Error involving use of device*
- *Study visit conducted outside of required timeframe, only if it affects subject safety*
- *Failure to follow safety monitoring plan*
- *Enrollment of subjects after IRB-approval of study expired*

“Minor Protocol Deviation”

A deviation that does not affect subject safety, rights, welfare, or data integrity. Examples of minor protocol deviations include (but are not limited to):

- *Missing original signed and dated consent form (only photocopy available)*
- *Inappropriate documentation of informed consent, including:*
 - *Copy not given to the person signing the consent form*
 - *Someone other than the subjects dated the consent form*
 - *Expired consent used, but the version letter is identical to the currently approved consent form.*
- *Deviations from the approved study procedure that do not affect subject safety or data integrity*
- *Study procedure conducted out of sequence*
- *Omitting an approved portion of the protocol*
- *Failure to perform a required lab test*
- *Missing lab results*
- *Study visit conducted outside of required timeframe*
- *Failure of subject to return study medication*

-- Yes - Minor Deviation --

Minor Protocol Deviation

You are not required to report a *Minor Deviation* as to BRANY IRB using this xForm.

*****Minor Deviations must be reported via the Minor Deviation Log at the time of Continuing Review*****

Please click close this form and DELETE it from IRBManager.

If you proceed and enter your password to submit, your PI will be required to authorize/sign this xForm in order to close it and remove it from both your and your PI's **IRBManager** dashboard.

-- No - NOT Minor Deviation --

You need to **modify** the question on this xForm that has the incorrect response:

1. *Click Save for Later;*
2. *Re-open the xForm (via study's xForms(#)) OR My IRBManager Dashboard *unsubmitted xForms*);*
3. *Re-read EACH question carefully;*
4. *Modify question(s) where needed.*

OR...



IRB STANDARD OPERATING PROCEDURES

1. Click the browser's *Back* button *TWO TIMES*, until you arrive at the page with the Protocol Deviation: Is this event a MAJOR or a Minor Protocol Deviation? question.
2. Modify question(s) where needed.

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IRB STANDARD OPERATING PROCEDURES

Appendix 14 – BRANY IRB Standard Operating Procedures

ARCHIVED – IND Safety Report Submission Form



IRB STANDARD OPERATING PROCEDURES

Appendix 15 – BRANY IRB Standard Operating Procedures

Request for IRB Review of Modifications Form [xForm #01]

-- Submission Review Instructions --

- **BRANY IRB File #** ⇒Displays the protocol code.
- **Site:** ⇒Display the name of this protocol site.
- **Protocol Title** ⇒Displays the protocol title.
- **Sponsor:** ⇒Display the sponsor for this protocol.
- **Sponsor Protocol #** ⇒Display the Sponsor's protocol name for this protocol.
- **Principal Investigator** ⇒The name and contact information of the Investigator for this protocol will be displayed.
- **xForm Submitter:** ⇒Displays the name of the user who submitted this form.

This xForm **IS** the ***BRANY IRB Request for IRB Review form*** and as such:

- is **required** for **ALL** requests for review of study modifications **and/or** study personnel additions.
- is **required** to be authorized/signed by the study's Principal Investigator (PI).

Please **CAREFULLY READ EACH informational Instruction** on **THIS** page! The following items are **NOT ELIGIBLE** to be submitted via the 01-Modification/Request for IRB Review xForm.

- **Change in PI:** complete and submit the paper **Change in PI** form. <-- click **blue** hyperlink for a copy of the paper form to be completed and submitted (faxed/mailed to BRANY IRB).
- **Status Changes: Study Closure or Enrollment Closure** Has its own xForm! Submit a copy of the 04-Study Status Change: Closed/Enrollment Closed xForm by clicking on "Start xForms" in the appropriate study.
- **Adverse Event and Deviation Submission:** Has its own xForm! Submit a copy of the 16-Reportable Event xForm by clicking on "Start xForms" in the appropriate study.

Principal Investigator (PI) xForm Reviewing Instructions

Please **CAREFULLY READ EACH** Question in the xForm. As the study's **Principal Investigator**, you are required to review and authorize this electronic xForm submission for the aforementioned study. Please **scroll through** and **review the contents** of this completed submission, then follow the directions **at the end** of this xForm.

-- User Access Form Screener --

[BRANY System User Access Form](#)

For xForm submissions to be valid, a copy of the signed, dated, completed (including attestation box checked off that you read the included BRANY compliance with 21 CFR Part 11) **[BRANY System User Access Form](#)** **MUST** be on file at BRANY for:

- the Principal Investigator of the study.
- the person adding a xForm into *IRBManager* (i.e., you).

EACH person that creates, submits and/or authorizes a xForm in *IRBManager* is **required** to have a signed, completed (including attestation box checked off that you read the included BRANY compliance with 21 CFR Part 11) copy of the **[BRANY System User Access Form](#)** on file with BRANY.



IRB STANDARD OPERATING PROCEDURES

*****If the [BRANY System User Access Form](#) is *NOT* on file at BRANY and *NOT* included with this submission, this xForm **WILL BE REJECTED*******

Principal Investigator - BRANY System User Access Form Status

- Is a signed, dated, completed (attestation box checked off that you read BRANY policy included with the form) copy of a BRANY System User Access Form on file for the **PRINCIPAL INVESTIGATOR** listed above? Click on the blue [BRANY System User Access Form](#) hyperlink for a copy of the user access form. Complete, sign and scan to an electronic document (e.g. PDF) so it can be attached to this xForm.

⇒Select *one* of the following options from the drop down list presented:

- No - submitting with this xForm submission
- Yes - on file at BRANY

xForm Submitter (You) - BRANY System User Access Form Status

- Is a signed, dated, completed (attestation box checked off that you read BRANY policy included with the form) copy of a BRANY System User Access Form on file for **YOU**, the **xForm submitter**? Click on the blue [BRANY System User Access Form](#) hyperlink for a copy of the user access form. Complete, sign and scan to an electronic document (e.g. PDF) so it can be attached to this xForm.

⇒Select *one* of the following options from the drop down list presented:

- No - submitting with this xForm submission
- Yes - on file at BRANY

xForm Submissions will be *rejected* as incomplete if the PI and/or xForm submitter listed above **DO NOT** have [BRANY Systems User Access Form](#)'s on file with BRANY or included with this xForm submission! ***All Incomplete submissions WILL BE REJECTED and delay the approval process!!!***

-- PI User Access Form Attachment --

Principal Investigator's [BRANY Systems User Access Form](#)

- Attach Principal Investigator's signed, dated, completed (attestation box checked off that you read BRANY policy included with the form) [BRANY Systems User Access Form](#)
⇒Attach a file of type "User Access Form BRANY Systems" to this xForm.

-- Submitter User Access Form Attachment --

xForm Submitter/Your [BRANY Systems User Access Form](#)

- Attach **YOUR** signed, dated, completed (attestation box checked off that you read BRANY policy included with the form) [BRANY Systems User Access Form](#)
⇒Attach a file of type "User Access Form BRANY Systems" to this xForm.

-- Instructions for Submission --

xForm Submissions will be *rejected* as incomplete if the PI and/or xForm submitter listed above **DO NOT** have [BRANY Systems User Access Form](#)'s on file with BRANY or included with this xForm submission! ***All Incomplete submissions WILL BE REJECTED and delay the approval process!!!***



IRB STANDARD OPERATING PROCEDURES

Request for IRB Review: Changes may not be initiated without prior IRB Approval EXCEPT when necessary to eliminate immediate hazards to subjects. Please **CAREFULLY READ EACH Question in the xForm!**

- xForms must be submitted **FOR EACH STUDY** the changes apply to, *as always!*
- This xForm **IS** the **Request for IRB Review form** and as such is required for all requests for review and/or study personnel additions.
- **ALL** Protocol Amendments and Investigator Brochure updates **REQUIRE:**
 1. The revised Protocol Amendment/Investigator Brochure document(s) **AND**;
 2. The related summary of changes and/or revision history document **AND**;
 3. Location of the summary of changes and/or revision history (page and/or section) **IF** contained within the revised Protocol Amendment/Investigator Brochure document
- **ALL** Informed Consent, Assent and/or **ADDENDUMS** to Informed Consent/Assent submissions are required to be:
 1. Submitted as Consent/Assent and Addendums to Consent/Assent in the xForm.
 2. Include rationale as to **WHY** the changes are being made.
 - 3.** **EACH** Consent, Assent, and/or Addendum to Consent/Assent submitted requires:
 - a. Electronic Word documents for **EACH** item:
 - b. Include the final **AND** tracked/highlighted version of **EACH** Informed Consent, Assent and/or **ADDENDUM** to Informed Consent/Assent;
 - c. **BOTH** versions of **EACH** document are required regardless of who is responsible for implementing Informed Consent, Assent and/or **ADDENDUM** to Informed Consent/Assent changes.
- **ALL** Study Personnel additions **REQUIRE:**
 1. Completed, signed, dated **BRANY IRB Conflict Disclosure Statement** **FOR EACH** individual and **FOR EACH STUDY** the individual is being added to and;
 2. Proof of Human Subject Protection training per your institution's training policy, unless current, unexpired certification(s) are on file at BRANY.
- Please use our updated, shorter version of the **BRANY IRB Conflict Disclosure Statement** which is available on our website.
 1. The individual completes part one: **BRANY IRB Conflict Disclosure Statement**, each time they are being added to a study **OR** if there is a change in their status.
 2. If the individual has any "YES" responses on part one: **BRANY IRB Conflict Disclosure Statement**, they **MUST** complete and submit part two: **BRANY IRB Conflict Report Form**.
 3. This will be one of the few paper forms that will continue to be required (except for the PI on new research applications).

Please contact the BRANY IRB Team at 516.470.6900 if you have any questions regarding submitting items for review via xForms! Thank you!

-- Study Status & Submission Type --

- **What is the current status of the study at your site?**
 - ⇒ Select *one* of the following options from the drop down list presented:
 - Approved - Study Open - Actively Enrolling
 - Enrollment Closed - Subjects in Follow-up
 - Study Closed - NO research activity

Please be sure **READ** each question **CAREFULLY** to ensure you answer each properly. For **EACH** item selected, you will be directed to at least one page of required attachments and questions.



IRB STANDARD OPERATING PROCEDURES

- Items to be reviewed (select **ALL** that apply):

For *EACH* item selected, you will be directed to at least one page of required attachments and questions.

Key personnel are defined as individuals who are responsible for the design and conduct of a study. Therefore, ALL investigators and key personnel, including but not limited to ALL sub-investigators, coordinators and others participating in the conduct of the research MUST satisfy this requirement and be added to the study.

⇒ Check *one or more* of the following items from the list of check boxes presented:

- Protocol Amendment (including summary of changes);
- Investigator Brochure (including summary of changes);
- Drug/Device/Combination-Instructions/IFU/Inserts/Prescribing Information;
- Consent/Assent and Addendums to Consent/Assent (Word documents including red-lined/highlighted copy);
- 1572 Form;
- Personnel Changes (including BRANY IRB Conflict of Interest forms for this study);
- Reports: DMSB Reports, Annual Reports (Device Studies), Safety Summary Reports (NOT INDs, Deviations or Adverse Events);
- Subject - Study Material;
- Advertisements - Recruitment;
- Press Releases;
- Translation;
- Modification to Eliminate Apparent Immediate Hazard(s);
- Request to Use Surrogate Consent/Legally Authorized Representative
- NONE OF THE ABOVE

-- Radiation Exposure --

- **Radiation Exposure - Does the study increase exposure, i.e. increase exposure compared to patients who do not participate in the study (e.g., Study participation requires two additional CT scans.)?**

⇒ Select either 'Yes' or 'No'

- **Optional Explanation:** ⇒ Enter an unlimited amount of text.

-- Protocol Amendment Details --

Protocol Amendment Update

- List the following for **EACH** Protocol Amendment you are requesting review of for this study:

1. Protocol Amendment Version **AND** Date.
2. Location of the summary of changes/revision history within the main Protocol Amendment document.

E.g., Amendment 1, Version 1 and 2, dated January 2012 & March 2012, resp. summary of changes listed in appendix A for each amendment.

⇒ Enter an unlimited amount of text.

- **Protocol Amendment Documents - EACH Protocol Amendment requires a copy of the Amendment AND Summary of Changes, if the Summary of Changes is not contained within**



IRB STANDARD OPERATING PROCEDURES

the Amended Protocol document. **Incomplete submissions will be rejected!** *If you received an email with the items you are submitting for review, please attach a copy and select Attachment type: Submission Email.*

⇒ Attach 1 to 20 files of type "Any" to this xForm.

- **Password, for password locked Protocol documents** ⇒ Enter an unlimited amount of text.
- **Do you have Consent/Assent and/or Consent/Assent Addendum form changes to submit?** ⇒ Select either 'Yes' or 'No'

-- Investigator Brochure Details --

Investigator Brochure Update

- **Identify EACH of the Investigator Brochures you are submitting by listing:**
 1. **Drug name of EACH Investigator Brochure AND;**
 2. **Version/Date of EACH Investigator Brochure AND;**
 3. **Location of the summary of changes/revision history within EACH Investigator Brochure.**

(E.g., Investigator Brochure Naproxin Tablet Version 1, 2 and 3, December 2011, January 2012 & March 2012, respectively. Investigator Brochure Imitrix Nasal Spray dated 30-JUN-2012. Revision History in Appendix 2.0)

⇒ Enter an unlimited amount of text.
- **Investigator Brochure Documents - EACH Investigator Brochure submitted requires a copy of the Investigator Brochure AND Summary of Changes, if the Summary of Changes is not contained within the updated Investigator Brochure document. **Incomplete submissions will be rejected!** *If you received an email with the items you are submitting for review, please attach a copy and select Attachment type: Submission Email.***
- **Password, for password locked investigator brochure documents.** ⇒ Enter an unlimited amount of text.
- **Do you have Consent/Assent form changes to submit?** ⇒ Select either 'Yes' or 'No'

-- Drug or Device Instructions/Inserts --

Drug/Device Package Insert Update

- **Version/Date -- List the following for EACH Drug/Device document you are requesting review of for this study:**
 1. **Title of document;**
 2. **Drug/Device name it is applicable to;**
 3. **Document's Version AND Date.**

(E.g., BrainStim2012 Instructions for Use (IFU) Version 1.0 dated 1/2/2012.)

⇒ Enter an unlimited amount of text.
- **Drug/Device Documents - *If you received an email with the items you are submitting for review, please attach a copy and select Attachment type: Submission Email.*** ⇒ Attach 1 to 20 files of type "Any" to this xForm.
- **Password, for password locked drug/device documents.** ⇒ Enter an unlimited amount of text.
- **Do you have Consent/Assent form changes to submit?** ⇒ Select either 'Yes' or 'No'

-- Subject and/or Subject Materials --

Subject and/or Study Material(s)

- **Describe item(s) submitted: Include any information you would like to provide the IRB regarding the document(s) you are submitting for review: description, version number, date, etc. (e.g. Patient Diary Version 1.1)**



IRB STANDARD OPERATING PROCEDURES

- ⇒Enter an unlimited amount of text.
- **Password, for password locked Subject/Subject Materials documents**
⇒Enter an unlimited amount of text.
- **Attach Subject and/or Study Material(s) - *If you received an email with the items you are submitting for review, please attach a copy and select Attachment type: Submission Email.***
⇒Attach 1 to 50 files of type "Any" to this xForm.
- **Do you have Consent/Assent form changes to submit?** ⇒Select either 'Yes' or 'No'

-- DMSB Report(s): --

Reports: DMSB Reports, Annual Reports (e.g. Device Studies), Safety Summary Reports, etc.

- **Describe item(s) submitted. Include any information you would like to provide the IRB regarding the document(s) you are submitting for review: description, version number, date, etc. (e.g. DMSB Q4 dated 01 Jan 2011). **DO NOT** submit SAEs or Deviations with this xForm!**
⇒Enter an unlimited amount of text.
- **Attach Report(s) - NOT for Reportable Events, INDs, or Deviations.**
You may attach up to ten (10) separate documents. If you received an email with the items you are submitting for review, please attach a copy and select Attachment type: Submission Email.
⇒Attach 1 to 10 files of type "Any" to this xForm.
- **Password, for password locked DMSB/Safety Report documents**
⇒Enter an unlimited amount of text.
- **Do you have Consent/Assent form changes to submit?**
⇒Select either 'Yes' or 'No'

-- Modifications to Eliminate Apparent Immediate Hazards --

Report of Modifications to Eliminate Apparent Immediate Hazards to the Patient

- **Describe the modifications that were initiated *without IRB approval* in order to eliminate apparent immediate hazards to the patient and indicate whether this report was consistent in assuring the patient's welfare. Describe and/or attach documentation below.**
⇒Enter an unlimited amount of text.
- **Report of Modifications Attachment**
You may attach up to five (5) separate documents. If you received an email with the items you are submitting for review, please attach a copy and select Attachment type: Submission Email.
⇒Attach 1 to 5 files of type "Site Correspondence" to this xForm.
- **Do you have Consent/Assent form changes to submit?**
⇒Select either 'Yes' or 'No'

-- Request to Use Surrogate Consent/ Legally Authorized Representative (LAR) --

Research involving Adult Individuals Who May Lack Capacity to Provide Informed Consent or May Require Surrogate Consent (Consent by LAR - Legally Authorized Representative)

1. **Who will decide whether an individual subject is competent to consent? (Required)**
⇒Enter an unlimited amount of text.
2. **How will this assessment be made? (Required)**
⇒Enter an unlimited amount of text.



IRB STANDARD OPERATING PROCEDURES

3. Will you obtain assent from adult participants who may lack capacity to consent? When NO: answer question 3a. (Required)

⇒Select either 'Yes' or 'No'

3a. No - Why not?

⇒Enter an unlimited amount of text.

4. Yes - What is the plan for obtaining the assent?

Choices:

- Assent Form - must be submitted for IRB review
- Documented Assent Discussion
- Other (explain) - answer 4a

⇒Check *one or more* of the following items from the list of check boxes presented:

- Assent Form - must be submitted for IRB review
- Documented Assent Discussion
- Other (explain)

4a. Other (explain):

⇒Enter an unlimited amount of text.

5. Does this study meet all of the following criteria?

If the study *DOES NOT* meet ALL five (5) of the criteria listed, you will be required to Comment/supply further justification to the BRANY IRB in question 5a. (Required)

⇒Check *one or more* of the following items from the list of check boxes presented:

- There is a potential benefit over standard treatment
- Standard treatment is not being withheld
- There is no alternative standard treatment
- Enrollment in the study is in the best interest of the patient
- Participation in the research would not be contrary to the known wishes of the patient

5a. Comments/Further Justification:

⇒Enter an unlimited amount of text.

-- Advertisements-Recruitment --

Advertisement/Recruitment Material

NOTE: The final copy of a printed advertisement must be submitted; BRANY IRB will not approve incomplete or template forms of advertisements. BRANY IRB will review a script of an audio/video tape advertisement; however, the advertisement may not be broadcast until the final audio/video advertisement is submitted for BRANY IRB review and approval.

- **Select the Advertisement type(s) below (select ALL that apply). All ads must be submitted in their final format. Final Format = Includes contact information for potential subjects.**

⇒Check *one or more* of the following items from the list of check boxes presented:

- Clinical trial website
- Flyer
- Print advertisement
- Internet advertisement
- Brochure
- Revision to previously submitted advertisement
- Other (explain in the following question)
- **If you selected OTHER Advertisement type, please explain here:**



IRB STANDARD OPERATING PROCEDURES

⇒Enter an unlimited amount of text.

- **Please attach an electronic version of the advertisement(s) and/or recruitment material(s).** You may attach up to twenty (20) separate documents. If you received an email with the items you are submitting for review, please attach a copy and select Attachment type: Submission Email.
⇒Attach 1 to 20 files of type "Any" to this xForm.
- **Is Advertisement in its Final Format?**

Submitted Advertisements **MUST** include contact information, if not, add the Contact Information to the Advertisement, attach the final format copy and select Yes for this question BEFORE submitting this xForm OR fill in the complete Contact information in the following question.

NOTE: If you add the missing contact information to the copy of the Advertisement submitted/attached with this form, please be sure to select the Yes response for this answer or xForms will require you to enter a response in the contact information question.

If the Advertisement submitted IS NOT IN FINAL FORMAT, i.e. does not include contact information, the approval process of your submission(s) will be **DELAYED**.

⇒Select either 'Yes' or 'No'

- **Contact Information to be included on the Advertisement(s)**

Submitted Advertisements **MUST** include contact information, if not, please add the Contact Information to the Advertisement BEFORE submitting with this form *OR* fill in the complete Contact information here.

If the Advertisement submitted IS NOT IN FINAL FORMAT, i.e. does not include contact information, the approval process of your submission(s) will be **DELAYED**.

⇒Enter an unlimited amount of text.

- **Is the Advertisement a script for a future audio/video recording?**

PLEASE NOTE: BRANY IRB will review a script of an audio/video tape advertisement; however, the advertisement **MAY NOT BE BROADCAST** until the final audio/video advertisement is submitted to BRANY IRB for review AND **APPROVED**.

⇒Select *one* of the following options from the list of radio buttons presented:

- Yes
- No

-- Press Releases --

- **Who is the target audience?**
⇒Select *one* of the following options from the drop down list presented:
 - Potential subject population
 - Medical community
 - Both potential subjects & medical community
- **Press Release Attachments**
You may attach up to 25 separate items.
⇒Attach 1 to 25 files of type "Press Release" to this xForm.

-- Press Releases-Method of Distribution --

Press Release to Potential Subject Population



IRB STANDARD OPERATING PROCEDURES

- **By what method will the press release be provided to prospective subjects (e.g., published on a web-site directed at study subjects, handed out to subjects at next visit, published in subject newsletter, published in local newspaper with my PI's contact information)?**
⇒Enter an unlimited amount of text.

-- Press Releases - Affect Subject Willingness to Participate --

- **Does the information in the press release provide new information that may affect a subject's willingness to continue participation (e.g., new risk or benefit information, new safety information)?**
When **Yes**: You will be required to answer questions on another page.
When **No**: Click **Next**.
⇒Select either 'Yes' or 'No'

-- Press Releases-Medical Community --

You indicated that the submitted press release is intended for the medical community and not for the subjects. BRANY IRB policy indicates that "advertisements" to the medical community need not be reviewed by the IRB, unless it is likely that prospective subjects will see the advertisement.

- **Does the information in the press release provide new information that may affect a subject's willingness to continue participation (e.g., new risk or benefit information, new safety information)?**
When **Yes**: You will be required to answer questions on another page.
When **No**: Click **Next**.
⇒Select either 'Yes' or 'No'

-- Press Releases - How Subjects Informed --

- **What is the new information that may affect a subject's willingness to continue participation?**
⇒Enter an unlimited amount of text.
- **Please attach a revised consent form or other documentation (e.g., consent addendum or draft letter to subjects) that the IRB will review to inform subjects of the new information.**
You may attach up to five (5) separate documents.
⇒Attach 1 to 5 files of type "Any" to this xForm.

-- Press Releases-Medical Community-CLOSE xFORM --

Press Release - Released to Medical Community ONLY!

You are not required to submit this press release for IRB review since you stated in responses to the previous question(s) that the information in the press release **DOES NOT** provide new information that may affect a subject's willingness to continue participation (e.g., new risk or benefit information, new safety information).

If this press release is the only item included in this xForm submission, this xForm will be *closed as complete* AFTER the PI authorizes/signs this xForm.

-- Revised FDA Form 1572 Required --

FDA Form 1572



IRB STANDARD OPERATING PROCEDURES

You indicated a revised FDA Form 1572 is required for the changes you are submitting. You are required to attach the revised document below.

If this is **NOT** the case:

- press "Previous" to get to the first page *OR* "Save for Later" and re-open the xForm you just created.
 - select Items to be reviewed "Personnel Changes" for personnel change(s).
 - continue completing the xForm.
- Describe the changes to the 1572 including the date the PI signed the 1572 form. *For example: 1572 (dated February 7, 2012) Box 4 Change address for ChemLab: typo in zip code of Port Jefferson facility. 1572 (dated 20 June 2012) Box 6 Add Dr. Isaac; Remove Dr. Smith and Dr. Jones.*
⇒Enter an unlimited amount of text.
 - Attach revised FDA Form 1572
⇒Attach 1 to 5 files of type "1572/IDE" to this xForm.
 - Are **Research Site Locations** being added, modified or removed? When **YES** you will be required to supply additional information for each Research Site Location.
⇒Select either 'Yes' or 'No'
Are Clinical Laboratory Facilities being added, modified or removed? When **YES** you will be required to supply additional information for each Clinical Laboratory Facility.
⇒Select either 'Yes' or 'No'
 - Are **Personnel** being added, modified or removed? When **YES**, you will be required to enter information for each personnel being added or removed from the 1572.
⇒Select either 'Yes' or 'No'
 - Do you have Consent/Assent form changes to submit?
⇒Select either 'Yes' or 'No'

1572 Research Location ***Repeatable***

This Group of pages will repeat.

-- Research Location: Change Type --

Research Location Action

⇒Select *one* of the following options from the drop down list presented:

‡ ‡Remove ‡Add ‡Modify ‡DONE

-- Research Location: Remove from Study - Details --

Research Location to **REMOVE**

⇒Enter one line of text.

Address of Research Location to **REMOVE**

⇒Enter an unlimited amount of text.

-- Research Location: Modify Location - Details --

Full Name of previously approved Research Location being **MODIFIED** (Required)

⇒Enter one line of text.

Specify the changes to the previously approved research location listed above:

e.g. Please change suite number from 220 to 202, etc. (Required)



IRB STANDARD OPERATING PROCEDURES

⇒Enter an unlimited amount of text.

-- **Research Location: Add to Study - Details --**

Research Location Name **ADD NEW**

⇒Enter one line of text.

Research Location Physical Address:

Please include Street, City, State/Province, ZIP and Country (if NOT USA)

⇒Enter an unlimited amount of text.

Research Location Telephone

⇒Enter one line of text.

Research Location 24 Hour Telephone

⇒Enter one line of text.

Facility Type

Choices:

Medical Office

Hospital

University

Psychiatric Institution

Nursing Home

Laboratory

Research Clinic

Dialysis Center

Other (specify below)

⇒Select *one* of the following options from the list of radio buttons presented:

‡Medical Office ‡Hospital ‡University ‡Psychiatric Institution ‡Nursing Home ‡Laboratory ‡Research Clinic ‡Dialysis Center ‡Other (specify below)

Other Facility Type:

⇒Enter one line of text.

Does the Investigator have an obligation to submit this project to another committee or obtain other organizational/institutional approval for conducting this study at this research location?

• **Example: Radiation Safety, Protocol Review Committee, GCRC Pharmacy, Hospital/Department approval, Institutional approval, etc.**

If YES, it is the Principal Investigator's obligation to ensure other required approvals are in place BEFORE initiating BRANY IRB approved research.

⇒Select either 'Yes' or 'No'

Does this site have an obligation to submit this project to another IRB?

If Yes, and the documentation was provided to you, please attach the documentation in the following question.

If the document was **NOT provided to you, xForms will allow you to proceed without attaching the document **HOWEVER**, this will *delay the review of your request* **AND** you are still required to submit this documentation to the BRANY IRB.**

⇒Select either 'Yes' or 'No'

Other IRB Documentation authorizing review by BRANY IRB



IRB STANDARD OPERATING PROCEDURES

Please attach copies of the other IRB Documentation, if available to you at this time. These document(s) WILL be required by the BRANY IRB to complete the review of your request.

⇒ Attach a file of type "Any" to this xForm.

Does the Research Location need to be added to the consent form?

⇒ Select either 'Yes' or 'No'

-- **Research Location: Add to Study - Emergency Plan --**

The Investigator should ensure a plan is in place to have trained staff available to provide coverage in emergency situations.

Describe the emergency equipment available at this site (select ALL that apply):

Selections:

Crash Cart

Emergency Medications

CPR Trained Staff

Access to 911

When OTHER, you will be required to explain other emergency equipment available at the site.

When N/A, Not Applicable you will be required to explain why availability to emergency equipment at the site is not applicable (N/A).

⇒ Check *one or more* of the following items from the list of check boxes presented:

‡ Crash Cart ‡ Emergency Medications ‡ CPR Trained Staff ‡ Access to 911 ‡ Other (specify below) ‡ N/A (explain below)

Describe Other Emergency Equipment Available at Site:

⇒ Enter an unlimited amount of text.

N/A Emergency Equipment - Why?

Explain why emergency equipment is not available (N/A) at this site.

⇒ Enter an unlimited amount of text.

Are research personnel available to subjects 24 hours a day?

When **NO, you will be required to explain how subjects can contact research personnel.**

When **N/A, you will be required to explain why access to research personnel 24/7 is not applicable (N/A).**

⇒ Select *one* of the following options from the drop down list presented:

‡ ‡ Yes ‡ No (explain below) ‡ N/A - Not Applicable (explain why)

When **NO, Research Personnel are NOT available 24/7, explain how subjects can contact research personnel:**

⇒ Enter an unlimited amount of text.

When **N/A (not applicable) for Research Personnel to be available 24/7 you are required to explain why access to research personnel 24/7 is not applicable (N/A).**

e.g. this is a questionnaire/survey study, etc.

⇒ Enter an unlimited amount of text.

Describe any additional resources available to subjects (select ALL that apply):

If there are none, please select None.

⇒ Check *one or more* of the following items from the list of check boxes presented:

‡ Counseling Services ‡ Certified Medical Interpreters ‡ Other (explain below) ‡ None



IRB STANDARD OPERATING PROCEDURES

Other Additional Resources Available to Subjects:

⇒Enter an unlimited amount of text.

-- Research Location End Page --

Do you have additional **Research Locations** you are adding/removing/modifying for the 1572?

If **YES**, press **Repeat** to add/remove/modify another **Research Location**.

If **NO**, press **Next** to continue completing this xForm.

1572 Clinical Laboratory Location *Repeatable*****

This Group of pages will repeat.

-- **Clinical Location: Change Type** --

Clinical Laboratory Location Action

⇒Select *one* of the following options from the drop down list presented:

‡ ‡Remove ‡Add ‡Modify ‡DONE

-- **Clinical Location: Remove from Study Details** --

Clinical Laboratory Location to **REMOVE**

Name and Address

Please include Street, City, State/Province, ZIP and Country (if NOT USA)

⇒Enter an unlimited amount of text.

-- **Clinical Location: Modify Location - Details** --

Full Name of previously approved Clinical Laboratory Location being **MODIFIED**

Full Name of previously approved Clinical Laboratory Location being **MODIFIED**

⇒Enter one line of text.

Specify the changes:

⇒Enter an unlimited amount of text.

-- **Clinical Location: Add to Study Details** --

Clinical Location Name and Address:

Please include Street, City, State/Province, ZIP and Country (if NOT USA)

⇒Enter an unlimited amount of text.

Clinical Location Telephone

⇒Enter one line of text.

-- **Clinical Location End Page** --

Do you have additional **Clinical Laboratory Locations** to add/remove/modify from the 1572?

If **YES**, press **Repeat** to add/remove/modify another **Clinical Laboratory Location**.

If **NO**, press **Next** to continue completing this xForm.

Personnel Changes *Repeatable*****

This Group of pages will repeat.

-- **Personnel Change: Change Type** --

Each person to be added, removed or modified from the study **MUST** be listed **INDIVIDUALLY** so the correct questions will be displayed to you on subsequent pages.



IRB STANDARD OPERATING PROCEDURES

When **Adding** personnel, you will be required to attach electronic copies of:

- A completed, signed, dated BRANY IRB Financial Conflict of Interest form for the individual listing **THIS** study only and;
- Proof of Human Subject Protection training per your institution's training policy, unless current, unexpired certification(s) are on file at BRANY.

Please note: this xForm will be rejected for ANY missing required documentation.

Personnel Action

⇒Select *one* of the following options from the drop down list presented:

‡ ‡Remove ‡Add ‡Modify Previously Approved ‡DONE

-- Personnel Change: Remove from Study - Details --

Full Name of Individual to **REMOVE**

⇒Enter one line of text.

-- Personnel Change: Add to Study - Details --

Full Name of Individual to **ADD**

⇒Enter one line of text.

Email

⇒Enter a valid e-mail address.

Phone

⇒Enter one line of text.

Research Role

When "**Other/Not Listed (explain)**" is selected, you will be required to explain in the following question.

⇒Select *one* of the following options from the drop down list presented:

‡ ‡Sub-Investigator ‡Coordinator ‡CC Recipient ‡Faculty Adviser ‡Research Assistant ‡Regulatory Coordinator ‡Other/Not Listed (explain)

Other Role Not Listed Above, explain.

⇒Enter an unlimited amount of text.

Will the newly added individual obtain informed consent from subjects?

⇒Select either 'Yes' or 'No'

Completed [BRANY IRB Conflict Disclosure Statement](#) for the newly added individual

Please use our updated, shorter version of the BRANY IRB Conflict Disclosure Statement which is available on our website.

1. The individual completes part one: BRANY IRB Conflict Disclosure Statement, each time they are being added to a study

OR if there is a change in their status.

2. If the individual has any "YES" responses on part one: BRANY IRB Conflict Disclosure Statement, they **MUST**

complete and submit part two: [BRANY IRB Conflict Report Form](#).

3. This will be one of the few paper forms that will continue to be required (except for the PI on new research applications).

NOTE: BRANY IRB Conflict Report Form is required to be completed and attached **ONLY** if the individual answered **YES to any question** on part one: the BRANY IRB Conflict Disclosure Statement.

You may attach up to two (2) separate documents.



IRB STANDARD OPERATING PROCEDURES

BOTH forms available on the BRANY IRB Website via the above blue hyperlinks **OR** going directly to the [BRANY IRB Forms and Downloads web page](#) under "Personnel Changes".
⇒Attach 1 to 10 files of type "Any" to this xForm.

Human Subject Protection Training Completion Training

Is the current individual's current, non-expired, Human Subject Protection Training completion certification(s) on file at BRANY? (e.g. CITI, NIH, etc.)

When **NO – attaching current, non-expired copies of training completion certification with submission**, you will be required to attach copies of current, non-expired training completion certificates below.

⇒Select *one* of the following options from the drop down list presented:

‡ ‡NO – attaching current, non-expired copies of training completion certification with application ‡YES – current, non-expired training completion certification on file at BRANY

Evidence of Training in Human Subject Protections attachment(s) for the newly added individual

You may attach up to five (5) separate documents.

⇒Attach 1 to 15 files of type "Human Sub. Prot. Training" to this xForm.

Require IRBManager Access to this study?

NOTE: IRBManager access is only required for the study's PI and individuals creating and submitting xForms to BRANY.

⇒Select *one* of the following options from the drop down list presented:

‡No ‡Yes - attaching completed, signed BRANY User Access Form ‡Yes - BRANY User Access Form on file

BRANY User Access Form

⇒Attach 1 to 5 files of type "User Access Form BRANY Systems" to this xForm.

-- Personnel Change: Modify Previously Approved - Details --

Full Name of previously approved individual being **MODIFIED**

⇒Enter one line of text.

Specify the changes to the previously approved study personnel listed above:

Please note if this person was NOT previously approved for this study, additional document(s) may be required to add them to the study.

⇒Enter an unlimited amount of text.

-- Personnel Change: End --

Do you have additional Key Study Personnel to Add/Remove/Modify from this study?

When **YES**: I need to process more personnel, press **Repeat** to Add/Remove/Modify additional Key Study Personnel.

When **NO**, press **Next** to continue with the next section of this xForm.

NONE OF THE ABOVE

-- NONE OF THE ABOVE --

NONE OF THE ABOVE

If your submission does not fit into one of the listed categories listed below, then why does it need IRB review?



IRB STANDARD OPERATING PROCEDURES

Submission Types:

Protocol Amendment;
Investigator Brochure;
Drug/Device/Combination-Instructions/IFU/Inserts/Prescribing Information;
Consent/Assent Form;
1572 Form;
Personnel Changes;
Reports: DMSB Reports, Annual Reports (Device Studies), Safety Summary Reports (NOT INDs or Deviations!);
Subject/Study Material;
Advertisements - Recruitment;
Press Releases;
Translation;
Modification to Eliminate Apparent Immediate Hazard(s)

Refer to the guidance available by clicking: [Items that DO and DO NOT Need BRANY IRB Review](#)

Please do one (1) of the following:

1. If you *do not want to request review for this item*, click Save for Later then delete this xForm from your My *IRBManager* dashboard's unsubmitted xForms or via the My Forms & Documents list.

2. If the item *DOES fall into one of the existing types*, click Back, modify the submission type selection and click Next to continue

3. If you still believe the item(s) require IRB review *AND* they do not fall into any of the listed submission types, complete all the questions on this page.

Clearly explain why you are requesting IRB review for this item.

⇒Enter an unlimited amount of text.

Attachment(s)

This xForm is NOT for submitting Reportable Events, SAEs, INDs or Deviations

You may attach up to fifty (50) separate documents.

If you received an email with the items you are submitting for review, please attach a copy and select Attachment type: Submission Email.

⇒Attach 1 to 50 files of type "Submitted Item(s)" to this xForm.

Do you have Consent/Assent form changes to submit due to this submission?

⇒Select either 'Yes' or 'No'

Consent Form Revisions

-- Consent Form Revision Details --

Consent/Assent and/or ADDENDUM to Consent/Assent

Clearly describe the rationale for the Consent/Assent and/OR ADDENDUM to Consent/Assent revisions

e.g. Amendment 1 revisions, Change in Sponsor Name, ADDENDUM added for New/Additional



IRB STANDARD OPERATING PROCEDURES

Genetic Testing, etc.

⇒Enter an unlimited amount of text.

Version/Date

List the version/date of *EACH* of the revised Consent/Assent and/OR ADDENDUM to Consent/Assent documents you are submitting for the aforementioned study.

e.g. Main ICF dated 1/11/2011, Sub-study ICF B (12DEC2012), Main ICF Addendum 12December2012, etc.

⇒Enter an unlimited amount of text.

Password, for password locked consent/assent documents.

⇒Enter an unlimited amount of text.

Consent/Assent and/OR ADDENDUM to Consent/Assent Documents:

EACH Consent/Assent and/OR ADDENDUM to Consent/Assent requires a copy of the **red-lined/highlighted Word version AND the final Word version.**

Incomplete submissions will be rejected!

If you have questions about what to attach for consent changes, please contact a BRANY IRB Associate at 516.470.6900.

You may attach up to twenty (30) separate documents.

If you received an email with the items you are submitting for review, please attach a copy and select Attachment type: Submission Email.

⇒Attach 1 to 30 files of type "Any" to this xForm.

-- Translation --

- **Please select the appropriate choice:**

⇒Select *one* of the following options from the list of radio buttons presented:

- **FIRST TIME: Requesting translations to be obtained for the FIRST TIME.**
- **Submitting translations for review and approval (translation AND certificate of authenticity).**

-- First Time Translation Submission --

Translation Information

A. For which language(s) will you require translation?

⇒Enter an unlimited amount of text.

B. Who will provide translations?

⇒Select *one* of the following options from the drop down list presented:

- BRANY IRB Vendor
- Sponsor/CRO

C. Describe the plan for conducting the consent discussion and ongoing communication with non-English speaking subjects:

⇒Check *one or more* of the following items from the list of check boxes presented:

- Staff member fluent in foreign language
- Use a certified medical interpreter



IRB STANDARD OPERATING PROCEDURES

- Other (specify)
- D. Other (specify):**
⇒Enter an unlimited amount of text.
- E. Do you have translated item(s), i.e. translated item paired with its certificate of authenticity, to submit now?** You must select **YES** if you have completed translations, i.e. translated item paired with its certificate of authenticity, **to submit now**.
⇒Select either 'Yes' or 'No'

-- Submitting Translated Item(s) for Review/Approval --

Translated Study Items - Certificate of Accuracy is required for EACH translated item!

Describe the translated item(s): Language and Items description. (e.g. Spanish Patient Diary, French ICF AB, etc.)

⇒Enter an unlimited amount of text.

Attach Translated Item(s)

You may attach up to thirty (30) separate documents.

⇒Attach 1 to 30 files of type "Any" to this xForm.

Attach Certificate(s) of Accuracy

You may attach up to thirty (30) separate documents.

⇒Attach 1 to 30 files of type "Translation - Auth Certificate" to this xForm.

end

-- PI Submission Review Instructions (end) --

Principal Investigator (PI) xForm Reviewing Instructions

Now that you have reviewed the information within this electronic xForm submission, please follow the appropriate instructions, a or b, below:

a. **Modifications required**: alert your study coordinator that modifications are required on this xForm and click on the **Close** button to close the xForm. Once the modifications are complete, you will receive another email alert to review and authorize the updated xForm.

b. **Complete/Submit to BRANY**: if the content of this xForm is complete, click the **Next** button to display the **"Form Signatures Stage"**. Enter your *IRBManager* password into the empty box on the row your name is listed, then click the **Sign** button to submit the xForm to **BRANY**.

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IRB STANDARD OPERATING PROCEDURES

Appendix 16 – BRANY IRB Standard Operating Procedures

FDA List of NSR and SR Devices

NONSIGNIFICANT RISK DEVICES (NSR)

- Low Power Lasers for treatment of pain
- Caries Removal Solution
- Daily Wear Contact Lenses and Associated Lens Care Products not intended for use directly in the eye (e.g., cleaners; disinfecting, rinsing and storage solutions)
- Contact Lens Solution intended for use directly in the eye (e.g., lubricating/rewetting solutions) using active ingredients or preservation systems with a history of prior ophthalmic/contact lens use or generally recognized as safe for ophthalmic use
- Conventional Gastroenterology and Urology Endoscopes and/or Accessories
- Conventional General Hospital Catheters (long-term percutaneous, implanted, subcutaneous and intravascular)
- Conventional implantable Vascular Access Devices (Ports)
- Conventional Laparoscopes, Culdoscopes, and Hysteroscopes
- Dental Filling Materials, Cushions or Pads made from traditional materials and designs
- Denture Repair Kits and Realignment
- Digital Mammography [Note: an IDE is required when safety and effectiveness data are collected which will be submitted in support of a marketing application.]
- Electroencephalography (e.g., new recording and analysis methods, enhanced diagnostic capabilities)
- Externally Worn Monitors for Insulin Reactions
- Functional Electrical Neuromuscular Stimulators
- General Biliary Catheters General Urological Catheters (e.g., Foley and diagnostic catheters)
- Jaundice Monitors for Infants
- Magnetic Resonance Imaging (MRI) Devices within FDA specified parameters
- Manual Image Guided Surgery
- Menstrual Pads (Cotton or Rayon, only)
- Menstrual Tampons (Cotton or Rayon, only)
- Nonimplantable Electrical Incontinence Devices
- Nonimplantable Male Reproductive Aids with no components that enter the vagina
- Ob/Gyn Diagnostic Ultrasound within FDA approved parameters
- Transcutaneous Electric Nerve Stimulation (TENS) Devices for treatment of pain
- Wound Dressings, excluding absorbable hemostatic devices and dressings (also excluding Interactive Wound and Burn Dressings)

SIGNIFICANT RISK DEVICES (SR)

General Medical Use

Catheters:

- Urology- urologic with anti-infective coatings
- General Hospital- except for conventional long-term percutaneous, implanted, subcutaneous and intravascular
- Neurological- cerebrovascular, occlusion balloon
- Cardiology- transluminal coronary angioplasty, intra-aortic balloon with control system
- Collagen Implant Material for use in ear, nose and throat, orthopedics, plastic surgery, urological and dental applications
- Surgical Lasers for use in various medical specialties



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- Tissue Adhesives for use in neurosurgery, Gastroenterology, ophthalmology, general and plastic surgery, and cardiology

Anesthesiology

- Breathing Gas Mixers
- Bronchial Tubes
- Electroanesthesia Apparatus
- Epidural and Spinal Catheters
- Epidural and Spinal Needles
- Esophageal Obturators
- Gas Machines for anesthesia or analgesia
- High Frequency Jet Ventilators greater than 150 BPM
- Rebreathing Devices
- Respiratory Ventilators
- Tracheal Tubes

Cardiovascular

- Aortic and Mitral Valvuloplasty Catheters
- Arterial Embolization Devices Cardiac Assist Devices: artificial heart (permanent implant and short term use), cardiomyoplasty devices, intra-aortic balloon pumps, ventricular assist devices
- Cardiac Bypass Devices: oxygenators, cardiopulmonary non-roller blood pumps, closed chest devices
- Cardiac Pacemaker/Pulse Generators: antitachycardia, esophageal, external transcutaneous, implantable
- Cardiopulmonary Resuscitation (CPR) Devices
- Cardiovascular/Intravascular Filters
- Coronary Artery Retroperfusion Systems
- Coronary Occluders for ductus arteriosus, atrial and septal defects
- Coronary and Peripheral Arthrectomy Devices
- Extracorporeal Membrane Oxygenators (ECMO)
- Implantable Cardioverters/Defibrillators
- Laser Coronary and Peripheral Angioplasty Devices
- Myoplasty Laser Catheters
- Organ Storage/Transport Units
- Pacing Leads
- Percutaneous Conduction Tissue Ablation Electrodes
- Peripheral, Coronary, Pulmonary, Renal, Vena Caval and Peripheral Stents
- Replacement Heart Valves
- RF Catheter Ablation and Mapping Systems
- Ultrasonic Angioplasty Catheters
- Vascular and Arterial Graft Prostheses
- Vascular Hemostasis Devices

Dental

- Absorbable Materials to aid in the healing of periodontal defects and other maxillofacial applications
- Bone Morphogenic Proteins with and without bone, e.g., Hydroxyapatite (HA)
- Dental Lasers for hard tissue applications
- Endosseous Implants and associated bone filling and augmentation materials used in conjunction with the implants
- Subperiosteal implants
- Temporomandibular Joint (TMJ) Prostheses



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Ear, Nose, and Throat

- Auditory Brainstem Implants
- Cochlear Implants
- Laryngeal Implants
- Total Ossicular Prosthesis Replacements

Gastroenterology and Urology

- Anastomosis Devices
- Balloon Dilation Catheters for benign prostatic hyperplasia (BPH)
- Biliary Stents
- Components of Water Treatment Systems for Hemodialysis
- Dialysis Delivery Systems
- Electrical Stimulation Devices for sperm collection
- Embolization Devices for general urological use
- Extracorporeal Circulation Systems
- Extracorporeal Hyperthermia Systems
- Extracorporeal Photopheresis Systems
- Femoral, Jugular and Subclavian Catheters
- Hemodialyzers
- Hemofilters
- Implantable Electrical Urinary Incontinence Systems
- Implantable Penile Protheses
- Injectable Bulking Agents for incontinence
- Lithotripters (e.g., electrohydraulic extracorporeal shock-wave, laser, powered mechanical, ultrasonic)
- Mechanical/Hydraulic Urinary Incontinence Devices
- Penetrating External Penile Rigidity Devices with components that enter the vagina
- Peritoneal Dialysis Devices
- Peritoneal Shunt
- Plasmapheresis Systems
- Prostatic Hyperthermia Devices
- Urethral Occlusion Devices
- Urethral Sphincter Protheses
- Urological Stents (e.g., ureteral, prostaG)

General and Plastic Surgery

- Absorbable Adhesion Barrier Devices
- Absorbable Hemostatic Agents
- Artificial Skin and Interactive Wound and Burn Dressings
- Injectable Collagen
- Implantable Craniofacial Protheses
- Repeat Access Devices for surgical procedures
- Sutures

General Hospital

- Implantable Vascular Access Devices (Ports)- if new routes of administration or new design
- Infusion Pumps (implantable and closed- loop- depending on the infused drug)

Neurological

- Electroconvulsive Therapy (ECT) Devices
- Hydrocephalus Shunts
- Implanted Intracerebral/Subcortical Stimulators
- Implanted Intracranial Pressure Monitors



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Implanted Spinal Cord and Nerve Stimulators and Electrodes

Obstetrics and Gynecology

- Antepartum Home Monitors for Non-Stress Tests
- Antepartum Home Uterine Activity Monitors
- Catheters for Chorionic Villus Sampling (CVS)
- Catheters Introduced into the Fallopian Tubes
- Cervical Dilatation Devices
- Contraceptive Devices:
 - Cervical Caps
 - Condoms (for men) made from new materials (e.g., polyurethane)
 - Contraceptive in Vitro Diagnostics (IVDs)
 - Diaphragms
 - Female Condoms
 - Intrauterine Devices (IUDs)
 - New Electrosurgical Instruments for Tubal Coagulation
 - New Devices for Occulsion of the Vas Deferens
 - Sponges
 - Tubal Occlusion Devices (Bands or Clips)
- Devices to Prevent Post-op Pelvic Adhesions
- Embryoscopes and Devices intended for fetal surgery
- Falloscopes and Falloposcopic Delivery Systems
- Intrapartum Fetal Monitors using new physiological markers
- New Devices to Facilitate Assisted Vaginal Delivery
- Thermal Systems for Endometrial Ablation

Ophthalmics

- Class III Ophthalmic Lasers
- Contact Lens Solutions intended for direct instillation (e.g., lubrication/rewetting solutions) in the eye using new active agents or preservatives with no history or prior ophthalmic/contact lens use or not generally recognized as safe for ophthalmic use
- Corneal Implants
- Corneal Storage Media
- Epikeratophakia Lenticules
- Extended Wear Contact Lens
- Eye Valve Implants (glaucoma implant)
- Intraocular Lenses (IOLs) [21 CFR part 813]
- Keratoprotheses Retinal Reattachment Systems: fluids, gases, perfluorocarbons, perfluoropropane, silicone oil, sulfur hexafluorine, tacks
- Viscosurgical Fluids

Orthopedics and Restorative

- Bone Growth Stimulators
- Calcium Tri-Phosphate Hydroxyapatite
- Ceramics Collagen and Bone Morphogenic Protein Meniscus Replacements
- Implantable Prostheses (ligament, tendon, hip, knee, finger)
- Computer Guided Robotic Surgery

Radiology

- Boron Neutron Capture Therapy
- Hyperthermia Systems and Applicators

Appendix 17 – BRANY IRB Standard Operating Procedures

Risks and Procedures – Lay Terminology**Allergic Reactions**

(Drug Name) may cause allergic reactions in some people. In general, allergic reactions to medicines are more likely to occur in people who have allergies to other drugs, foods, or environmental elements such as dust or grass. If you have allergies to other medicines, food products, environmental elements or if you have asthma, you should tell my doctor.

Barium enema with air contrast

A barium enema with air contrast, also called a *double contrast barium enema* or *lower GI series*, uses x-rays to view the large intestine. The procedure takes about 30 to 45 minutes to perform. A barium enema may cause discomfort and a feeling of fullness.

You will be told how to cleanse your bowel the night before and the morning of the exam. This bowel preparation usually includes a liquid diet for 2 days before the procedure and clear liquids the day before the procedure. Avoid eating or drinking dairy products the day before the test. You should not eat or drink anything after midnight the night before the procedure. Be sure to follow your doctor's instructions for bowel preparation. A laxative or enema may be given before the procedure to make sure your colon is empty. Check with your doctor for specific instructions.

Barium sulfate, a chalky substance, is used to partially fill and open up the colon. The barium sulfate is given in the anus. When the colon is about half-full of barium, the patient is turned on the x-ray table so the barium spreads throughout the colon. Then air is inserted to cause the colon to expand. This allows good x-ray films to be taken. You may be asked to change positions so that different views of the colon and rectum can be seen on the x-rays. The doctor can then see the size and shape of the colon and rectum. The barium can cause constipation and your stool may appear gray or white for a few days after the procedure.

Blood Sampling

I may experience slight bruising or pain on my arm or my finger where blood samples will be taken for my blood tests. There is also the slight risk of infection, light headedness, and/or fainting. The total amount of blood taken for samples over the course of the study will approximate (# of teaspoons).

Bone marrow biopsy

A needle is used to remove a small piece of bone, usually from the back of the hip bone. The sample is checked for cancer cells.

Bronchoscopy

A lighted, flexible tube is passed through the mouth into the bronchi. This test can help find tumors or it can be used to take samples of tissue or fluids to see if cancer cells are present.

Cervical Coloposcopy and Biopsy

The side effects associated with cervical coloposcopy and biopsy are usually limited to mild pain and cramping. There is also a risk of minor bleeding and infection associated with these procedures. The study doctor can explain these potential side effects and risks completely to you, and will also be able to answer any other questions that you might have about these procedures. Patients may experience the following psychological symptoms: anxiety, worry, fear and tension.

Colonoscopy

A colonoscopy is a test used to view the lining of the colon using a colonoscope. A colonoscope is a slender, flexible, hollow lighted tube about the thickness of a finger. It is inserted through the rectum up into the colon. A colonoscope is much longer than a sigmoidoscope, and in most cases allows the doctor to see the lining of the entire colon. The colonoscope is connected to a video camera and video display monitor so the doctor can closely examine the inside of the colon.

Preparation for the test usually includes the following:



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- You will need to drink only clear liquids (water, any Jell-O except red, and grape, apple, or cranberry juice). Do not eat or drink anything after midnight the night before your test. Check with your doctor for your specific instructions.
- The large intestine must be cleaned out so that is visible during the test. Your doctor will prescribe a bowel preparation to cleanse the area the night before your test.

A colonoscopy usually lasts 30 to 60 minutes. You will get an I.V. (intravenous line) so that medicine can be given through a vein. The medicine will relax you and make you feel sleepy but you will be awake. You should arrange for someone to drive you home from the test because the sedative can affect your ability to drive. You will be placed on your side with your knees flexed and a drape will cover you. Your blood pressure, heart rate, and breathing rate will be monitored during and after the test. Bleeding and puncture of the colon are possible complications of colonoscopy. However, they are uncommon.

Colonoscopy is generally a safe test although rare complications can occur. These can include a reaction to the sedative or numbing medication that is spread on the tube that is passed into the colon. Usually there is some pain or discomfort, like a feeling of fullness, felt during this test. Even more rarely, a hole can be made in the side of the colon that can require surgery.

The colonoscope is lubricated so it can be easily inserted into the rectum. Once inserted into the rectum, the colonoscope is passed through the transverse colon and into the ascending colon and rectum. You may feel an urge to have a bowel movement when the colonoscope is inserted or pushed further up the colon. To ease any discomfort it is helpful to breathe deeply but slowly through your mouth. The colonoscope will deliver air into the colon so that it is easier to see the lining of the colon and use the instruments to perform the test. Suction will be used to remove any blood or liquid stools.

If a polyp is found, the doctor may remove it. Polyps, even those that are not cancerous, can cause bleeding and may become cancerous. For this reason, they are usually removed. This is done by passing a wire loop through the colonoscope to sever the polyp from the wall of the colon using an electrical current. The polyp can then be sent to a lab to be checked under a microscope to see if it has any areas that have changed into cancer.

If the doctor sees anything else abnormal, a *biopsy* may be done. To do this, a small piece of tissue is taken out through the colonoscope. Examination of the tissue can help determine if it is a cancer, a benign (non-cancerous) growth, or a result of inflammation. Patients receive instructions on how to cleanse their colon at home before the exam so that there will not be any stool to block the view.

Colonoscopy usually does not cause pain, although it may be uncomfortable. If a polyp is removed or a biopsy is done during the colonoscopy, you may notice some blood in your stool after the test.

Cystoscopy

A cystoscope is a slender tube with a lens and a light. It is placed into the bladder through the urethra and allows the doctor to look at the inside of the bladder. If anything looks abnormal, a small piece of tissue will be removed for a biopsy.

A cystometrogram (CMG) The cystometric study uses a device to pump water into the bladder through a catheter (tube) in the urethra (canal that carries urine from the bladder). The device then measures the amount of fluid that goes into the bladder when you first feel the desire to void, when you are able to sense fullness, and when your bladder is completely full. The study doctor will then provoke stress incontinence by asking you to cough or by having you apply pressure to your belly. During the cystometrogram, there may be some discomfort. You may experience pain, flushing, sweating, nausea, bladder filling, and an urgency to go to the bathroom.

Dependency

(Drug Name) has the potential to cause psychological or physical dependence. You should not participate in this study if you have had previous problems with drug or alcohol abuse. Withdrawal symptoms (such



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as anxiety, sweating, difficulty sleeping, and shakiness) may occur if (Drug Name) is discontinued over a very short period of time.

Digital Rectal Exam (DRE)

The doctor or health care provider inserts a gloved finger into the rectum to feel for anything not normal. This simple test, which is not painful, can detect many rectal cancers.

Ductogram

A ductogram is a test that is sometimes helpful in determining the cause of a nipple discharge. This is a type of x-ray test in which a fine plastic tube is placed into the opening of the duct onto the nipple. A small amount of dye is injected, which outlines the shape of the duct on an x-ray image and will show whether there is a mass inside the duct.

ECG

A test of the electrical activity of your heart. This test does not emit electricity and there is no risk of shock. An ECG is painless. When first applied, the disks may be cold and in rare circumstances, a person may develop a localized rash or irritation where the patches are placed.

Endoscopic Assessment

A process using special tubes with lights at the end to look at the mouth, voicebox, esophagus and breathing tubes.

Fecal Occult Blood Test (FOBT)

In this context, the word *occult* means *hidden*. The FOBT is used to find small amounts of blood in the stool that can't normally be seen. A sample of stool is tested for traces of blood. People having this test will receive a test kit with instructions that explain how to take a stool sample at home. The kit is then sent to a lab for testing.

Genetic Research

(Identified Sample Only)

The sponsor of the genetic research is (Sponsor Name). (Sponsor name) wants to protect your confidentiality. In order to do this your sample will be identified by your subject number, not your name. (Sponsor Name) plans to study genes or pieces of DNA smaller than genes that might be related to (disease name). Additionally, genes or pieces of DNA that may affect your response to the study medication will be studied. (Sponsor Name) may also look for other genes or pieces of DNA involved in (disease name) and the response to medicines for (disease name).

Medical information collected for this genetic research will also be labeled with your subject number, not your name. As an identified sample, only your study doctor will be able to link your subject number to your name.

(Sponsor Name) will keep your identified sample for about 6 months after the main study results are reviewed and the results are written up for use within (Sponsor Name). [Although it is not possible to know the exact date that the review will be completed, it is likely that this will happen approximately 6-8 months after the study ends at your doctor's office (the study end is defined as the last visit for the last patient in the main study)]. (Sponsor Name) will then destroy your identified sample. If for some reason the review of the main study results is very delayed, (Sponsor Name) will keep your identified sample for no more than 10 years after you gave the sample. It is very unlikely that the review of the main study results will be significantly delayed.

(Non-Identified Sample)

(Sponsor Name) will study your sample as an identified sample and a non-identified sample. About 6 months after the study is over and the results have been reviewed, (Sponsor Name) will take your subject number off of your identified sample. A new number will be given to your sample, medical information and genetic results. This number is not associated with your subject number or your name. Your sample is now a non-identified sample.



IRB STANDARD OPERATING PROCEDURES

Even though you may not be affected by conditions other than Type 2 diabetes, your non-identified sample and information may be used for other genetic research related to many different diseases and responses to a range of medicines. (Sponsor Name) is asking patients from many different studies to participate in non-identified research. Your sample will be stored together with those of thousands of other non-identified samples from (Sponsor Name) clinical trials and will become part of a valuable resource of genetic information for future research that will allow (Sponsor Name) to develop medicines to treat many diseases such as (list diseases). This genetic resource will also help (Sponsor Name) to understand which genes or pieces of genes may be involved in these or other diseases. There is no time limit on how long (Sponsor Name) can store or use your non-identified sample and medical information for genetic research. (Sponsor Name) will have the ability to screen thousands of genes or pieces of genes from your non-identified sample.

Social and Psychological Risks:

When the patient learns the results of a test:

There is a potential of discrimination in employment or insurance coverage should the results of the genetic testing prove to confirm a genetic disorder. Someone with a known genetic condition indicating a susceptibility to develop a disease or condition might be denied a job or a promotion, or denied health or life insurance, because they are regarded as a health risks and therefore an economic risk. Carriers for a genetic disorder might be discriminated against and viewed as having the potential to have a child with a genetic condition.

A potential risk of genetic testing includes the burden of knowing. Some people who discover that they have a genetic risk which makes them likely to develop a disease or condition could become depressed. The quality of life, joy and purpose of their lives would decrease. You and/or your family members may have mixed or unpleasant reactions (such as guilt, fear, anxiety, anger) to news of positive test results. In the case of negative results, feelings of guilt may occur if less fortunate siblings or other relatives test positive.

Genetic risk counselors are trained to help people decide whether to have a genetic test and to interpret test results. A genetic risk counselor can help you sort through results. They can help you sort through both information and feelings, and help you decide 1) whether to raise questions with your family, and 2) how best to talk about the test and the concerns it raises. In some instances, you may want members of your family to meet with you and the genetic risk counselor. Each person and every family is different, the decision to undergo genetic testing is personal, and the process you go through to make your decisions will be your own.

When the patient doesn't learn the results of the test:

In the case that confidentiality has been breached, positive results of genetic testing may have become available to insurance carriers or employers. The knowledge of this information has the potential to lead to discrimination in employment or insurance. Someone with a known genetic condition indicating a susceptibility to develop a disease or condition might be denied a job or a promotion, or denied health or life insurance, because they are regarded as a health risks and therefore an economic risk. Carriers for a genetic disorder might be discriminated against and viewed as having the potential to have a child with a genetic condition

Gene Therapy

Introductory Language:

Human gene therapy involves inserting healthy genes into your body to correct serious medical conditions. The healthy gene is attached to a carrier known as a vector, often a virus that carries the gene to the target area of the body. In general, a gene cannot be directly inserted into a person's cell. It must be carried to the cell using what is known as a "vector." The most common types of vectors used in gene therapy are viruses because of their ability to enter a cell's DNA. One major goal of gene therapy is to supply cells with healthy copies of damaged genes.



IRB STANDARD OPERATING PROCEDURES

Risks

Viruses usually can infect more than one type of cell and cause a change in more than the targeted cells. Whenever a gene is added to DNA, there is the danger that the new gene could be inserted in the wrong place, possibly causing cancer or other damage.

Other worries include the possibility that inserted genes could be “over expressed”, causing the virus to be transmitted from the patient to other individuals or into the environment.

Adenoviruses

Adenoviruses are a frequent cause of acute upper respiratory tract (URT) infections, the common cold and are used in gene therapy experiments.

Retroviruses

Retroviruses contain RNA (ribonucleic acid) as their genetic material instead of DNA.

Retroviruses can cause AIDS and other diseases. In gene therapy, scientists inactivate certain retroviruses to prevent them from causing disease and to make them safe for use. This enables scientists to take advantage of the retroviruses’ ability to deliver genes into the DNA of the host.

Intravenous line

The discomforts associated with an intravenous line (a small tube inserted in the vein) are similar to the discomforts associated with taking blood from a vein (venipuncture), and include pain, bruising or swelling at the site, infiltration (fluid leaking into the tissues below the skin), and more rarely, inflammation and/or infection of the skin (cellulitis).

Intravenous pyelogram (IVP)

In this test, a dye is put into the bloodstream and then x-rays are taken. They will show a clear picture of the kidney, bladder and other nearby organs.

Magnetic Resonance Imaging (MRI)

An MRI uses magnets and radio waves, instead of x-rays to produce very detailed images of the area of the body being studied.

Mammography

Mammography refers to x-ray examination of the breast. Mammography is used to detect and diagnose breast disease both in women who have breast symptoms (problems such as a lump, pain or nipple discharge) and women who are asymptomatic (no breast complaints). To perform a mammography, the breast is compressed to spread the tissue apart and allow a lower dose of x-ray. Although this may be temporarily uncomfortable, it is necessary in order to produce a good mammogram. The compression is only in place a few seconds of the examination and the entire procedure for screening mammography takes about 20 minutes. This x-ray does not penetrate tissue as easily as the x-ray used for routine chest films or x-rays of the limbs (arm, legs). To put dose into perspective, a woman who receives radiation as a treatment for breast cancer will receive several thousand rads. If a woman had yearly mammograms beginning at age 40 years and continuing until 90, she will have received 10 rads.

Mediastinoscopy

With the patient asleep, tissue samples are taken from the lymph nodes along the windpipe through a small hole cut into the neck. Again, looking at the tissue under a microscope can show if cancer cells are present.

Magnetic Resonance Imaging (MRI)

The MRI involves scanning the body using magnetic energy in order to get detailed pictures. There are currently no known side effects of the MRI other than possible anxiety or distress due to being confined to a small space while in the MRI machine.

Needle biopsy

A needle is placed into the tumor to remove a piece of tissue. The tissue is looked at in the lab to see if cancer cells are present.



IRB STANDARD OPERATING PROCEDURES

Out of Reach of Children / Others who are unable to read or understand

The study medication must be taken only by the person for whom it has been prescribed. Caution should be used to keep this medication out of the reach of children and other people who are unable to read or understand written directions. **Pelvic Examination**

Some women experience discomfort during a pelvic examination. You may feel embarrassed or shy during this next part of the exam: you will be asked to take off your clothes and lie down on the exam table. You can ask to have your partner, a friend or a nurse stay in the room if it makes you feel more comfortable. It may feel uncomfortable having the speculum inserted, but it should not hurt.

Pelvic Ultrasound

Ultrasound is a painless way to show the structures inside your pelvis using sound waves and a type of sonar detection system to generate a black and white picture. Depending on the view of your pelvic organs, the ultrasound technician may position the ultrasound machine's wand to look through your abdominal wall ("pelvic ultrasound"). During the pelvic ultrasound, you will lie on your back on a table. A technician or doctor will first squirt some clear jelly onto your lower abdomen to help the ultrasound sensor slide around easily, and then will place the sensor against your skin in this jelly. Sometimes you will feel pressure during this procedure. There are generally no other risks or discomforts associated with a pelvic ultrasound.

Precautions during study treatment

Because of possible dizziness or drowsiness you are cautioned regarding operating a vehicle or heavy equipment while in this study. Until you know how you will be affected by the study drug, you should exercise special caution when driving or using machinery.

Pregnancy – Cannot Take Part

(A) There may be unforeseen risks to an unborn child associated with your participating in this study. If you are of childbearing potential, you may enter this study only if you are practicing (and have been for at least one month prior to the start of the study) a medically approved, effective method of birth control, such as hormonal contraceptives, intrauterine device or spermicide and barrier (for example, condom or diaphragm), or you are practicing abstinence. If you become pregnant while participating in the study, you must contact your study doctor immediately.

(B) There may be unforeseen risks to an unborn child associated with your taking (Drug Name). For this reason, you must agree to be abstinent or to use highly effective means of birth control such as IUD (Intrauterine device), an implantable contraceptive (such as Norplant®), an injectable contraceptive (Depo-Provera®), a barrier method of contraception (such as a condom or diaphragm with spermicide). Your doctor and you must discuss your methods of birth control. Your doctor and you must agree that they are effective. You are responsible for advising your doctor if you suspect that you may be pregnant or if you are a male and suspect your partner may be pregnant. The effects of (Drug Name) on a nursing infant are unknown; if you are breastfeeding, you cannot participate in the study.

Unknown Risks

There may be risks or side effects related to the study drug that are unknown at this time. You will be notified if significant new findings become known that may affect your willingness to continue in the study.

Pulmonary Angiography & Venography

Procedures:

Pulmonary angiography: an injection of x-ray dye into an artery in the lungs to check for clots in the blood vessels of the lungs.

Venography: An x-ray which involves the injection of a contrast dye through a small needle inserted in the top of the feet to examine the deep veins in your legs.

Some of the potential risks and discomforts associated with pulmonary angiography and venography include irritation, pain, bleeding, and/or tissue damage at the injection site. Angiography and venography rarely may cause or worsen inflammation of the veins and/or blood clots. A small number of people have had changes in kidney function after x-ray dye injection. Angiography may also cause



IRB STANDARD OPERATING PROCEDURES

coughing, an increase in the pressure in the arteries of the lung, and damage to the arteries. Also, you may have an allergic reaction to the x-ray dye and/or study medication, which may include itching, rash, hives, swelling, low blood pressure and possible difficult breathing. As with any x-ray procedure, there will also be exposure to low doses of radiation.

Pulmonary Catheter

Placement of a catheter into a vein in the chest also carries a number of risks, which could be mild or life threatening. The process of inserting the catheter could cause pain, bleeding, or rarely, collapse of the lung. If these occur, I could require blood transfusions, hospitalization, or in the unlikely event of a collapse of the lung, placement of a tube in the side of my chest to allow the lung to re-expand. After placement, the catheter could become infected, requiring treatment with antibiotics, or a blood clot could develop around the catheter, requiring treatment with blood thinners. Treatment for infections or blood clots around the catheter often requires hospitalization.

Quinolone Usage

A small number of people taking quinolones have reported shakiness, headache, dizziness, anxiety, confusion, restlessness, lightheadedness, difficulty sleeping, and, very rarely, seizures. Vomiting has also been reported. Some quinolones may rarely cause an increased sensitivity to sunlight; therefore, you should avoid excessive exposure to sunlight or artificial ultraviolet light while taking the study medicine. You should immediately contact the study doctor or study staff if a rash, skin burning, redness, swelling, or blisters or any other kind of skin abnormality occurs. Tendonitis (inflammation of tendons and muscles) and tendon rupture (tearing of the fibers of the tendon) have been associated with quinolone usage in a very small number of adults. Therefore, if you have tendon pain or swelling, you should call your study doctor immediately.

It is advised that patients taking quinolones should drink plenty of fluids; in addition, quinolones may affect your blood sugar. If you are a diabetic, you should watch your blood sugar readings closely. If you are diabetic and being treated with insulin or an oral hypoglycemic agent and a hypoglycemic reaction occurs, you should immediately contact the study doctor.

If you are taking theophylline, warfarin, or cyclosporin, you must tell the study doctor because quinolones may cause an increase of levels of these drugs in the blood. Your theophylline, warfarin, or cyclosporin levels may be measured at each study visit

Radiation exposure

Diagnostic (i.e. Chest x-ray, CT Scan)

The radiation you receive from the x-ray is minimal. The more radiation you receive over the course of your life, however, the greater the risk of inducing changes to the cells in your body or of having cancerous tumors. The changes to your body's cells possibly could cause abnormalities or diseases in your future offspring. The radiation from this study is not expected to greatly increase these risks, but the exact increase in such risks is not known. Women who are pregnant should receive no unnecessary radiation and should not participate in this trial.

Risk of Radiation Therapy

General Description:

Radiation therapy is a treatment with high energy rays (such as x-rays) to kill or shrink cancer cells. The radiation may come from outside the body (external radiation) or from radioactive materials placed directly in the tumor (internal or implant radiation).

After surgery, radiation can kill small areas of cancer that may not be seen during surgery. If the size or location of a tumor makes surgery hard, radiation may be used before the surgery to shrink the tumor.



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Radiation Therapy for Bladder Cancer

Radiation therapy is a treatment with high energy rays (such as x-rays) to kill or shrink cancer cells. The radiation may come from outside the body (external radiation) or from radioactive materials placed directly in the tumor (internal or implant radiation).

After surgery, radiation can kill small areas of cancer that may not be seen during surgery. If the size or location of a tumor makes surgery hard, radiation may be used before the surgery to shrink the tumor.

There can be side effects from radiation. These side effects can include mild skin irritation, nausea, bladder irritation, diarrhea and fatigue. Most of these problems will go away after a short while.

Radiation Therapy for Breast Cancer

Radiation therapy is treatment with high-energy rays (such as x-rays) to kill or shrink cancer cells. The radiation may come from outside the body (external radiation) or from radioactive materials placed directly in the tumor (internal or implant radiation).

Most often, external radiation is used for treating breast cancer. It is much like getting a regular x-ray, but for a longer period of time. Radiation therapy may be used to destroy cancer cells remaining in the breast, chest wall, or underarm area after surgery or, less often, to reduce the size of a tumor before surgery. Patients are usually treated five days per week in an outpatient center over a period of about six weeks, beginning around a month after surgery. Each treatment lasts a few minutes. The treatment itself is painless.

The main side effects of radiation therapy are swelling and heaviness in the breast, sunburn-like changes in the treated area, and possibly fatigue. These changes to the breast tissue and skin usually go away in 6-12 months. In some women, the breast becomes smaller and firmer after radiation therapy. Radiation therapy is usually not given during pregnancy because it can be harmful to the fetus.

Radiation Therapy for Colon and Rectal Cancer

Radiation therapy is treatment with high-energy rays (such as x-rays) to kill or shrink cancer cells. The radiation may come from outside the body (external radiation) or from radioactive materials placed directly in the tumor (internal or implant radiation).

After surgery, radiation can kill small areas of cancer that may not be seen during surgery. If the size or location of a tumor makes surgery hard, radiation may be used before the surgery to shrink the tumor.

Radiation also may be used to ease (palliate) symptoms of advanced cancer such as intestinal blockage, bleeding, or pain.

External radiation is most often used for people with colon or rectal cancer. Treatments are given five days a week for several weeks. Each treatment lasts only a few minutes and is something like having an x-ray for a broken bone.

A different approach may be used for some cases of rectal cancer. The radiation can be aimed through the anus and reaches the rectum without passing through the skin of the abdomen.

Side effects of radiation therapy for colon or rectal cancer include mild skin irritation, nausea, diarrhea, or tiredness. These often go away after a while. If you have these or other side effects, talk to your doctor.

There are ways to lessen many of these problems.

Radiation Therapy for Head/Neck Cancers

Radiation therapy is a treatment with high-energy rays (such as x-rays) to kill or shrink cancer cells. The radiation may come from outside the body (external radiation) or from radioactive materials placed directly in the tumor (internal or implant radiation).



IRB STANDARD OPERATING PROCEDURES

After surgery, radiation can kill small areas of cancer that may not be seen during surgery. If the size or location of a tumor makes surgery hard, radiation may be used before the surgery to shrink the tumor.

The administration of standard radiation therapy with or without (Drug Name) could have a potential for risks and discomforts. The most frequent side effects associated with radiotherapy to the head and neck region include skin toxicity in the involved area receiving radiation therapy, inflammation of the linings of the mouth and throat producing pain and difficulty in swallowing, inflammation of the esophagus, and moderate to complete dryness of the mouth and throat due to changes in the salivary glands. A moderate loss of taste may also be experienced. It is recommended that you wear sunscreen when you are outdoors. The above side effects can make eating difficult or may lead to poor nutrition or weight loss. Sometimes, this requires placement of a feeding tube into the stomach until therapy is finished.

Radiation Therapy for Lung Cancer

Radiation therapy is treatment with high-energy rays (such as x-rays) to kill or shrink cancer cells. The radiation may come from outside the body (external radiation) or from radioactive materials placed directly in the tumor (internal or implant radiation). External radiation is the type most often used to treat lung cancer.

Radiation is sometimes used as the main treatment of lung cancer, for example, for those people who may not be healthy enough to have surgery. For other patients, radiation might be used after surgery to kill small areas of cancer that can't be seen and removed during surgery. Radiation can also be used to relieve symptoms such as pain, bleeding, and trouble swallowing.

Side effects of radiation therapy could include mild skin problems, nausea, vomiting, and tiredness. Often these go away after a short while. Chest radiation may cause lung damage and difficulty breathing. Side effects of radiation therapy to the brain (to treat metastasis) usually become most serious one or two years after treatment, and include headaches and trouble with thinking. Be sure to talk with your doctor if you have any side effects.

Radiation Therapy for Prostate Cancer

Radiation therapy is another way to treat prostate cancer. In this treatment, high-energy x-rays are used to kill cancer cells. Radiation is used most often for cancer that has not spread outside the prostate gland, or has spread only to nearby tissue. If the disease is more advanced, radiation may be used to shrink the tumor and provide pain relief. While radiation usually eliminates the need for surgery, men who do not have a good response to radiation might still have surgery at a later date.

Two methods of giving radiation are used to treat prostate cancer:

External beam radiation is much like getting a regular x-ray, but for a longer time. Each treatment lasts only a few minutes. Patients usually have five treatments per week on an outpatient center over a period of seven or eight weeks. The treatment itself is painless.

Side effects can include diarrhea with or without blood in the stool, and irritated intestines. Sometimes, normal bowel function does not return after treatment is stopped. Both during and after treatment, other side effects might include frequent urination, feeling like you have to urinate all the time, burning while urinating, and blood in the urine.

Also, external radiation therapy can cause tiredness that may not go away until a month or two after treatment stops. In about half the men, some degree of impotence may occur within two years of radiation. Impotence usually does not begin right after treatment (as it often does with surgery) but develops slowly over one or more years.

Internal radiation uses small radioactive pellets (each about the size of a grain of rice) placed directly into the prostate. They may be permanent or temporary. Because they are so small, they cause little discomfort and are simply left in place after their radioactive material is used up. In another method, needles containing a higher amount of radioactive material can be used to place



IRB STANDARD OPERATING PROCEDURES

the material for less than a day. This approach is called *high dose rate brachytherapy*. For about a week after the needles are put in place, there may be some pain in the area and a red-brown color to the urine.

While radiation therapy can be used as the main treatment for prostate cancer, it can also be used to treat bone pain for cancer that has spread to the bone. Strontium 89 (Metastron) is the substance used for this

Side effects of internal radiation therapy can include impotence, urinary incontinence, and bowel problems. Rectal problems such as burning, pain, and diarrhea may occur in a small number of men. They can be hard to treat once they develop. Impotence is less likely to be a problem after internal radiation than after surgery or external beam radiation. Be sure to talk to your doctor if you have any of these side effects. Often there are medicines or other methods to help.

Sigmoidoscopy

A sigmoidoscopy allows a doctor to look at the inside of *the sigmoid colon* (the lower part of the large intestine or colon) and the rectum. The doctor will use a *sigmoidoscope*, a slender, flexible, hollow, lighted tube to do the test. A sigmoidoscope is about the thickness of a finger and is inserted through the rectum up into the colon. The sigmoidoscope is connected to a video camera and a video display monitor. This allows the doctor to look for bleeding, cancer, and polyps. Polyps are small growths that can become cancerous. The length of a sigmoidoscope is about 60 centimeters (about 2 feet), allowing the doctor to see about half of the colon. A sigmoidoscope is shorter in length than a colonoscope.

A sigmoidoscopy may be somewhat uncomfortable, but it should not be painful.

The colon and rectum must be cleansed so your doctor can view the lining of the sigmoid colon and rectum. There are a few different regimens for bowel preparation. You may be asked to use two enemas prior to the exam. Another bowel preparation consists of drinking only clear liquids for a day or two before the exam in addition to an enema prior to the exam. Your doctor will give you specific instructions that you should follow.

A sigmoidoscopy takes 10 to 20 minutes. Bleeding and puncture of the colon are possible complications of sigmoidoscopy. However, such complications are uncommon. You may receive medicine before the test to help you relax but you will be awake for the test. You may be placed on your side or on your back with your knees positioned near your chest. Your doctor may also have a special table that rotates to ease positioning.

The sigmoidoscope is lubricated so it is easy to insert into your rectum. Your right buttock will be raised as the sigmoidoscope is inserted into your rectum. It may feel cool. To ease discomfort and the urge to have a bowel movement, it is helpful to breathe deeply but slowly through your mouth. The sigmoidoscope may stretch the wall of the colon so you may feel muscle spasms or lower abdominal pain. Air will be placed into the sigmoid colon through the sigmoidoscope so the doctor can see the colon better. The air can cause gas.

During the procedure, you might feel pressure and slight cramping in your lower abdomen. You will feel better afterwards when the air leaves your colon.

Flexible sigmoidoscopy is generally a safe test although rare complications can occur. These can include a reaction to the sedative or numbing medication that is spread on the tube that is passed into the rectum. Usually there is some pain or discomfort, like feeling of fullness, felt during this test. Even more rarely, a hold can be made in the side of the rectum or colon that can require surgery.

Sputum cytology

A sample of phlegm (mucous or spit) is looked at under a microscope to see if cancer cells are present.



IRB STANDARD OPERATING PROCEDURES

Tympanocentesis

Tympanocentesis is a procedure where the doctor uses a knife to make an incision in the eardrum, and is usually done in the operating room under general anesthesia. This temporarily allows drainage of fluid and relieves pain. Because the incision heals within a day or two, the symptoms usually return, especially if the underlying infection is still present.

Risks with Procedure

The instruments used as part of the ear evaluation may cause some children to feel slight discomfort, or they may not like the sound of the instrument. In addition, temporary pain and a very small chance of bleeding or further infection may occur from the tympanocentesis. There is also a small risk that the tympanocentesis may cause a permanent hole in the eardrum and loss of hearing.

Ultrasound

Also known as sonography, and ultrasound is an imaging method in which sound waves are used to outline a part of the body. Sound waves are transmitted through the area of the body being studied. The sound wave echoes are picked up and translated by a computer into an image that is displayed on a computer screen. No radiation exposure occurs during this test.

Venography

The venography (x-ray of the veins in the legs) will require the introduction of dye into a vein of the foot; and, as with any venous puncture, increased bleeding, bruising and/or pain may occur. The dye may cause pain or burning when it is injected, and may worsen kidney function in people who have kidney disease or who are dehydrated. The contrast dye may also cause an allergic reaction, which could be severe and life threatening. There is a risk of clot formation after the venography procedure takes place.

If this procedure is being performed for research purposes only:

This procedure is performed as part of this study for evaluation purposes and is not routinely performed after (name of procedure).

If the procedure that is being performed is standard of care:

This procedure is performed as standard of care for (name of procedure).

V/Q Scan

A V/Q scan (x-ray of the lungs) will require an introduction of radioactive substance into a vein of the arm, which may cause increased bleeding, bruising and/or pain at the site where the substance is introduced. This scan also requires breathing a radioactive gas into a tube for a few minutes, and being able to hold your breath for a short period. This may cause some anxiety. If you are unable to complete this part of the test due to anxiety, notify the doctor. The amount of radioactivity received by this test is about the same as with a chest x-ray.

Withdrawal from medications

The symptoms of your illness may become worse after withdrawal of the medications that you were taking to treat these symptoms. If you are treated with a placebo in the trial, your symptoms might get worse. If you are treated with (Drug Name), your condition might not respond to (drug name) or your symptoms might become worse. Your condition will be monitored closely by the trial doctor and his/her staff. If you or your trial doctor decide to stop your participation in the trial because of worsened symptoms of your illness or side effects of your trial medication, you will receive appropriate follow up treatment as determined by you trial doctor.



IRB STANDARD OPERATING PROCEDURES

Appendix 18 – BRANY IRB Standard Operating Procedures

HIPAA Authorization Template Language

AUTHORIZATION TO USE AND DISCLOSE PERSONAL HEALTH INFORMATION

Federal regulations give you certain rights related to your health information. These include the right to know who will be able to get the information and why they may be able to get it. The study doctor must get your authorization (permission) to use or give out any health information that might identify you.

If you choose to be in this study, the study doctor will get personal information about you. This may include information that might identify you. The study doctor may also get information about your health, including:

- Past and present medical records
- Research records
- Records about phone calls made as part of this research
- Records about your study visits
- Information obtained during this research about laboratory test results
- Results from diagnostic and medical procedures including but not limited to X-rays, physical examinations and medical history
- Billing records

Information about your health may be used and given to others by the study doctor and staff. They might see the research information during and after the study.

Your information may be given to the sponsor of this research. “Sponsor” includes any persons or companies that are working for or with the sponsor, or are owned by the sponsor. Information about you and your health which might identify you may be given to:

- The U.S. Food and Drug Administration
- Department of Health and Human Services agencies
- Governmental agencies in other countries
- Biomedical Research Alliance of New York (BRANY)
- The Institutional Review Board
- HHC Corporate Research Staff Members {for HHC sites only}
- Accrediting agencies
- Data Safety Monitoring Boards
- Health Insurers/Payers

Your personal health information may be further shared by the groups above. If shared by them, the information will no longer be covered by the U.S. federal privacy laws. However, these groups are committed to keeping your personal health confidential.

If you give permission to give your identifiable health information to a person or business, the information may no longer be protected. There is a risk that your information will be released to others without your permission.

Information about you and your health that might identify you may be given to others to carry out the research study. The sponsor will analyze and evaluate the results of the study. In addition, people from the sponsor and its consultants will be visiting the research site. They will follow how the study is done, and they will be reviewing your information for this purpose. The information may be given to the FDA. It may also be given to governmental agencies in other countries. This is done so the sponsor can receive marketing approval for new products resulting from this research. The information may also be used to meet the reporting requirements of governmental agencies.



IRB STANDARD OPERATING PROCEDURES

This Authorization does not have an expiration date. If you do not withdraw this Authorization in writing, it will remain in effect indefinitely.

By signing this consent form, you are giving permission to use and give out the health information listed above for the purposes described above. You do not have to sign this consent form. If you choose not to sign this consent form, you will not be able to be in this research study. Your decision not to sign this consent form will not have any effect on your medical care and you will not lose any benefits or legal rights to which you are entitled.

You have the right to review and copy your health information. However, if you decide to be in this study and sign this permission form, you may not be allowed to look at or copy your information until after the research is completed.

You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the study doctor at the address on the front of this informed consent form. If you withdraw your permission, you will not be able to continue being in this study, but you will not have any penalty or loss of access to treatment or other benefits to which you are entitled.

When you withdraw your permission, no new health information which might identify you will be gathered after that date.

Notice Concerning HIV-Related Information: The recipients of HIV-related information are prohibited from redisclosing it without your authorization unless permitted to do so under federal or state law. You also have a right to request a list of people who may receive or use your HIV-related information without authorization. If you experience discrimination because of the release or disclosure of HIV-related information, you may contact the agencies responsible for protecting your rights.



IRB STANDARD OPERATING PROCEDURES

Appendix 19 – BRANY IRB Standard Operating Procedures

Sample Informed Consent Form

SAMPLE ICF - the text in this document describing specific procedures, illnesses, etc. are given as EXAMPLES of the information that should be included, where applicable. Please view the embedded comments for additional guidance.

BIOMEDICAL RESEARCH ALLIANCE OF NEW YORK INSTITUTION NAME

SUBJECT INFORMATION AND INFORMED CONSENT FORM

Protocol Title:

Protocol #:

Sponsor:

Principal Investigator: , (MD, PhD, etc.)

Institution:

Address:

Telephone:

INTRODUCTION

You are being asked to be a subject in a research study because you have been diagnosed with _____. Insert 1-2 sentence definition of illness/symptoms in lay terms. This consent form explains the research study. Before you decide to be a part of this study, you need to know why the research is being done, what it will involve and the risks and benefits. Ask the study doctor and study staff to explain anything in this form or about the study that is unclear. Please take time to read this information carefully. Feel free to discuss it with your relatives, friends and your primary care physician. If you agree to take part in the research study, you must sign this consent form.

DISCLOSURE OF FINANCIAL INTERESTS

Sponsor Name is providing funds to the (study doctor or institution) on a per subject basis for conducting this research study.

PURPOSE OF THE STUDY

The purpose of this study is to evaluate the safety and effectiveness of an experimental drug called _____. An experimental drug is not approved by the United States Food and Drug Administration (FDA) for use except in research studies. Some subjects will receive either Antibiotic A or Antibiotic B. These are both approved by the FDA to treat your illness. The results will be compared among the different study drug regimens.

NUMBER OF SUBJECTS AND LENGTH OF STUDY

Your participation in this study will last 6 weeks.



IRB STANDARD OPERATING PROCEDURES

About 75 subjects will participate in this study at research sites around the world. This study site is expected to enroll 5 subjects.

STUDY PROCEDURES

A description of visits and procedures including but not limited to blood draws (with amount drawn), ECGs, injections, follow up phone calls, pulmonary function testing, pregnancy test, X-rays, questionnaires, diaries, etc.

- ◆ If the study requires subjects to be “*randomized*” or “*randomly assigned*” this process must be explained to the subject in the consent form. Common phrases that can be used to describe randomization may include “*like the flip of a coin*” (if the chances are 50/50), “*Like the roll of the dice*”, “*by chance*”, “*like a lottery*”, or “*picking chances from a hat*”.
- ◆ The dosage of study drug being administered to the subject should be included in this section of the consent form. “*If you are randomized to receive drug XXX, you will receive one of the following doses: 3 mg/kg/day, 6mg/kg/day, or 12 mg/kg/day. Your chances of receiving placebo are 1 in 4.*”
- ◆ Route of study drug administration (by mouth, injection, intravenous infusion)
- ◆ Is the study double blind? This too must be explained. “*Neither you nor the study doctor will know which treatment you receive. In the event of an emergency your study doctor can discover which drug you are receiving.*”
- ◆ Does the protocol require a washout period? This process must be explained to the patient. “*A period of time in which you will be asked not to take your current medication.*”
- ◆ Is the study open-label, placebo controlled, or evaluator blind? These phrases are not lay language and need to be described.
- ◆ The consent form should address the duration of individual visits and procedures including questionnaires. “*Visit one is expected to last about 1 hour.*”
- ◆ If a drug, device, test, or procedure employed in the course of the research study is considered part of routine clinical practice or standard patient care, this should be noted. Conversely, if participation in the research project entails an extra spinal tap, endoscopy, EKG, chest x-ray, blood drawing, etc., this must also be noted. “*Carotid angioplasty and stent implantation are an alternative to surgery but are considered experimental.*”
- ◆ The chances of receiving study drug vs. placebo should be documented in the consent form, for example, “*Your chances of receiving study drug are 50/50*”.
- ◆ If certain foods must be avoided or if specific medications are contra-indicated, please note.
- ◆ If patient must be accompanied home, this must be noted.
- ◆ If the patient will not be able to perform everyday functions, this must also be noted.
- ◆ Any videotaping or photography should be noted.
- ◆ If patient is expected to wear a holter monitor, keep a diary; respond to telephone inquiries, this information should appear.
- ◆ If subjects will undergo surgery, the administration of anesthesia should be included as well as its use for procedures such as bronchoscopies.

The study has a two week drug regimen period, during which you will be given one of the following drugs: the study drug, antibiotic A or antibiotic B. The drug regimen period is followed by a 4 week follow-up period when you will be asked questions by telephone or in person by the study staff once each week.

Screening:

No study procedures are done without a signed consent form. The screening visit tests and procedures are done to see if you are eligible to be in the study. You will need to come to this visit fasting, that is, no food or drink (except water) for 8 hours before the visit. This visit will take



IRB STANDARD OPERATING PROCEDURES

about 3 hours. The tests and procedures will be:

- A physical examination
- Your vital signs (blood pressure, pulse, heart rate) will be taken
- A review of your medical history and what medications you are taking.
- A blood sample [about 1 tablespoon] will be drawn for routine laboratory tests. A total of about 7 tablespoons of blood will be drawn during the study.
- Women who can have children will take a blood pregnancy test. The test must be negative for you to be in this study.
- A urine sample collected for routine laboratory tests.
- An electrocardiogram (ECG) - a test that measures the electrical activity of the heart
- Fill out a questionnaire about your quality of life, such as your ability to do daily activities

You cannot eat grapefruit or Seville oranges or drink grapefruit juice during the study and should have no more than one alcoholic drink a day.

Washout Period: Certain medications are not allowed during this study. The study doctor will tell you if you have to stop any medications. If you do have to stop any, you will stop taking those medicines 2 weeks before the Drug Regimen period. This is called a Washout period. It is done so all of that medicine is out of your body before you start the study drug.

Randomization: Subjects will be randomly assigned (by chance, like rolling dice) into one of these three study groups:

- Study drug (15 grams each day) plus placebo.
- Antibiotic A (250 milligrams each day) plus placebo
- Antibiotic B (1000 milligrams each day) plus placebo

A placebo contains no active ingredients, but looks like the active drug. Each of the drugs is a tablet, taken by mouth. Two pills will be taken each morning for two weeks.

You will have an equal chance (1 out of 3 or 33%) of being chosen for any group. Which group you are assigned to will be selected by a computer. Neither you nor the study doctor will know which drug you are receiving. However, your study doctor can find this out in an emergency.

You will be given a study drug diary to write down each time you take the study drug. the study staff will show you how to use the diary.

Drug Regimen Period (Days 1-14):

All subjects will receive study drug for 14 days.

Subjects in the hospital will have the number of headaches and abdominal (stomach) discomfort they have each day, if any, evaluated daily by the study doctor. Each day you will also be asked about any health problems and changes in medications. If you are still having headaches or vomiting and you are still taking the study drug, you will be asked to give a blood sample (about 1 teaspoon) every 4 days to check your blood level of potassium, a salt in the blood. A blood sample (about 1 tablespoon) will also be drawn on Day 8 to monitor your safety.



IRB STANDARD OPERATING PROCEDURES

If you are an outpatient or you are released from the hospital during the Drug Regimen period, you will take your study drug at home. You will be given the name of a contact person and you will be instructed to phone this person to report new or worsening headaches. You will receive a telephone call each day from the study staff. They will ask about your health and medications, your number of headaches per day and the greatest amount of stomach discomfort, if any. On Day 8, you will be asked to return to the clinic for a complete physical examination and blood draw (about 1 tablespoon). On Day 15, you will be asked to return to the clinic for an End of Drug Regimen visit.

Photographs: Some subjects in previous studies with this study drug had a rash on their back. If this happens to you, a member of the study staff will take pictures of your rash. You will not be identified in the photographs, so no one will be able to recognize you. The photographs will be part of your research study files.

Holter Monitor Sub-Study (optional)

Some subjects will be asked to take part in an optional sub-study to check if the study drug affects the heart. You can still be in the main study even if you do not want to be in this Holter monitor sub-study. The Holter is a small box, worn on the waist, which continually measures the person's heart rate. You will be shown how to wear the device. You cannot shower or do heavy exercise when wearing this device. You will come back to the clinic the next day to have the monitor removed. Please initial below if you want to be in the Holter Monitor sub-study:

I agree to be in the 24-hour Holter Monitor study: _____ YES _____ NO

End of Drug Regimen Visit: Once you have finished taking the study drug you will have an end of drug regimen evaluation. You will be examined by the study doctor, a blood sample [about 1 tablespoon] will be drawn, and you will be asked about any health problems and changes in the medications that you take. You will need to bring all unused study drug with you to this visit. The study doctor will discuss what needs to be done during the follow-up period and give you the telephone number of a person who you should call immediately to report health problems during the follow-up period.

Follow-up:

There will be a 4 week follow-up period once you have completed taking the study drug. Each week you will be interviewed (either in person or by phone) and asked about any health problems that have occurred and any changes in the medications that you take. You will also be questioned as to whether you have had headaches. If you have a headache at any time you should call, right away, the person whose phone number you received at your end of drug regimen visit. Within 3 days of the return of a headache you will be asked about your recent number of headaches, any stomach pain, hospitalizations, medication changes and any other possible causes for your headaches. You may also be asked to return to the clinic for an exam by the study doctor and to provide a blood sample (about 1 tablespoon) for laboratory tests.

RISKS AND DISCOMFORTS

Include risks and/or discomfort that subjects may encounter. Where possible state common/uncommon/rare. Note the possibility of side effects that are not yet known.



IRB STANDARD OPERATING PROCEDURES

There may be risks or side effects related to the study drug that are unknown at this time. You will be notified if significant new findings become known that may affect your willingness to continue in the study.

Study Drug:

The side effects associated with the study drug that were reported most frequently include cough, headache, dizziness and sore throat. Rarely, side effects such as swelling of the face, lips, hands, or feet, and allergic reaction have occurred. Some allergic reactions can be severe and even life threatening.

Pregnancy Risks, Birth Control: The effects of the study drug on a nursing infant are unknown. If you are breastfeeding, you cannot participate in the study.

You may not participate in this study if you are currently pregnant or if you are trying to become pregnant. There may be risks to an unborn child associated with your taking the study drug. For this reason, you must agree to be abstinent or to use a highly effective means of birth control, such as hormonal contraceptives (birth control pills), intrauterine device (IUD), an injectable contraceptive (Depo-Provera), or a barrier method of contraception (such as a condom and/or diaphragm with spermicide). The study doctor will discuss with you the acceptable methods of birth control. You are responsible for notifying the study doctor if you think that you may be pregnant or if you are a male subject and think your partner may be pregnant. The study drug may involve risks to you or to the embryo or fetus which are currently unknown.

Drug Combinations: The study drug may interact with other drugs you are taking. This may change the way the study drug or the other drugs work. Be sure to tell the study doctor about any medications, prescribed or over the counter, vitamins and herbal supplements that you are taking or before starting any new ones.

Other Risks of Study Drug: The study drug must only be taken by the person for whom it has been prescribed and must be kept out of the reach of children and persons of limited capacity to read or understand. There may be risks or side effects related to the study drug that are unknown at this time.

The study drug will not be made available to you once your participation in the study ends whether or not you have a positive response to the study drug.

Placebo Group: Placebo may be one of the study drugs you receive during the study. If you receive placebo your condition may go untreated and may worsen as a result.

Washout Period, Stopping Medications: You will be asked to stop any current treatment for your high blood pressure, including prescribed medications or herbal therapy, for the duration of the study. If your condition does not improve or gets worse, you should contact the study doctor immediately.

Radiation: The radiation you receive from the chest x-ray is minimal. However, the more radiation you receive during your life, the greater the risk of inducing changes to the cells in your body or of having cancerous tumors. The changes to your body's cells possibly could cause



IRB STANDARD OPERATING PROCEDURES

abnormalities or disease in your future children. The radiation from this study is not expected to greatly increase these risks, but the exact increase in such risks is not known. Pregnant women should receive no unnecessary radiation and should not take part in this study.

Blood Draw: Risks and discomforts associated with drawing blood samples may include pain, bruising, bleeding and on rare occasions, infection at the needle stick site. Other risks are feeling lightheaded and faint.

Electrocardiogram, MRI, CT, etc - include risks.

NEW INFORMATION

You will be notified in a timely way if important new findings become known that may affect your willingness to continue in the study.

BENEFITS

There is no guarantee that your condition will improve as a result of your participation in this study. It may stay the same or worsen. However, the information learned from this study may help other people with this disease in the future.

ALTERNATIVES TO STUDY PARTICIPATION

You do not have to participate in this study to receive treatment for your condition. There are FDA-approved treatments such as XXX, YYY or ZZZ that your doctor can prescribe to treat your condition. You may also choose to have treatment for your symptoms (palliative care) or to have no treatment. The study doctor will discuss study alternatives with you and their risks and benefits.

COSTS OF PARTICIPATION

The study drug will be provided to you at no cost. The sponsor will cover the cost of all study visits and procedures and tests that are done as part of this study.

You and/or your insurance will be responsible for the costs of the regular treatment for your condition. These would be done even if you were not in this study. The costs for these procedures will be billed to your insurance in the usual way. If you are uninsured, you will be billed for them. You will be responsible for any costs your insurance does not cover. You will not be responsible for the procedures that are experimental.

REIMBURSEMENT FOR PARTICIPATION

You will receive \$50 per visit toward your study related expenses such as travel and parking. If you leave the study early, you will be reimbursed only for visits you complete. You will receive reimbursement by check, 4 to 6 weeks after completion of each study visit.

Note the following limitations for Department of Defense supported research that involves U.S. military personnel:

1. Individuals cannot be compensated for *research taking place during duty hours.*
2. Federal employees while on duty and non-federal individuals may be compensated for research blood draws up to \$50 per blood draw.
3. Non-federal individuals may be compensated for research participating other than blood

446

Version A

Protocol [Add sponsor's protocol # here]

Page 446 of 595

IRB approved from _____ through _____.

Revision dated 04.17.2015



IRB STANDARD OPERATING PROCEDURES

draws in a reasonable amount, to be reviewed/approved by the IRB.

COMPENSATION FOR INJURY

If you become ill or injured as a result of participating in this research study, medical care to treat such illness or injury will be made available to you. The cost of such treatment will be covered by the study sponsor (to the extent such costs are not covered by your commercial health insurance, non-government program or other third party). No other compensation will be offered by {Institution/Private Practice}, the sponsor or the Biomedical Research Alliance of New York.

You are not waiving any legal right to seek additional compensation through the courts by signing this form.

For Department of Defense (DoD) research, provisions to be outlined in the *Compensation for Injury* section depend upon whether DoD supports, conducts, or is engaged in the research. Please refer to DoD Instruction 3216.02, Section 10, Protecting Human Subjects From Medical Expenses If Injured.

CONFIDENTIALITY

To the extent allowed by law, every effort will be made to keep your personal information confidential. However, information from this study will be submitted to the study sponsor and to the U.S. Food and Drug Administration (FDA). It may be submitted to governmental agencies in other countries where the study drug may be considered for approval. Medical records, which identify you and the consent form signed by you, will be looked at by the sponsor or the sponsor's representatives and may be looked at by the FDA and other regulatory agencies, the Institutional Review Board, and the Biomedical Research Alliance of New York. While these parties are aware of the need to keep your information confidential, total confidentiality cannot be guaranteed. The results of this research project may be presented at meetings or in publications; however, you will not be identified in these presentations and/ or publications.

Effective March 2011, FDA requires the informed consent form contain the following statement for applicable clinical trials, as defined in 42 U.S.C. 282(j)(1)(A),

- *Trials of Drugs and Biologics: controlled clinical investigations, other than Phase 1 investigations, of a product subject to FDA regulation (not generics)*
- *Trials of Devices: Controlled trials with health outcomes of devices subject to FDA regulation, other than small feasibility studies, and pediatric postmarket surveillance*

A description of this clinical trial will be available on www.ClinicalTrials.gov, as required by U.S. law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

AUTHORIZATION TO USE AND DISCLOSE PERSONAL HEALTH INFORMATION

Federal regulations give you certain rights related to your health information. These include the right to know who will be able to get the information and why they may be able to get it. The study doctor must get your authorization (permission) to use or give out any health information that might identify you.



IRB STANDARD OPERATING PROCEDURES

If you choose to be in this study, the study doctor will get personal information about you. This may include information that might identify you. The study doctor may also get information about your health, including:

- Past and present medical records
- Research records
- Records about phone calls made as part of this research
- Records about your study visits
- Information obtained during this research about laboratory test results
- Results from diagnostic and medical procedures including but not limited to X-rays, physical examinations and medical history
- Billing records

Information about your health may be used and given to others by the study doctor and staff. They might see the research information during and after the study.

Your information may be given to the sponsor of this research. "Sponsor" includes any persons or companies that are working for or with the sponsor, or are owned by the sponsor. Information about you and your health which might identify you may be given to:

- The U.S. Food and Drug Administration
- Department of Health and Human Services agencies
- Governmental agencies in other countries
- Biomedical Research Alliance of New York (BRANY)
- The Institutional Review Board
- HHC Corporate Research Staff Members {for HHC sites only}
- Accrediting agencies
- Data Safety Monitoring Boards
- Health Insurers/Payers

Your personal health information may be further shared by the groups above. If shared by them, the information will no longer be covered by the U.S. federal privacy laws. However, these groups are committed to keeping your personal health confidential.

If you give permission to give your identifiable health information to a person or business, the information may no longer be protected. There is a risk that your information will be released to others without your permission.

Information about you and your health that might identify you may be given to others to carry out the research study. The sponsor will analyze and evaluate the results of the study. In addition, people from the sponsor and its consultants will be visiting the research site. They will follow how the study is done, and they will be reviewing your information for this purpose. The information may be given to the FDA. It may also be given to governmental agencies in other countries. This is done so the sponsor can receive marketing approval for new products resulting from this research. The information may also be used to meet the reporting requirements of governmental agencies.

This Authorization does not have an expiration date. If you do not withdraw this Authorization in

448

Version A

Protocol [Add sponsor's protocol # here]

Page 448 of 595

IRB approved from _____ through _____.

Revision dated 04.17.2015



IRB STANDARD OPERATING PROCEDURES

writing, it will remain in effect indefinitely.

By signing this consent form, you are giving permission to use and give out the health information listed above for the purposes described above. You do not have to sign this consent form. If you choose not to sign this consent form, you will not be able to be in this research study. Your decision not to sign this consent form will not have any effect on your medical care and you will not lose any benefits or legal rights to which you are entitled.

You have the right to review and copy your health information. However, if you decide to be in this study and sign this permission form, you may not be allowed to look at or copy your information until after the research is completed.

You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the study doctor at the address on the front of this informed consent form. If you withdraw your permission, you will not be able to continue being in this study, but you will not have any penalty or loss of access to treatment or other benefits to which you are entitled.

When you withdraw your permission, no new health information which might identify you will be gathered after that date.

Notice Concerning HIV-Related Information: The recipients of HIV-related information are prohibited from redisclosing it without your authorization unless permitted to do so under federal or state law. You also have a right to request a list of people who may receive or use your HIV-related information without authorization. If you experience discrimination because of the release or disclosure of HIV-related information, you may contact the agencies responsible for protecting your rights.

VOLUNTARY PARTICIPATION / WITHDRAWAL

Your participation in this study is voluntary. You may decide not to participate or you may discontinue your participation at any time during the study, without penalty or loss of benefits or medical care to which you are otherwise entitled. If you decide to leave the study, please tell the study doctor.

If you choose to withdraw from the study early, it is important to know that data collected up until the time you withdraw will remain part of the study database and cannot be removed, and will still be used and given to others. *[Note: This must remain for FDA regulated research.]*

Additional note: An investigator may choose to ask the subject permission to provide continued follow-up and further data collection subsequent to their withdrawal from the interventional portion of the research, and the investigator must obtain the subject's consent to do so. It is expected that the investigator's discussion with the subject will distinguish between study-related interventions and standard care procedures. If the BRANY IRB approved consent form does not already address this information, a consent form revision (or consent addendum) must be submitted for IRB review prior to implementation

Your participation in this study may be stopped without your consent at any time and for any reason by the study doctor, the sponsor, the FDA and other regulatory authorities. Reasons you



IRB STANDARD OPERATING PROCEDURES

may be withdrawn from the study include it is determined to be in your best interest, you need treatment not allowed in this study, you do not follow the study instructions, the study is stopped, or for other administrative reasons. If you leave the study early, you may be asked to return to the study doctor's office for a final study visit for your safety.

*For DoD supported research with an independent research monitor, you must include a statement indicating **the research monitor will have the authority to stop a research study in progress, remove individuals from study, and take any steps to protect the safety and well-being of subjects.***

PRIMARY CARE PHYSICIAN/SPECIALIST NOTIFICATION

Your primary care physician and/or other physicians you are seeing may be notified of your participation in this study so that they can provide you with appropriate, ongoing medical care.

QUESTIONS/COMPLAINTS/CONCERNS

If you have any questions or requests for information relating to this research study or your participation in it, or if you want to voice a complaint or concern about this research, you may contact {Principal Investigator/Research Team Contact} at {PI Phone Number}.

If you have any questions about your rights as a research subject or complaints regarding this research study, or you are unable to reach the research staff, you may contact a person independent of the research team at the Biomedical Research Alliance of New York Institutional Review Board at 516-318-6877. Questions, concerns or complaints about research can also be registered with the Biomedical Research Alliance of New York Institutional Review Board at www.branyirb.com/concerns-about-research.

STATEMENT OF CONSENT

I have read this consent form. I have been informed of the risks and benefits involved. All of my questions have been answered to my satisfaction. I know that the study doctor or study staff will answer any future questions I may have. I will be given a copy of this signed consent form to keep.

By signing this consent form I voluntarily agree to participate in this study.

Subject's Name (Printed)

Subject's Signature

Date

[Only add signature lines for Legally Authorized Representatives if applicable to your research (e.g., research involves individuals who cannot consent for themselves and you're requesting IRB approval to obtain consent from a legally authorized representative for the research)]

Legally Authorized Representative Name (Printed)



IRB STANDARD OPERATING PROCEDURES

Legally Authorized Representative Signature

Date

Name of Person Obtaining Consent (Printed)

Signature of Person Obtaining Consent

Date

{If your Institution's policy requires additional signature lines for the Investigator or Witness, add them here.}



IRB STANDARD OPERATING PROCEDURES

Appendix 20 – BRANY IRB Standard Operating Procedures

Sample Assent Form and Preparation Guidelines

Biomedical Research Alliance of New York, LLC

{INSERT NAME OF INSTITUTION}

PEDIATRIC SUBJECT ASSENT FORM

Project Title:

Protocol Number:

Investigator(s):

Sponsor:

We are doing a research study. A research study is a special way to find out about something. We are trying to find out how a *special drug can be used to treat ...{Insert disease under study}*

There will be about {INSERT TOTAL NUMBER OF SUBJECTS TO BE ENROLLED} other children in this study.

If you decide that you want to be in this study, you will come back to see the study doctor about {Insert Total Number of Study Visits times} over the next few months. We will ask you to tell us how you feel, what medicines you are taking, and what problems you are having, if any.

We want to tell you about some of the things that might happen to you if you are in this study. The study doctor will give you a physical exam and measure your height and weight. This will not hurt. Your blood will be drawn with a needle about {INSERT NUMBER OF BLOOD DRAWS} times and that may hurt a little. You may get a small bruise or a sore where the needle went into your skin. We will look at your heartbeat with a special machine called an ECG; this will not hurt at all. We will take your blood pressure and heart rate at every visit. The blood pressure cuff will squeeze your arm and you may feel it as a pressure for a little while. We will count your heart rate to see how fast your heart is beating; this will not hurt. We will ask you to give us some of your urine in a cup about three times. If you are female and have started your menstrual periods your urine will be tested to see if you are pregnant at the beginning of the study and at the end.

The study drug will be assigned by chance, like pulling numbers from a hat, to see which strength of study drug you will receive. There are 5 different strengths of active study drug and placebo tablets (it looks like the study drug, but it does not have any of the ingredients medication the study drug has) that you could receive during this study.

If you weigh less than 110 lbs., you will be randomly assigned to one of four treatment groups below:

- *Placebo (no active medication)*
- *2 mg of study drug*



IRB STANDARD OPERATING PROCEDURES

- 8 mg of study drug or
- 16 mg of study drug

If you weigh more than 110 lbs., you will be randomly assigned to one of the four treatment groups below:

- *Placebo (no active medication)*
- *4mg of study drug*
- *16 mg of study drug*
- *32 mg of study drug*

There is a 1 in 7 chance that you will not receive active study drug for the entire study. Everyone who decides to enter this study will be on placebo (no active medication) for 1 week.

You should take the study drug whenever your parents (or guardian) tell you to take it. You will be asked to take the study drug once a day at about the same time for 5 weeks. The study drug may make you feel tired, dizzy, may give you a headache, runny nose, sore throat, a cough, make your stomach hurt, may make you feel like you have to throw up or make you throw up, may give you diarrhea (the runs), make your back or chest hurt, cause your arms, legs, hands, and feet to hurt or to puff out or you might have other problems. Be sure to tell your parent/guardian when if you feel any of these things.

If you decide to be in this study, some good things might happen to you. Your blood pressure may not be high while you are taking the study drug. But we don't know for sure that these things will happen. There is a possibility that your blood pressure will not be lowered. Your blood pressure may not get better or may get worse if you are taking the placebo (no active medication) tablets. We might also find out things that will help other children some day.

There are definite risks to an unborn child if you became pregnant during the study. During pregnancy, this study drug can cause injury and even death to a developing unborn baby.

If you have started menstrual periods:

- **By signing this form, you confirm you are as sure as can be that you are not pregnant now and have no intention of becoming pregnant during this study.**
- **By signing this form, you agree that you will not have sex or if you do, you will use one of the following birth control methods: barrier method (sponge, diaphragm or condom) plus spermicidal foam, oral (the "pill") or implanted contraceptives (Norplant).**
- **A urine pregnancy test will be done to confirm that you are not pregnant before you take part in this study as well as at the end of the study.**

Throughout the study, the study doctor or a member of the study staff will ask you about your menstrual period and the possibility of pregnancy. If they feel it is necessary, the study doctor or a member of the study staff can request additional pregnancy tests.



IRB STANDARD OPERATING PROCEDURES

If at any time during this study you think you might be pregnant, or later learn that you were pregnant during the study, you must contact the study doctor immediately for further instructions. Your parent(s) or guardian(s) may have access to the pregnancy test results taken during this study.

Your parents (or guardian) must say it is okay for you to be in this study.

This study will not cost you or your parents (or guardian) any money.

You can ask the nurses and doctors questions any time.

You don't have to be in this study. We will tell you about the other things we can do for your high blood pressure.

When we are done with the study, we will write a report about what we found out. We won't use your name in the report.

You don't have to be in this study. It's up to you. If you say okay now, but you want to stop later, that's okay too. All you have to do is tell us.

If you want to be in this study, please sign your name. We will give you a copy of this form for you to keep.

I, _____, want to be in this research study.
(Print your name here)

(Sign your name here)

(Date)

Signature of person
obtaining this assent

Date of Signature

Printed name of person obtaining this assent

Witness* Signature

Date of Signature

Printed name of Witness*

**Witness is a 3rd party not related to the subject.*



IRB STANDARD OPERATING PROCEDURES

Appendix 21 – BRANY IRB Standard Operating Procedures

Genetic Research Consent Template

Sample language to be used in developing consent forms for genetic research and tissue banking.

An Introduction of Genetic Testing and Voluntary Participation

(1) Introduction: a general description of the test, explaining genetic testing and voluntary participation.

For example:

“You are being asked to provide one [additional, if applicable] blood sample (about __ teaspoonfuls) for the study described below. [You do not have to agree to be in this additional study in order to be in the main study of [name of study drug], if applicable].

DNA is the material in your body’s cells (genes) that pass on characteristics that are inherited from one generation to the next (like hair and eye color).

DNA will be extracted from your blood sample in a laboratory so that your genetic information can be used to study [fill in]”

(2) **Statement of Purpose:** what information is expected to result from the research

(3) Scope of the Project:

“This study is being conducted at approximately __ research centers [in the US, or in ____ and _____, or worldwide] and is expected to involve about ____ subjects.”

(4) **Statement Regarding Identification of Samples:**

For identified samples:

“In order to protect your privacy, your sample will be identified by your subject number, not your name. Only the study doctor and the sponsor of the study, [name of sponsor], will be able to link your subject number with your name. Neither you nor your doctor will be given the results of the testing [where applicable].”

For non-identified samples:

“Your sample will be given a number that cannot be linked with you. Your sample will be stored with thousands [or hundreds or many] of other non-identified samples from [name of institution]. Neither you nor your doctor will be given the results of the testing.”

(5) Physical/Non-Physical Risks and Benefits:

a. Physical Risks:

For blood draws:

“Although the taking of the blood sample causes no serious problems for most people, it can cause some bleeding, bruising, tiredness, dizziness, and/or discomfort at the injection site”

For skin biopsies:

Describe the procedure and the risk of pain and possible infection. Also address whether or not any topical or other anesthetic will be used and any attendant risks associated with the anesthesia.



IRB STANDARD OPERATING PROCEDURES

For other collection procedures:

Describe procedure(s) and attendant risks.

b. Non-Physical Risks:

"There is a chance of future discrimination if the results of the testing show a genetic disorder. You might be denied a job or promotion, or denied health or life insurance if employers or insurance companies find out. You may experience other forms of discrimination. We will not release any information to anyone without your written permission. However, it is possible that genetic information may be gotten through legal means and then affects your ability to get insurance or a job. In cases where parents and children are both tested, tests may reveal the possibility that the father is not the biological parent."

c. Potential Benefits of Genetic Testing:

"This study may improve our understanding of the role of genes in [genetic condition]. Information learned about the gene may increase general knowledge, provide scientists with information about disease and/or eventually lead to improved treatment. There will [or "may" if results will be available and may allow for informed healthcare decisions] be no direct benefit to you or your family from participating in this study."

(6) Statements Regarding Subject's Authorized Disclosure:

All consents must include **confidentiality and authorized disclosure statement** to the effect of:

"Your test results may be disclosed to [name of organizations, persons, or categories of persons] [use your institution's standard consent form confidentiality and disclosure language here]."

(7) Statement regarding contact:

"If you have questions about the research at any time, you may contact [Investigator name and phone number]. If you have questions about your rights as a study subject, please call [IRB name and phone number]."

(8) Statement regarding subject injury:

"If you believe you have been injured as a result of your participation in this research, please call [Investigator name and phone number]. ["Medical care will be provided at [name of Institution]" **OR** ["Dr. _____ will assist you in obtaining appropriate medical care."]
["The costs of this medical care will be paid for by _____" **OR** "You will be expected to pay for this medical care."]

"No other compensation will be offered by [Institution]. However, you are not waiving any legal right to seek additional compensation through the courts by signing this form"

(9) Statement regarding copy of consent:

"You will receive a copy of this consent form."

(10) Statement regarding withdrawal:

"You are free to withdraw from this study at any time without giving up anything you might otherwise be entitled to. Withdrawal will not have any negative effect on your medical care or anything else. The Investigator may also decide to end your participation in the study at any time. You may request that your sample and data relating to it be destroyed at any time, but this will only be possible if the sample and data can be identified."



IRB STANDARD OPERATING PROCEDURES

(11) Statement Regarding Use and Storage of Samples

"No tests other than those described in this form will be performed on your sample without your permission. Your sample will be destroyed at the end of the testing process, which is estimated to take approximately [or specify longer period]

OR

(12) For Storage of Samples for Other Research Purposes:

"We would like to store a sample of your blood or tissue that will be obtained from you during this current research study. We need to ask your permission to store this sample, and we would like to know how we might use it in future approved research studies.

1. Do you give permission for the samples to be used by the study doctor in future research studies that are directly related to the current research?

Please initial your choice: Yes ____ No ____

2. Do you give permission for the samples to be used by the study doctor in future research studies that are unrelated to the purpose(s) of the current research?

Please initial your choice: Yes ____ No ____

3. Do you give permission for the samples to be given to other investigators at this Institution or other institutions for use in research that is either related or unrelated to the purpose of this study?

Please initial your choice: Yes ____ No ____

4. If you agree to have the samples stored for future research do you consent to have your sample stored and labeled in a way that it will be possible to identify you as the donor of the sample?

Please initial your choice: Yes ____ No ____

Please note: If you agree then because the blood/tissue will be linked to you, if you change your mind and ask in writing, we will destroy the sample. If we have already shared the blood/tissue with other researchers we will ask that they destroy the sample.

[If the answer is no, please skip down to Question 5, as the text between questions 4 and 5 will not apply.]

- a. If the future research can be done without having to know who you are or any information about you then we will remove all identifying information from the sample before doing any of the types of research you agreed to above.
- b. If the future research requires that we know who the sample came from and information about the donor of the sample then we will do one of the following:
 - i. If you allow us to contact you in the future, we will be able to explain to you why we wish to use your blood/tissue and your associated information in future research, and we will tell you what we will do with the sample and the information about you. We will then ask your permission to use your blood or tissue in that research project.

May we have your permission to contact you in the future?



IRB STANDARD OPERATING PROCEDURES

Please initial your choice: Yes ____ No ____

- ii. If you do not give us permission to contact you in the future, or if we find that contacting you is not practical, for example because you have moved, we may still use your blood and tissue. Either we will use it after we have removed all links to you and your identifiable health information, or will ask the Institutional Review Board for permission to use the sample. The IRB can give permission to the researcher to use and share your health information and the associated blood/tissue, but only if it determines that doing this will be more than a minimal risk to you or your privacy.

5. Do you consent to have your sample stored and labeled in a way that will make it impossible to identify you as the donor of the sample?

Please initial your choice: Yes ____ No ____

Note: If you agree to have the sample and information stored without any way of identifying you, then you will not be able to change your mind and ask for the blood/tissue to be destroyed at a future date.

(13) For cell lines, where applicable:

"The Investigator may want to use your sample to make a cell line, which means that the cells from my sample would be treated in such a way that they may live and divide outside the body, be frozen for storage indefinitely, and be thawed in the future and used for future genetic research. There are no plans to share with you any financial profits that may result from this research.

Please tell us (by initialing the applicable line) whether you authorize the Investigator to use your sample to make a cell line:

_____ I consent to using my sample to make a cell line

_____ I do not consent to my sample being used for a cell line."

(14) Statement of Consent:

"I have read this consent form and all of my questions have been answered to my satisfaction. I voluntarily consent to be a subject in this research study and to the procedures described in this form. I have been told that there are no plans to share with me any financial profits resulting from the use of my sample. I am not waiving any legal rights by signing this form."

Printed Name of Subject

Subject Signature

Date

Signature of Person Obtaining Consent



IRB STANDARD OPERATING PROCEDURES

Appendix 22 – BRANY IRB Standard Operating Procedures

Sample QA Review Report

\$\$generationdate\$\$

Via email

RE: **Dr.** \$\$PIFirstName\$\$ \$\$PILastName\$\$
BRANY IRB File # \$\$ProtocolCode\$\$-\$\$\$SiteCode\$\$
\$\$sponsorname\$\$ Protocol # \$\$sponsorprotocol\$\$
Protocol Title: \$\$ProtocolDescription\$\$

Dear **Dr.** \$\$PIFirstName\$\$ \$\$PILastName\$\$:

I visited your site for a review of the above referenced protocol on [redacted], 2013.

The above mentioned protocol is subject to Title 45, Code of Federal Regulations (CFR), part 46 – Protection of Human Subjects, Title 21, Code of Federal Regulations (CFR), Part 50 - Protection of Human Subjects, Part 56 - Institutional Review Boards (IRB), Part 312 - Investigational New Drugs, Part 812 – Investigational Device Exemptions, and Title 49 - Transportation of Infectious Substances, as applicable.

In addition, the observations herein contain recommendations intended to keep investigators in compliance with the International Conference of Harmonization/Good Clinical Practice (ICH GCP) Guidelines. ICH GCP is the international ethical and scientific quality standard for designing, conducting, recording and reporting trials that involve participation of human subjects. Compliance with this standard provides public assurance that the rights, safety, and well being of trial subjects are protected, consistent with the principles that have their origin in the Declaration of Helsinki.

During this review I discussed with you and your staff some findings and regulatory issues pertaining to this research project. Items reviewed included the Investigator's regulatory files, including records of IRB/site/sponsor communications, medical records, informed consent, and source documentation for # enrolled subjects.

The status of the trial is open / closed to enrollment.

- # subjects have been enrolled.

This was a routine / for cause quality assurance review. Following is a summary of findings noted during the review.



IRB STANDARD OPERATING PROCEDURES

Key Personnel

<u>Name</u>	<u>CV</u>	<u>License</u>	<u>FDF *</u>	<u>Del. of Authority</u>

- *Reference: 21CFR 312.64(d) financial disclosure reports states “The clinical investigator shall provide the sponsor with sufficient accurate financial information to allow an applicant to submit complete and accurate certification or disclosure statements...The clinical investigator shall promptly update this information if any relevant changes occur during the course of the investigation and for 1 year following the completion of the study.”*
- *Reference: ICH 8.2.10, “Essential Documents For The Conduct Of A Clinical Trial” states, Curriculum Vitae and / or other relevant documents evidencing qualifications of investigator(s) and sub-investigators to conduct the trial and / or provide medical supervision of subjects should be located in the files of the sponsor and the investigator/institution.*
- *Reference: According to ICH/GCP Guidelines 4.1.5, “The investigator should maintain a list of appropriately qualified persons to whom the investigator has delegated significant trial-related duties.”*

IRB Approvals

- The original IRB approval () is on file in the site regulatory binder.
- Continuing review approval () is also on file.
- IRB submissions and corresponding approval letters are on file.
- IRB approval for this project expires **add date**.
- *Reference: ICH 8.2.7“Essential Documents for the Conduct of a Clinical Trial” states that the dated, documented approval / favorable opinion of the IRB /IEC should be located in the files of the investigator/institution to document that the trial has been subject to IRB / IEC review and given approval /favorable opinion.*
- *Reference: ICH 8.3.3“Essential Documents for the Conduct of a Clinical Trial” states that the dated, documented approval / favorable opinion of the IRB /IEC should be located in the files of the investigator/institution to document that amendments and / or revisions have been subject to IRB / IEC review and were given approval / favorable opinion.*

Clinical Protocol

- The originally approved protocol (**Version / date**) is on file.
- Protocol revision (**date**) is also on file.



IRB STANDARD OPERATING PROCEDURES

- *Reference: ICH 8.2.2, "Essential Documents for the Conduct of a Clinical Trial" states that the signed protocol and amendments should be located in the files of the investigator/institution to document investigator and sponsor agreement to the protocol / amendment(s).*

Investigational Brochure

- The originally approved IB (Version / Date) is on file.
- *Reference: ICH 8.2.1, "Essential Documents for the Conduct of a Clinical Trial" states that the investigator's brochure should be located in the files of the investigator/institution to document that relevant and current scientific information about the investigational product has been provided to the investigator.*

1572 Form

- The originally approved 1572 (signed) is on file.

Investigator Statement

- The investigator statement (signed) is on file.
- *Reference: 21CFR 812.43 "Selecting investigators and monitors" states, (c) Obtaining agreements. A sponsor shall obtain from each participating investigator a signed agreement that includes:*
 - (4) *A statement of the investigator's commitment to:*
 - (i) *Conduct the investigation in accordance with the agreement, the investigational plan, this part and other applicable FDA regulations, and conditions of approval imposed by the reviewing IRB or FDA;*
 - (ii) *Supervise all testing of the device involving human subjects; and*
 - (iii) *Ensure that the requirements for obtaining informed consent are met.*

Laboratory / Facility Certifications & Accreditations

- The New York State Department of Health license is on file and current (exp.).
- The College of American Pathologists (CAP) certification is on file and current (exp.).
- The Clinical Laboratory Improvement Amendments (CLIA) certificate is on file and current (exp.).
- Reference ranges (dated) are on file.
 - *Reference: ICH 8.2.11 and 8.2.12, "Essential Documents for the Conduct of a Clinical Trial" state that normal values/ranges for laboratory tests, certifications, or accreditations document the competence of the facility to perform required tests, and support reliability of the data. These documents should be located in the files of the sponsor and the investigator/institution.*

Shipping Infectious Substances

- Documentation of training (exp.) is on file.



IRB STANDARD OPERATING PROCEDURES

- *Reference: The Federal Code of Regulations Title 49 requires that shipping personnel complete training every 3 years. When shipping by air, International Air Transport Association regulations require that shippers receive recurrent training every 2 years.*

Investigational Product Accountability

(include shipping receipts, storage, temperature logs, dispensing records, individual accountability and compliance as appropriate)

- *Reference: 21CFR 312.62(a) states “An investigator is required to maintain adequate records of the disposition of study drug, including dates, quantity, and use by subjects.”*
- *Reference: 21CFR812.140 “Records and Reports” states the following:*
- *Reference: (a) Investigator Records. A participating investigator shall maintain the following accurate, complete, and current records relating to the investigator’s participation in an investigation:*
 - (2) *Records of receipt, use, or disposition of a device that relate to:*
 - (i) *The type and quantity of the device, the dates of its receipt, and the batch number or code mark.*
 - (ii) *The names of all persons who received, used, or disposed of each device.*
 - (iii) *Why and how many units of the device have been returned to the sponsor, repaired, or otherwise disposed of.*
- *Reference: According to ICH guideline 4.6.1, “Responsibility for investigational product(s) accountability at the trial site rests with the investigator/institution.”*

Monitoring

- A monitoring visit log is on file.
- The most current visit was conducted on **date**.
- There were no significant issues noted in the most recent monitoring report.

Source Document Review

Subject

- The subject originally signed the most current version of the consent (**Version**) on **(DATE)**.
- A note documenting the process of consent is on file.
- The subject was re-consented with a revised consent (**Version**) on **(DATE)** .
- Documentation indicates the subject met inclusion criteria as follows:
 - Age > **18: xx**
- Documentation indicates the subject did not meet exclusion criteria as follows:
 - Hgb. < **10: 12.5**
- Documentation indicates the subject’s randomization number (). IVRS documents are consistent with source document records.

References



IRB STANDARD OPERATING PROCEDURES

Consent

- Reference: ICH 4.8.11 states, "During a subject's participation in the trial, the subject should receive a copy of the signed and dated consent form updates and a copy of any amendments to the written information provided to subjects."
- Reference: 21CFR50.25, "Elements of Informed Consent" states, "...significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject."
- Reference: ICH 4.8.8 states "Prior to a subject's participation in the trial, the written informed consent form should be signed and personally dated by the subject or by the subject's legally acceptable representative, and by the person who conducted the informed consent discussion."
- Reference: 21CFR 50.20 "General Requirements for Informed consent" states "the information that is given to the subject or the representative shall be in language understandable to the subject or the representative."
- Reference: 21CFR312.62 (b) "Case Histories" states that the case history for each individual shall document that informed consent was obtained prior to participation in the study.
- BRANY IRB policy, "Investigations Involving Human Subjects and Informed Consent" states, "the informed consent information must be presented in language that is understandable to the subject."
- Reference: The FDA does not require a third person to witness the consent interview unless the subject or representative is not given the opportunity to read the consent form before it is signed, as per 21CFR 50.27(b). The consent document however, that was approved by the sponsor and the IRB, did require the signature of a witness and therefore one should have been obtained.
- Reference: ICH 4.8.9 states, "... the witness attests that the information in the consent form and any other written information was accurately explained to and apparently understood by, the subject or the subject's legally acceptable representative, and that informed consent was freely given...."
- Reference: ICH guidelines define an "impartial witness" as "a person who is independent of the trial, who cannot be unfairly influenced by people involved in the trial...."
- Reference: ICH guidelines (Glossary, 1.61) define vulnerable subjects as, "individuals whose willingness to volunteer in a clinical trial may be unduly influenced...by a retaliatory response from senior members of a hierarchy in case of refusal to participate." Examples are members of a group with a hierarchical structure, such as students and subordinate hospital and laboratory employees.

HIPAA

- Reference: The Health Insurance Portability and Accountability Act of 1996 requires that subjects enrolled in research studies after April 14, 2003 sign an authorization form.
- Reference: 45CFR Subtitle A 164.508...a covered entity may not use or disclose protected health information without an authorization that is valid....

IN SUMMARY:



IRB STANDARD OPERATING PROCEDURES

Please complete the Quality Assurance Audit Response and return via fax by **date**.

This report is a confidential BRANY document and is not to be included in the study file.

This quality assurance review of limited focus is conducted on behalf of the BRANY IRB. It is not intended to replace any required or voluntary monitoring or review function of the institution, the research sponsor, or any other entity. BRANY offers no warranty, guarantee, or certification of any kind with regard to the limited review or the results reported herein.

I would like to thank you, **and** for accommodating me during my QA review. If I can be of any assistance, please do not hesitate to call me at **\$\$userphone\$**.

Sincerely,

\$\$username\$\$, \$\$userdegree\$\$

cc: C. Hahn, Institutional Official
R. Hart, IRB Director
K. Irvine, VP Operations
M. Sinnet, IRB Chairperson
I. Leviton, IRB Chairperson
Site liaison



IRB STANDARD OPERATING PROCEDURES

Appendix 23 – BRANY IRB Standard Operating Procedures

Termination and Enrollment Closure Form

xForm #04-Study Status Change-Closed/Enrollment Closed

Study Status Change Data Entry

-- User Access Form Screener --

BRANY System User Access Form

For xForm submissions to be valid, a copy of the signed, dated, completed (including attestation box checked off that you read the included BRANY compliance with 21 CFR Part 11) **BRANY System User Access Form** ***MUST*** be on file at BRANY for:

- the Principal Investigator of the study.
- the person adding a xForm into *IRBManager*, i.e. you.

EACH person that creates, submits and/or authorizes a xForm in *IRBManager* is ***required*** to have a signed, completed (including attestation box checked off that you read the included BRANY compliance with 21 CFR Part 11) copy of the **BRANY System User Access Form** on file with BRANY.

*****If the BRANY System User Access Form is *NOT* on file at BRANY and *NOT* included with this submission, this xForm **WILL BE REJECTED*******

Principal Investigator - BRANY System User Access Form Status

Is a signed, dated, completed (attestation box checked off that you read BRANY policy included with the form) copy of a BRANY System User Access Form on file for the **PRINCIPAL INVESTIGATOR** listed above? (Required)

⇒Select *one* of the following options from the drop down list presented:

‡ ‡No - submitting with this xForm submission ‡Yes - on file at BRANY

xForm Submitter (You) - BRANY System User Access Form Status

Is a signed, dated, completed (attestation box checked off that you read BRANY policy included with the form) copy of a BRANY System User Access Form on file for **YOU**, the **xForm submitter**? (Required)

⇒Select *one* of the following options from the drop down list presented:

‡ ‡No - submitting with this xForm submission ‡Yes - on file at BRANY

-- PI User Access Form Attachment --

Principal Investigator's BRANY System User Access Form

Attach Principal Investigator's signed, dated, completed (attestation box checked off that you read BRANY policy included with the form) **BRANY System User Access Form**(Required)

*Click on the blue **BRANY System User Access Form** hyperlink for a copy of the user access form to attach a completed, sign form on another page.*

⇒Attach a file of type "User Access Form BRANY Systems" to this xForm.

-- Submitter User Access Form Attachment --



IRB STANDARD OPERATING PROCEDURES

xForm Submitter/Your BRANY System User Access Form

Attach **YOUR** signed, dated, completed (attestation box checked off that you read BRANY policy included with the form) **BRANY System User Access Form (Required)**

Click on the blue **BRANY System User Access Form** hyperlink for a copy of the user access form.

Complete, sign and scan to an electronic document (e.g. PDF) so it can be attached to this xForm page.

⇒ Attach a file of type "User Access Form BRANY Systems" to this xForm.

-- Change of Study Status --

Study Status Details

Date Status Changed (Required)

Enter the date the status changed.

⇒ Enter a valid date.

Indicate the status of this study at your site (Required)

• Study has been **Closed**: no subjects are in follow-up, no study activity is being conducted, no analysis of data from this site remains, and no private identifiable health information is being collected.

NOTE: Selecting this option will **mean you no longer have IRB approval**. No study-related activity may occur without IRB approval.

• Study is **Closed to Enrollment**: subjects are active in the study and/or remain in follow-up.

NOTE: You will still be required to file for continuing approval if the study is **not** terminated prior to expiration of IRB approval.

⇒ Select one of the following options from the drop down list presented:

‡ ‡Closed ‡Closed to Enrollment

Attach any Site Termination/Study Closure documents received from the Sponsor/CRO, if available.

E.g. Termination letter, Site close out letter, etc.

You may attach up to ten (10) separate documents.

⇒ Attach 1 to 10 files of type "Submitted Item(s)" to this xForm.

-- Study Subjects --

Does this study include a waiver of informed consent?

(Required)

When **YES**, you will be required to answer questions on another page.

⇒ Select either 'Yes' or 'No'

Does this study involve an *in vitro* diagnostic device used with de-identified, leftover/discarded samples?

(Required)

When **YES**, you will be required to answer questions on another page.

⇒ Select either 'Yes' or 'No'

-- Subject Status Breakdown Details --



IRB STANDARD OPERATING PROCEDURES

How many subjects signed consent for your study?

If study involves a waiver of consent or testing of an in vitro diagnostic device, enter 0 (zero). (Required)

⇒Enter a valid number. It must be ≥ 0 . It must be a whole number.

Ensure that $A + B + C + D + E + F + G + H = \text{number enrolled/signed consent you entered}$, above.

Please *breakdown* to ***explain the current status*** of *EACH* subject that **signed consent**:

A. #Screen Failures: (Required)

⇒Enter a valid number. It must be ≥ 0 . It must be a whole number.

B. #Lost to Follow-up: (Required)

⇒Enter a valid number. It must be ≥ 0 . It must be a whole number.

C. #Deceased: (Required)

⇒Enter a valid number. It must be ≥ 0 . It must be a whole number.

D. #Withdrawn:

When non-zero, you will be required to provide Withdrawal Reason(s) in question D.i. (Required)

⇒Enter a valid number. It must be ≥ 0 . It must be a whole number.

D.i. Withdrawal Reason(s) required when 1d. is non-zero: List the reason(s) for each withdrawn subject.

⇒Enter an unlimited amount of text.

E. #Completed the study: (Required)

⇒Enter a valid number. It must be ≥ 0 . It must be a whole number.

F. #Currently/actively receiving the study intervention: (Required)

⇒Enter a valid number. It must be ≥ 0 . It must be a whole number.

G. #Currently in Follow-up Only (Required)

Enter # of subjects involved in follow-up procedures. If a non-interventional study (e.g., observation of routine care/behavior) list subjects ABOVE in "Presently Active" section.

⇒Enter a valid number. It must be ≥ 0 . It must be a whole number.

H. Other Status Number

Enter TOTAL number of subjects in a status not listed above. When non-zero, you will be required to breakdown this number in the following question. (Required)

⇒Enter a valid number. It must be ≥ 0 . It must be a whole number.

H.i. Other Status (please specify) When H is \neq Zero, Please specify the Other Status and indicate the number of subjects in this status.



IRB STANDARD OPERATING PROCEDURES

For example:

Of the total 21 in other statuses:

12 - Other Status1

9 - Other Status2

Where "Other Status1" and "Other Status2" are the description/labels of the statuses not listed as a choice on this page.

⇒Enter an unlimited amount of text.

CalcFieldEnrolled

⇒Output field showing result of a calculation

CalcFieldTotal

⇒Output field showing result of a calculation

CalcFieldDevFromTotal

⇒Output field showing result of a calculation

-- Waiver of Informed Consent Details --

Waiver of Informed Consent

Indicate the # of the subjects/samples/specimens/records included in the research:

⇒Enter a valid number. It must be ≥ 0 . It must be a whole number.

-- In Vitro Diagnostic Study Details --

In Vitro Diagnostics Device

Indicate the # of samples included in the research: (Required)

⇒Enter a valid number. It must be ≥ 0 . It must be a whole number.

-- Serious Adverse Event (SAE) Detail --

Serious Adverse Events (SAEs)

Have there been any Serious Adverse Events at YOUR site? (Required)

When **YES** - answer the following question

When **NO** - click **Next** to continue

⇒Select either 'Yes' or 'No'

YES: Serious Adverse Events (SAEs) HAVE Occurred:

Have ALL the Serious Adverse Events (SAEs) been reported to the BRANY IRB?



IRB STANDARD OPERATING PROCEDURES

When **NO**, you will be **required** to:

1. Answer additional questions on the following page **AND**;

2. Report **each** of the outstanding SAEs to BRANY using the **16-Reportable Event** electronic xForm.

⇒Select either 'Yes' or 'No'

-- Serious Adverse Events --

SAEs Not Reported to BRANY

Describe ALL Serious Adverse Events (SAEs)

Include description of adverse events, their relationship to study agent (or relationship to source of DNA and/or the host vector system for recombinant DNA or gene transfer studies), and their expectedness.

Enter information in text box *and/or* attach separate documents **INCLUDING** when you reported the events to BRANY via the 16-Reportable Event xForm (required).

You are also **required** to report **each of the outstanding** SAEs to BRANY using the 16-Reportable Event *electronic* xForm.

⇒Enter an unlimited amount of text.

Attach Serious Adverse Events document

You may attach up to 100 separate documents.

⇒Attach 1 to 100 files of type "Reportable Event Form" to this xForm.

-- Minor Deviations --

Do you have any Minor Deviations to report since the study's last approval?

When **YES**, you will be required to complete and attach the **Minor Deviation Log**.

When **NO**, click **Next** (Required)

⇒Select *one* of the following options from the drop down list presented:

‡ ‡YES-Minor deviation log required ‡NO

Minor Deviation Log Attachment(s)

You may attach up to ten (10) separate items.

⇒Attach 1 to 10 files of type "Minor Deviation Log" to this xForm.

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IRB STANDARD OPERATING PROCEDURES

Appendix 24 – BRANY IRB Standard Operating Procedures

Confidentiality Agreement

I, _____, will for professional or educational purposes be participating in the review of proposed human subject research (i.e., convened meeting or expedited review) on behalf of or with the Biomedical Research Alliance of New York Institutional Review Board of BRANY. Regardless of my role, I understand and agree that the information and documentation that I will be exposed to during and related to my participation with the Institutional Review Board is confidential. I further acknowledge and agree that I will not, without appropriate authorization, access information that the IRB considers privileged or confidential, release such privileged or confidential information to anyone outside of the review process neither within nor outside the Biomedical Research Alliance of New York or use such information for unauthorized purposes.

I understand that such authorized purposes only include educational discussions or compositions that may describe general aspects of the review process but may not include specific information regarding any of the research proposals discussed by the Institutional Review Board. I also agree that I will not copy or otherwise take any documentation or written information from the Institutional Review Board without express permission from the director of the Institutional Review Board.

Regardless of my association with the Institutional Review Board, I further understand and agree that this confidentiality agreement continues after the end of my affiliation with the Biomedical Research Alliance of New York.

Signature: _____

Affiliation: _____

Date: _____



IRB STANDARD OPERATING PROCEDURES

Appendix 25 – BRANY IRB Standard Operating Procedures

Informed Consent Feedback Tool

BRANY IRB File # _____

TITLE OF THE STUDY:

1. The purpose of the research is: **or** I am not sure
2. Possible benefits of the research include: **or** I am not sure
3. Possible risks of the research include: **or** I am not sure

For items 4-6, please circle one:

4. Participation in this research is voluntary. TRUE / FALSE / NOT SURE
5. I must continue in the study until completion. TRUE / FALSE / NOT SURE
6. I may not benefit by taking part in this research study. TRUE / FALSE / NOT SURE

I have some questions for the research team:



IRB STANDARD OPERATING PROCEDURES

Appendix 26 – BRANY IRB Standard Operating Procedures

Continuing Review Multi-Center Sponsor Supplement

Table with 4 columns: BRANY PROTOCOL #, Sponsor Name and PROTOCOL #, EXPIRATION DATE OF STUDY, APPROVAL PERIOD (months), TITLE OF PROTOCOL, TO BE REVIEWED AT BRANY IRB MEETING OF:

STUDY SPONSOR INSTRUCTIONS:

For continuing review of multi-center research studies, BRANY IRB requires the STUDY SPONSOR provide a study-wide summary based on data gathered from all sites thus far. Please complete the following questions and return to BRANY IRB. For any of the items below, you may append an additional sheet with your response as needed.

- 1) The number of subjects accrued across all participating sites thus far:
a) Provide information regarding the race/ethnic classifications of subjects enrolled thus far:
b) Provide information regarding the gender distribution of subjects enrolled thus far (NOTE: This question does not apply if the study is gender-specific.)
c) Summarize any withdrawals of subjects, including reasons for withdrawal if known:
2) A summary of any unanticipated problems involving risks to participants or others (append additional sheets as necessary):
3) A summary of adverse events (indicate whether adverse events have occurred at the expected frequency and level of severity as documented in the research protocol, the informed consent document, and any investigator brochure/safety profile information that was already provided to the IRB)

NOTE: If this research is a clinical trial that is subject to oversight by a monitoring entity (e.g., the research sponsor, a coordinating or statistical center, or a DSMB/DMC), a current report (within 60 days) from the monitoring entity may be provided. The report must include:

- i) a statement indicating what information (e.g., study-wide adverse events, interim findings, and any recent literature that may be relevant to the research) was reviewed by the monitoring entity;
i) the date of the review; and



IRB STANDARD OPERATING PROCEDURES

ii) the monitoring entity's assessment of the information reviewed.

4) A summary of any complaints about the research

5) Provide or summarize any recent literature that may be relevant to the research and any amendments or modifications to the research since the last IRB review;

6) Any relevant multi-center trial reports;

7) Any other relevant information, especially information about risks associated with the research:

8) Any other interim findings since the last IRB review:

9) Based on study results thus far, please provide a current risk-potential benefit assessment (attach a separate sheet as necessary):

Submitted by:

Name

Title & Organization

Signature

Date



IRB STANDARD OPERATING PROCEDURES

Appendix 27 – BRANY IRB Standard Operating Procedures

Application for Determination of Exempt Status

Exempt: Exempt means that the research will be reviewed for exempt status approval by the IRB Chairperson or designee, and will not be subject to continuing review under the federal regulations. The IRB must be notified of any changes to a protocol that has been given exempt status, as the changes may require the project to undergo IRB review.

Sponsor Name and Protocol #:	BRANY IRB File #:
Principal Investigator:	Phone:
Name of person completing this form:	Study Title:
E-mail:	
Phone:	Fax:

1. **Does the research involve prisoners, pregnant women, fetuses, *In vitro* fertilization?** If so, BRANY IRB will not make a determination for exempt status. Please complete the Application for Review of a Research Project and **do not apply for exempt status.**

2. **Does this request for determination of exempt status involve the Emergency Use of a Test Article?** If so, the research may be exempt from IRB review. Please complete the Emergency Use Notification Form and do not complete this form. **Such emergency must be reported to the IRB within 5 working days. Any subsequent use of the test article at the institution is subject to IRB review.**

3. In order to qualify for exempt status, the research must fall into one of the following categories, as described in 45 CFR 46.101(b), 45 CFR 46.401(b), or 21 CFR 56.104. **Please select the category that describes your research:**
 - (1) Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as (i) research on regular and special education instructional strategies, or (ii) research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

 - (2) Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, **unless:**
 - (i) information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and (ii) any disclosure of the human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation.

NOTE: For research involving survey or interview procedures or observations of public behavior, this exemption category does not apply when the research involves children, except for research involving observation of public behavior when the investigator(s) do not participate in the activities being observed.



IRB STANDARD OPERATING PROCEDURES

- (3) Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior that is not exempt under paragraph (b)(2) of this section, if:
(i) the human subjects are elected or appointed public officials or candidates for public office; or (ii) federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.
- (4) Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.
- Did the data exist prior to the time the research was proposed?
 YES
 NO – If so, the research does not qualify for exempt status. Please complete the Application for Review of a Research Project and do not apply for exempt status.
- (5) Research and demonstration projects which are conducted by or subject to the approval of department or agency heads, and which are designed to study, evaluate, or otherwise examine:
(i) Public benefit or service programs;
(a) the program under study must deliver a public benefit (e.g., financial or medical benefits as provided under the Social Security Act) or service (e.g., social, supportive, or nutrition services as provided under the Older Americans Act);
(b) the research or demonstration project must be conducted pursuant to specific federal statutory authority;
(c) there must be no statutory requirement that the project be reviewed by an Institutional Review Board (IRB); and
(d) the project must not involve significant physical invasions or intrusions upon the privacy of participants (see 12/97 OPRR Guidance at <http://www.dhhs.gov/ohrp/humansubjects/guidance/exmpt-pb.htm>). This exemption is for projects conducted by or subject to approval of Federal agencies, and is most appropriately invoked with authorization or concurrence by the funding agency.
(ii) procedures for obtaining benefits or services under those programs;
(iii) possible changes in or alternatives to those programs or procedures; or
(iv) possible changes in methods or levels of payment for benefits or services under those programs.
- (6) Taste and food quality evaluation and consumer acceptance studies, (i) if wholesome foods without additives are consumed or (ii) if a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.
- (7) Any investigation which commenced before July 27, 1981 and was subject to requirements for IRB review under FDA regulations before that date, provided that the investigation remains subject to review of an IRB which meets the FDA requirements in effect before July 27, 1981.
- (8) Any investigation commenced before July 27, 1981 and was not otherwise subject to requirements for IRB review under Food and Drug Administration regulations before that date.



IRB STANDARD OPERATING PROCEDURES

4. Please append the following:
 - a. Protocol
 - b. HIPAA Authorization Form **or** HIPAA Waiver Request Form (with completed Data Use Agreement, if applicable)
 - c. Principal Investigator's Curriculum Vitae
 - d. Financial Conflict of Interest Disclosure forms for the Principal Investigator and all study personnel.
 - e. Evidence of training in human subject protections for the Principal Investigator and all study personnel.

Completed applications may be submitted to: **BRANY IRB**
 1981 Marcus Avenue, Suite 210
 Lake Success, NY 11042
 T: (516) 470-6900
 F: (516) 706-4985

Principal Investigator's Statement

I understand studies that qualify as exempt are subject to the same regulations and ethical principles governing all research (refer to BRANY Standard Operating Procedures). I will inform the IRB of any changes in the research submitted with this application (e.g., study design, procedures, etc.), as the changes may necessitate IRB review.

Principal Investigator's Signature

Signature Date

IRB Use Only

In addition to the categories listed in item 3 above, please also consider the following to ensure that subjects are protected for exempt research:

- The ethical principles of respect for persons, beneficence and autonomy
- Whether the proposed research involves no more than minimal risk to participants
- Whether informed consent will be sought from subjects
- Whether selection of subjects is equitable
- Whether there are adequate provisions to maintain the confidentiality of data and protect the privacy of subjects

Note: If necessary, expert opinion regarding the proposed research and conformity to the applicable regulations can be solicited.

Please check one:

- Project is **exempt** from IRB review. → Please indicate the category # from item 3. above: _____
- Project requires **expedited** IRB review.
- Project requires **full** IRB review.

Please check one:

- HIPAA applies (if the data collected is **NOT** de-identified)
- HIPAA does not apply (if the data collected is de-identified)

IRB Chairperson:	Name	Signature	Date
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IRB STANDARD OPERATING PROCEDURES

Appendix 28 – BRANY IRB Standard Operating Procedures

Research Participant Information Sheet and Consent for HIV Antibody Test

Research Participant Information Sheet and Consent for HIV Antibody Test

TITLE:

STUDY SPONSOR:

PROTOCOL NO.:

PRINCIPAL INVESTIGATOR:

You have been asked to participate in a research study, for which you have signed a separate consent. As indicated on that consent, part of your participation in that study will involve undergoing an HIV antibody test. This consent is specifically for the HIV antibody test. The HIV antibody test is a blood test used to ascertain whether you have antibodies to the Human Immunodeficiency Virus (HIV), the virus, which causes Acquired Immunodeficiency Syndrome (AIDS). Less than one teaspoon of blood will be drawn from a vein in your arm using a needle. This may cause some discomfort and you may develop a black and blue mark. It takes approximately one to two weeks between the time your blood is drawn and the time you are notified of the results.

Both before and after your blood is tested, you will receive counseling from trained HIV counselors involved in this research project about the implications of negative and positive results, how to prevent future transmission, and the options available to you. Your partners may be notified of the results of this test and urged to undergo testing as well. If you do not want to tell them, or you will not tell them, your doctor or local health official can inform them that a partner of theirs has been tested and what the results of the test were, but only if the doctor feels that telling them is medically appropriate. You will not incur any costs nor receive any payment for participating in this part of the study.

A positive HIV antibody test means that your body is making antibodies to HIV but it does not mean that you will necessarily develop AIDS in the future. A negative test means that you are probably not infected; however, it is possible that you may be infected but that your body has not produced antibodies to HIV. If your results are negative and you have been exposed to HIV recently, you should be retested in a few months to make sure you are not infected.

There are several possible benefits to taking the HIV antibody test. If your test results are negative, you can learn how to avoid becoming infected in the future. If your results are positive, you can learn how to avoid infecting other individuals, and if you are pregnant, or are thinking about having children, you can learn how being HIV positive will affect your decision to have children. Additionally, we can offer you enrollment in a wide variety of research projects for the treatment of AIDS or refer you to a doctor for non-experimental treatment.

This is a voluntary procedure, and all results, either positive or negative, are confidential. Under New York State law, information about your HIV antibody test can only be released to people who you designate by signing a release form, or to those people listed below:

- a) You (or a person authorized by law who consented to the test for you);



IRB STANDARD OPERATING PROCEDURES

- b) To a health care facility (such as a hospital, blood bank, or clinical laboratory) or a health care provider (such as a physician, nurse, or mental health counselor) providing care to
- c) you or your child, and anyone working for such a facility or provider who reasonably needs the information to supervise, monitor or administer health care;
- e) c) To a person whom your doctor believes is at significant risk for HIV infection, if you do not notify that person after being counseled to do so;
- f) d) To a committee or organization responsible for reviewing or monitoring a health facility;
- g) e) To a federal, state, county, or local health officer when state or federal law requires disclosure;
- h) f) To a government agency, when the agency needs the information to supervise, monitor, or administer a health or social service;
- i) g) To an authorized foster care or adoption agency;
- j) h) To insurance companies and other third party payers such as Medicaid necessary for the payment of services to you;
- k) i) To any person whom a court orders disclosure under limited circumstances set forth by law. Except in an emergency situation, advance notice and an opportunity to oppose the release of such information would be given to you;
- l) j) To the Division of Parole, the Division of Probation, the Commission of Correction, or a medical director of a local correctional facility, as permitted by HIV confidentiality regulations of such organization.
- m) k) By a physician to someone who may consent to health care for you if you have been counseled and won't inform such person and disclosure is medically necessary to provide timely care and treatment. Disclosure must not be against your best interest.

If you do not want anybody to know your tests results or that you have been tested, you can go to an anonymous test site. This is a place where you can have your blood tested and receive counseling without having to tell anybody your name or address. You can find the nearest anonymous test site by calling the AIDS Hotline at **1-(800)-541-2437**.

If your results are positive, you should be very careful who you disclose this information to. Some HIV positive people have been discriminated against by landlords, employers, and the like. If you believe you have been discriminated against, you should call the New York State Division of Human Rights at (212) 480-2522 or the New York City Commission on Human Rights at (212) 306-5070. If you have any further questions regarding AIDS or HIV antibody testing, you can contact the New York State Department of Health AIDS Hotline at 1-(800) - TALK-HIV / 1-(800)-825-5448.



IRB STANDARD OPERATING PROCEDURES

Appendix 29 – BRANY IRB Standard Operating Procedures

Request for Waiver or Alteration of Informed Consent

Principal Investigator: \$PIFirstName\$ \$PILastName\$
Protocol Title: \$ProtocolDescription\$
Sponsor's Name and Protocol Number/Identifier: \$SponsorName\$ Protocol # \$SponsorProtocol\$

INSTRUCTIONS: PLEASE SELECT ONE CHOICE THAT APPLIES TO YOUR RESEARCH: CHOICE 1, CHOICE 2, OR CHOICE 3. IF YOU FEEL THAT MORE THAN ONE CHOICE MAY APPLY, PLEASE CONTACT THE BRANY IRB TEAM AT 516-470-6900.

CHOICE 1 - REQUEST FOR WAIVER OF INFORMED CONSENT

COMPLETE THIS SECTION ONLY IF no form of consent (oral, written, or other) will be obtained from subjects. The IRB may waive the requirement to obtain informed consent if one of the two following sets of criteria in part B is met.

- A) ** Is this research subject to FDA regulation?
[] No -> Please move on to complete Part B of this section and fax to BRANY IRB at 516-706-5134.
[] Yes -> If yes, do NOT submit this form. A waiver of consent IS NOT allowed.

NOTE: Research that falls within the guidelines of FDA's guidance document, entitled Guidance on Informed Consent for In Vitro Diagnostic Device Studies Using Leftover Human Specimens that are Not Individually Identifiable, does not require consent. As such, this request for a consent waiver is not required for IVDD research.

- B) Check the box next to the criteria you believe should be applied to this research.
[] (1) The research or demonstration project is to be conducted by or subject to the approval of state or local government officials and is designed to study, evaluate, or otherwise examine: (i) public benefit or service programs; (ii) procedures for obtaining benefits or services under those programs; (iii) possible changes in or alternatives to those programs or procedures; or (iv) possible changes in methods or levels of payment for benefits or services under those programs; AND
(2) The research could not practicably be carried out without the waiver or alteration.
Or
[] (1) The research involves no more than minimal risk to the subjects;
(2) The waiver or alteration will not adversely affect the rights and welfare of the subjects;
(3) The research could not practicably be carried out without the waiver or alteration; and
(4) Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

C) PROVIDE EXPLANATIONS/JUSTIFICATIONS for selecting either choice above:

[Empty box for providing explanations/justifications]

- D) Will you be providing a written description of information to subjects?
[] YES -> Please attach the description to this form. [] NO



IRB STANDARD OPERATING PROCEDURES

CHOICE 2 - REQUEST FOR WAIVER OF DOCUMENTATION OF INFORMED CONSENT

COMPLETE THIS SECTION ONLY IF consent will be obtained from subjects but a consent form will not be signed. The IRB may waive documentation of informed consent for some or all of the subjects if one of the following conditions is met:

A) Check the box next to the applicable criteria.

- The research is not subject to FDA regulation and the only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality.
- If this is so, will each subject be asked if he/she wants documentation linking him/her with the research? (The subject's wishes would govern). Yes No
- OR**
- The research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside the research context.

B) PROVIDE EXPLANATIONS/JUSTIFICATIONS for selecting either choice above:

CHOICE 3 - REQUEST FOR WAIVER OF ELEMENTS OF INFORMED CONSENT

COMPLETE THIS SECTION ONLY IF there is a consent form/process planned but you are requesting to *not include some required elements of informed consent* – per 45CFR46.116 and 21CFR50.25. If it can be justified, the IRB may approve a consent procedure which does not include or which alters some of the required elements of informed consent.

Which elements of informed consent do you wish for the IRB to waive, and why?

END OF FORM



IRB STANDARD OPERATING PROCEDURES

Appendix 30 – BRANY IRB Standard Operating Procedures

ARCHIVED – Access to PHI in Preparation of Research Form



IRB STANDARD OPERATING PROCEDURES

Appendix 31 – BRANY IRB Standard Operating Procedures

Guidelines for Drafting Protocols *(Based on the International Conference on Harmonization GCP Guidelines for Clinical Trial Protocol Development. A version adapted for non-clinical protocols appears at the bottom of this)*

FOR CLINICAL TRAIL PROTOCOLS

To promote sound scientific design of research protocols, the BRANY IRB recommends that the following elements be included when designing a research protocol:

General Information to be included in the Protocol

- Protocol title, protocol number, and version date. Any protocol amendments should also include the amendment number and date.
- Name and address of the sponsor and monitor (if other than the sponsor).
- Name, title, address, and telephone number of the medical expert for the trial.

Background Information may include:

- Name and Description of the investigational product.
- Summary of results from prior clinical trials
- Summary of known and potential risks and benefits, if any, to subjects.
- Description and justification for the route of administration, dosing regimen and treatment period.
- A statement that the trial will be conducted in compliance with the protocol, GCP and the regulations.
- Description of the population to be studied.
- References to literature and data relevant to the trial that also provide background for the trial.

Objectives/Purpose of the study:

- Include a detailed description of the objectives and the purpose of the trial.

Trial Design:

- State the primary and secondary endpoints, if any, to be measured during the trial.
- Include the design of the trial (e.g., double-blind, placebo controlled, parallel design) and a schematic diagram of the trial design, procedures, and stages.
- Describe measures to minimize and/or avoid bias (e.g., Randomization, Blinding).
- Describe the treatment, dosage, dosing regimen of the drug, as well as description of the dosage form, packaging and labeling of the experimental product.
- Include the expected duration of subject participation and a description of the sequence and duration of all trial periods, including any follow up.
- Describe when a subject's participation in the trial may be discontinued.
- Include Accountability procedures for the investigational product, including placebo and any comparators.
- Maintenance of randomization codes and any procedures for breaking such codes when necessary.
- Include a Risk Benefit Analysis when appropriate.
- Describe the potential risks.
- Identify steps taken to minimize risk.
- Describe possible benefits.
- Describe alternative treatments that are available to treatment the condition under study.

Selection and withdrawal of Subjects:

- Include subject inclusion criteria
- Include subject exclusion criteria. Women of childbearing potential may not be routinely excluded from participating in research; however, pregnant women should be excluded unless there is clear



IRB STANDARD OPERATING PROCEDURES

justification why they should be included. Participation of adult subjects in research should not be age-restricted unless there is scientific or medical justification. Additional restrictions may apply to research involving minors or any other category of vulnerable subjects. Provide justification for any enrollment restrictions. Research should include sufficient enrollment of persons of diverse racial/ethnic backgrounds to ensure that the benefits and burdens of research participation are distributed in an equitable manner.

- Include withdrawal criteria and procedures specifying when and how to withdraw subjects from the trial and the investigational product; the type and timing of the data to be collected for withdrawn subjects; whether and how subjects are to be replaced; and the follow up for subjects that are withdraw from the trial and/or the experimental product. If applicable, describe how subjects terminating their participation will be returned to their standard care (e.g. taper off study medication and return to prior regimen of care)

Treatment of Subjects:

- Include medications permitted (including rescue medication) and permitted before and during the trial.
- Procedures for monitoring subject compliance

Assessment of Efficacy:

- Specify the efficacy parameters
- Include the methods and timing for assessing, recording, and analyzing efficacy parameters.

Assessment of Safety:

- Specify the safety parameters
- Include the methods and timing for assessing, recording, and analyzing efficacy parameters
- Procedures for eliciting, recording and reporting Adverse Events and intercurrent illnesses.
- Identify the type and duration of follow up for subjects that experience an adverse event.

Statistics:

- Describe the statistical methods employed and the timing of any interim analysis.
- Include the number of subjects planned to be enrolled. For multi-center studies, include the total number sites expected and the total number of subjects to be enrolled across all sites. Additionally, provide the rationale for the sample size, the calculations on the power of the trial and the clinical justification.
- Include the level of significance to be used.
- Criteria for the termination of the trial.
- Procedure of accounting for missing, unused and spurious data.
- Procedures for reporting deviations from the original statistical plan.
- Include the selections of subjects to be included in the analyses (e.g. all randomized subjects, all dosed subjects, evaluable subjects).

Direct Access to Source Data Documents:

- State who will have access to the data and how the data will be used. If data with subject identifiers will be released, specify the person(s) or agency to whom the information will be released and the purpose of the release.
- Address trial related monitoring, audits, and regulatory inspections.



IRB STANDARD OPERATING PROCEDURES

ADAPTED FOR NON-CLINICAL PROTOCOLS

To promote sound scientific design of research protocols, the BRANY IRB recommends that the following elements be included when designing a research protocol:

General Information to be included in the Protocol

- Protocol title, protocol number, and version date. Any protocol amendments should also include the amendment number and date.
- Name and address of the sponsor and monitor (if other than the sponsor).
- Name, title, address, and telephone number of the medical expert for the study (if applicable).

Background Information may include:

- Name and Description of the investigational product.
- Summary of results from prior studies
- Summary of known and potential risks and benefits, if any, to subjects.
- Description and justification for the route of administration, dosing regimen and treatment period.
- A statement that the study will be conducted in compliance with the protocol, GCP (if applicable) and applicable regulations.
- Description of the population to be studied.
- References to literature and data relevant to the study that also provide background for the study.

Objectives/Purpose of the study:

- Include a detailed description of the objectives and the purpose of the study.

Study Design:

- State the primary and secondary endpoints, if any, to be measured during the study.
- Describe the design of the study (e.g., double-blind, placebo controlled, parallel design) and a possibly include a schematic diagram of the study design, procedures, and stages (if appropriate and necessary)
- Describe measures to minimize and/or avoid bias (e.g., Randomization, Blinding).
- Describe when a subject's participation in the study may be discontinued.
- Maintenance of randomization codes and any procedures for breaking such codes when necessary.
- Include a Risk Benefit Analysis when appropriate.
- Describe the potential risks.
- Identify steps taken to minimize risk.
- Describe possible benefits.

Selection and withdrawal of Subjects:

- Include subject inclusion criteria
- Include subject exclusion criteria. Women of childbearing potential may not be routinely excluded from participating in research; however, pregnant women should be excluded unless there is clear justification why they should be included. Participation of adult subjects in research should not be age-restricted unless there is scientific or medical justification. Additional restrictions may apply to research involving minors or any other category of vulnerable subjects. Provide justification for any enrollment restrictions. Research should include sufficient enrollment of persons of diverse racial/ethnic backgrounds to ensure that the benefits and burdens of research participation are distributed in an equitable manner.
- Include withdrawal criteria and procedures specifying when and how to withdraw subjects from the study (and the investigational product, if applicable); the type and timing of the data to be collected for withdrawn subjects; whether and how subjects are to be replaced; and the follow up for subjects that are withdraw from the study (and/or the experimental product, if applicable). If applicable, describe how subjects terminating their participation will be returned to their standard care (e.g. taper off study medication and return to prior regimen of care)



IRB STANDARD OPERATING PROCEDURES

Treatment of Subjects (if applicable):

- Include medications permitted (including rescue medication) and permitted before and during the study.
- Procedures for monitoring subject compliance

Assessment of Efficacy (if applicable):

- Specify the efficacy parameters
- Include the methods and timing for assessing, recording, and analyzing efficacy parameters.

Assessment of Safety (if applicable):

- Specify the safety parameters
- Include the methods and timing for assessing, recording, and analyzing efficacy parameters
- Procedures for eliciting, recording and reporting Adverse Events and intercurrent illnesses.
- Identify the type and duration of follow up for subjects that experience an adverse event.

Statistics:

- Describe the statistical methods employed and the timing of any interim analysis.
- Include the number of subjects planned to be enrolled. For multi-center studies, include the total number sites expected and the total number of subjects to be enrolled across all sites. Additionally, provide the rationale for the sample size, the calculations on the power of the study and the justification.
- Include the level of significance to be used.
- Criteria for the termination of the study, if applicable.
- Procedure of accounting for missing, unused and spurious data.
- Procedures for reporting deviations from the original statistical plan.
- Include the selections of subjects to be included in the analyses (e.g. all randomized subjects, all dosed subjects, evaluable subjects).

Direct Access to Source Data Documents:

- State who will have access to the data and how the data will be used. If data with subject identifiers will be released, specify the person(s) or agency to whom the information will be released and the purpose of the release.
- Address study-related monitoring, audits, and regulatory inspections, as applicable.



IRB STANDARD OPERATING PROCEDURES

Appendix 32 – BRANY IRB Standard Operating Procedures

Binder Organization List

STATUS OF STUDY

1. Closed to enrollment letter
2. Notification of Study Termination (*in front if study is closed*)
3. *Out Tab (to replace binder in cabinet when file is out and in use)*

1572 AND APPLICATION

1. Personnel Changes
2. 1572 Forms & Acknowledgements (Revisions when necessary)
3. Application for initial review
4. IDE letter (if applicable for device studies only) -or- FDA letter regarding IND #s (if applicable)
5. Principal Investigator's CV (academic and training credentials) & medical license (if applicable)
6. Human Subject Protections Training Documentation
7. HSPC/COI Requirements Checklist for Study Staff
8. Correspondence regarding COI Forms (Actual COI Forms kept in separate COI file)

INITIAL REVIEW INFORMATION

1. IRB Initial Approval Letter (and/or Deferral Letter)
2. Reviewer Checklists & Addendum Checklists (relating to initial review)
3. Full Board Review approvals & supporting documentation (assignment pages, checklists, materials reviewed, reviewer correspondence, etc...) if the initial approval has not yet been issued.
4. Other materials such as: advertisements, articles, etc...
5. Internal checklists
6. Reviewer Assignments pages
7. ICFs that were submitted with initial submission
8. HIPAA Form
9. Project Summary
10. Initial Submission from Grants

CORRESPONDENCE (*in reverse chronological order*)

1. All Approval Letters (and supporting documents for item reviewed), for example:
 - a. Continuing Approval (attach checklists from reviewers)
 - b. Protocol and/or IDB Amendments (*letter & supporting documents only; actual protocol/IDB filed in separate sections*)
 - c. ICF Revisions
 - d. Advertisements
 - e. Subject materials
 - f. DSMB
2. QA Audits and/or Responses to QA Audits from PI
3. Acknowledgement Review Approvals & supporting documentation (assignment pages, checklists, materials reviewed, reviewer correspondence, etc...)
4. Deviations
5. Full Board Review Documents (after Initial Approval is issued)
6. Communication between site, sponsor and BRANY



IRB STANDARD OPERATING PROCEDURES

PROTOCOL

1. All versions of the protocol and amendments
2. All protocol summary of changes

IDB

1. All versions of the IDB, amendments and summary of changes
2. If study involves a device, the Device brochure
3. Drug package inserts/product information pamphlets

CONTINUING REVIEW

1. Application
2. Assignment page for the reviewer
3. Continuing Review Process Checklist (*if completed by IRB staff*)



IRB STANDARD OPERATING PROCEDURES

Appendix 33 – BRANY IRB Standard Operating Procedures

ARCHIVED – Document Retention Schedule



IRB STANDARD OPERATING PROCEDURES

Appendix 34 – BRANY IRB Standard Operating Procedures

Sample Subject Enrollment Note

Date:

Protocol:

Subject:

Subject A-B has been enrolled in the *Sponsor name/study*. The study was explained, the subject was given a copy of the consent and an opportunity to ask questions. A signed copy was given to the subject. Consent was obtained prior to the performance of any study procedures.

(For women of child bearing potential)

The procedures listed in the consent with regard to pregnancy were reviewed with the subject. The subject agreed to continue abstinence or a medically accepted method of birth control as defined in the consent for the entire study. The subject was informed to notify the study doctor immediately if she suspects she has become pregnant.

The subject meets all inclusion criteria and does not meet any exclusion criteria. A laboratory specimen for screening was drawn and shipped to *Lab name* as per protocol.

Physical exam by Dr. X.

Past Medical History: *include all medical and surgical history.*

Current medications: *include name, dose, frequency, indication and date started.*

Next study visit is *date and time.*

Sign and date



IRB STANDARD OPERATING PROCEDURES

Appendix 35 – BRANY IRB Standard Operating Procedures

Investigator Database Information Form

INVESTIGATOR DATABASE INFORMATION FORM U.S. SITES

There is never an ongoing fee for a site to be part of the BRANY alliance or to be presented with opportunities. Please complete and submit the registration form below and we will contact you. For investigators already affiliated with or employed by an existing BRANY alliance member site, please complete the short form provided by the link at the bottom of this page.

Please attach an electronic version of your current CV.

Fields in blue are optional

STUDY SITE OR PRINCIPAL INVESTIGATOR

TITLE

NAME OF PRACTICE/SITE WHERE STUDY WILL BE PERFORMED

INSTITUTION OR ORGANIZATION

ADDRESS WHERE STUDY WILL BE PERFORMED

CITY

STATE OR PROVINCE

COUNTRY

ZIP OR POSTAL CODE

TELEPHONE

FAX

E-MAIL ADDRESS

CONTACT PERSON

ADDRESS

EMAIL

TELEPHONE

Principle Investigator

ARE THERE MULTIPLE PIS Yes No

HOW MANY? If multiple PIs, **click here** to fill out short info form for each.

Specialty

SPECIALTY BOARD CERTIFIED?

Yes No

SPECIALTY BOARD CERTIFIED?



IRB STANDARD OPERATING PROCEDURES

Yes No

Trials

WHAT TYPE OF TRIALS WOULD YOU LIKE TO RECEIVE?

ATTENTION

(Multiple types may be selected by using the Control key when making a selection) Adult Medicine

Adult Neurology

Anesthesia

Dentistry

Dermatology

Emergency Medicine

ENT

OB GYN

Ophthalmology

Pediatrics

Podiatry

Psychiatry

Radiology

Surgery

Urology



IRB STANDARD OPERATING PROCEDURES

List additional areas of expertise if not included above.

Practice Setting What is your Practice Setting: (Check all that Apply)

University Based Research Center Solo/Group Practice Hospital Staff Medical School

Faculty Urgent Care Center Consortium/Network Rehab Hospital /Clinic Nursing

Home/Extended Care Research center

HOW MANY STUDIES ARE YOU PARTICIPATING IN NOW?

Support Staff

HOW MANY COORDINATORS DO YOU HAVE?

HOW MANY ARE CCRC CERTIFIED?

HOW MANY STUDIES ARE ASSIGNED TO A COORDINATOR AT ONE TIME?

Primary Coordinator Contact

SAME AS CONTACT PERSON

NAME

ADDRESS

TELEPHONE

EMAIL

STAFF ON CALL

MD Coordinator Other

Training

DOES THE PI HAVE CERTIFICATION OF TRAINING IN HUMAN SUBJECTS PROTECTION?

Yes No

Acceptable certificates include academic medical center earned CME, Dunn and Chadwick's Protecting Study Volunteers in Research or <http://phrp.nihtraining.com/users/login.php>

DOES THE COORDINATOR(S) HAVE CERTIFICATION OF TRAINING IN HUMAN SUBJECT PROTECTION?

Yes No

Certificates are required for IRB approvals.

Facilities

ARE YOUR INVESTIGATIVE PRODUCTS STORED IN A LOCKED AREA?

Yes No

WHO DISPENSES THE TEST ARTICLE?

PI RN Non-RN

Equipment

DO YOU HAVE ACCESS TO DRY ICE?

Yes No

DO YOU USE ELECTRONIC MEDICAL RECORDS?



IRB STANDARD OPERATING PROCEDURES

Yes No

HAVE YOU EVER HAD AN FDA AUDIT?

Yes No

WAS A 483 ISSUED?

Yes No

If Yes, please fax the 483 form to 516-470-6903

WHO PRESENTS THE INFORMED CONSENT TO THE PATIENT AT YOUR SITE?

PLEASE DESCRIBE THE INVESTIGATOR'S LEVEL OF INVOLVEMENT IN THE RESEARCH THAT IS PERFORMED AT THE SITE.

ARE THERE ANY SPECIFIC LAWS GOVERNING MEDICAL RESEARCH IN YOUR U.S. STATE OR COUNTRY?

References

We will be contacting Sponsors and CRAs you have worked within the past to assess GCP compliance.

Please list two references

NAME

COMPANY

TELEPHONE

EMAIL ADDRESS

NAME

COMPANY

TELEPHONE NUMBER

EMAIL ADDRESS

DID YOU EVER HAVE ANY MEDICAL LICENSE ISSUES IE, SUSPENSIONS OR PROBATION PERIOD?'

Yes? No?

IF YES, EXPLAIN?

Attachments

ATTACHMENT(e.g.: CVs, 483 Reports)

For investigators who are affiliated with or employed by a BRANY alliance member site, please complete the short form provided at this link **click here**.



IRB STANDARD OPERATING PROCEDURES



IRB STANDARD OPERATING PROCEDURES

Appendix 36 – BRANY IRB Standard Operating Procedures

Revocation of Authorization to Release PHI for Research Purposes

TO: *Insert name of Principal Investigator*

I revoke my previous authorization for you to use or disclose my protected health information as part of your study.

I understand that the research team will continue to use and disclose health information about me that has already been collected. However, they will only use and disclose the information only for the reasons discussed in the Consent Form I signed when I joined the study.

I understand the revoking this authorization may mean that my participation in the study will also end. It will not affect my rights as a patient, including health care I may need when I am no longer in the study.

Signed:

Participant Signature

Date



IRB STANDARD OPERATING PROCEDURES

Appendix 37 – BRANY IRB Standard Operating Procedures

Chairperson Evaluation Form

In accordance with BRANY IRB policy, we must conduct an evaluation of the IRB chairpersons every 2 years. Therefore, BRANY IRB would like your feedback regarding the IRB Chairperson. Your responses will remain anonymous, and will assist BRANY in ensuring effective operation of BRANY IRB. Please respond to the questions that follow for the BRANY IRB Chairpersons noted at the top of the page. If you have any questions or require any additional information, please contact the IRB office at (516) 4706909. Thank you for your assistance!

Please respond to the questions below with regard to BRANY IRB Co-Chairperson [CHAIRPERSON NAME].

1. Rate [CHAIRPERSON NAME], based on the criteria listed below.

	Strongly Agree	Agree	Somewh at Agree	Somewh at Disagree	Disagree	Strongly Disagree
1. Chairperson portrays diplomacy and allows the interests of the members to be fully expressed and mediated.						
2. Chairperson allows nonscientific (lay) members the ability to participate in discussions equally.						
3. Chairperson is knowledgeable about the federal, state and local regulations governing research with human subjects.						
4. Chairperson is an expert on the legal, biomedical, behavioral and ethical issues that may be faced by IRBs.						
5. In your opinion, the Chairperson remains unbiased thorough out the duration of the meeting(s).						
6. Chairperson helps enlist the advice of appropriate, expert consultants to help advise the members of the IRB.						
7. Chairperson presents the discussion and materials at the meetings in an organized fashion.						
8. In my opinion, the Chairperson is an effective synthesizer (i.e. demands clear and concise restatement if decisions are made expeditiously).						
9. Chairperson is knowledgeable about the requirements for the informed consent process and document, and ensures IRB review considers appropriateness of consent disclosure, as well as the competence and capacity of the potential subject.						
10. The Chairperson answers questions appropriately and effectively.						
Additional comments may be added here:						

BRANY IRB truly appreciates your input! Thank you for taking the time to complete this survey. Results will be summarized and provided to the Chairpersons and BRANY IRB administration.



IRB STANDARD OPERATING PROCEDURES

Appendix 38 – BRANY IRB Standard Operating Procedures

IRB Checklist – Emergency Use

Sponsor Name and IND #:		BRANY IRB File #:	
Investigator:		Phone:	
Name of person completing this form:		Study Title:	
E-mail:			
Phone:	Fax:		

Emergency Use of a Test Article Without IRB Review: FDA regulations may allow the use of a test article with an IND without IRB review in an emergency situation when the certain circumstances are met. Although the FDA regulations allow for an exemption from prior review and approval by the IRB for emergency use, the BRANY IRB requires prior notification, if possible, of emergency use of test article so that the investigator’s intent for such use can be reviewed to determine if the circumstances of the emergency are in accord with FDA regulations. All instances of emergency use of a test article without prior IRB review must be reported to the IRB within 5 working days.

IRB Chairperson’s Use Only

- (1) Is this activity considered “research” as defined by DHHS regulations (a systematic investigational designed to develop or contribute to generalizable knowledge) and involve “subjects” as defined by DHHS regulations (a living individual about whom an investigator conducting research obtains (1) data through intervention or interaction with the individual) or (2) identifiable private information?
 NO – If NO, continue to item (2)
 YES – *If YES, this activity will be (was) subject to DHHS regulation & is not exempt from IRB Review.*
- (2) This Emergency Use was reported to BRANY IRB within 5 working days of (or prior to) the intended use.
 NO – *If NO, does (did) not meet FDA requirements for emergency use*
 YES – If YES, continue to item (3).
- (3) Did the Investigator attest that any subsequent use would be submitted for prior IRB review and approval?
 NO – *If NO, does (did) not meet FDA requirements for emergency use*
 YES – If YES, continue to item (4).
- (4) The human subject is (was) in a life-threatening situation or the subject’s disease or condition is severely debilitating (e.g. blindness, loss of limb, paralysis or stroke).
 NO -- *If NO, does (did) not meet FDA requirements for emergency use*
 YES – If YES, continue to item (5)
- (5) The situation necessitates the use of the test article.
 NO -- *If NO, does (did) not meet FDA requirements for emergency use*
 YES – If YES, continue to item (6)



IRB STANDARD OPERATING PROCEDURES

- (6) No standard acceptable treatment is available.
 - NO -- *If NO, does (did) not meet FDA requirements for emergency use*
 - YES – *If YES, continue to item (7)*

- (7) There is insufficient time to obtain IRB approval.
 - NO -- *If NO, does (did) not meet FDA requirements for emergency use*
 - YES – *If YES, continue to item (8) below*

- (8) If the Emergency Use is (was) carried out without obtaining informed consent (a-c below must be true in order for the criteria for emergency use without informed consent to be met):
 - a. Is (was) informed consent not able to be obtained because of an inability to communicate with, or obtain legally effective consent from, the subject?
 - NO – *If NO, continue to determinations below*
 - YES – *If YES, continue to item (8)b. below*
 - b. Is (was) time not sufficient to obtain consent from the subject’s legally authorized representative (if your institution allows surrogate consent)?
 - NO – *If NO, does (did) not meet FDA requirements for emergency use without informed consent.*
 - YES – *If YES, continue to item (8)c. below*
 - c. Is (was) an alternative method of approved or generally recognized therapy available that provides an equal or greater likelihood of saving the subjects life?
 - NO – *If NO, continue to determinations below.*
 - YES – *If YES, does (did) not meet FDA requirements for emergency use without informed consent*

Determination for the ACTIVITY – Please Check One:

- (1) Does this activity meet FDA requirements for emergency use of a test article in a life-threatening situation?
 - YES
 - NO

- (2) Does this activity meet FDA requirements for emergency use of a test article in a life-threatening situation without Informed Consent?
 - YES
 - NO

Chairperson’s Comments:

IRB Chairperson: _____ Name _____ Signature _____ Date _____



IRB STANDARD OPERATING PROCEDURES

Appendix 39 – BRANY IRB Standard Operating Procedures

Emergency Use Notification Form

Form with fields: Sponsor Name and IND/IDE #, BRANY IRB File #, Investigator, Phone, Name of person completing this form, Study Title, E-mail, Phone, Fax.

Emergency Use of a Test Article Without IRB Review: FDA regulations may allow the use of a test article with an IND without IRB review in an emergency situation when the certain circumstances are met. Although the FDA regulations allow for an exemption from prior review and approval by the IRB for emergency use, the BRANY IRB requires prior notification, if possible, of emergency use of test article so that the investigator’s intent for such use can be reviewed to determine if the circumstances of the emergency are in accord with FDA regulations. All instances of emergency use of a test article without prior IRB review must be reported to the IRB within 5 working days.

Please answer the questions below to report this emergency use to the IRB:

Principal Investigator’s Report → TO BE SUBMITTED PRIOR TO USE (or within 5 working days of event)

(1) For whom was the emergency use performed? Subject Initials: _____ Age: _____

(2) When will (did) the Emergency Use occur? Date: _____ Time: _____

NOTE: The emergency use must be reported to the IRB within five working days.

(3) Where will (did) the Emergency Use occur? _____

(4) Any subsequent use of the test article at the institution will be submitted for prior IRB review and approval.

- NO
YES

(5) Is/Was the human subject in a life-threatening situation or the subject’s disease or condition severely debilitating (e.g. blindness, loss of limb, paralysis or stroke)?

- NO
YES – Describe: _____

(6) Why does/did the situation necessitate the use of the test article?



IRB STANDARD OPERATING PROCEDURES

(7) Do you attest that no standard acceptable treatment is/was available?
 NO
 YES – On what basis is this claim made? _____

(8) Please describe why there is/was insufficient time to obtain IRB approval:

(9) Was Informed Consent obtained prior to the Emergency Use?
 YES
 NO – If NO, please answer the items a-c below:
a. Is (was) informed consent not able to be obtained because of an inability to communicate with, or obtain legally effective consent from, the subject?
 NO
 YES – On what basis is this claim made? _____
b. Is (was) time not sufficient to obtain consent from the subject’s legally authorized representative (if your institution allows surrogate consent)?
 NO
 YES – On what basis is this claim made? _____
c. Is (was) an alternative method of approved or generally recognized therapy available that provides an equal or greater likelihood of saving the subjects life?
 NO – On what basis is this claim made? _____
 YES

Completed applications may be submitted to: BRANY IRB
1981 Marcus Avenue, Suite 201
, Lake Success, NY 11042
T: (516) 470-6900
F: (516) 470-6903

Investigator’s Statement

I understand that Emergency Use of a Test Article without prior IRB review is subject to the same regulations and ethical principles governing all activities involving FDA regulated test articles (refer to BRANY Standard Operating Procedures). I will submit any subsequent use of the test article to the IRB for PRIOR review and approval.

Investigator’s Signature

Date



IRB STANDARD OPERATING PROCEDURES

[Appendix 40 – BRANY IRB Standard Operating Procedures](#)

ARCHIVED – CIRB IND Safety Report Submission Form



IRB STANDARD OPERATING PROCEDURES

Appendix 41 – BRANY IRB Standard Operating Procedures

Site Research Application (CIRB)

Instructions

Thank you for selecting the BRANY IRB. This application is designed to provide information necessary for the IRB to complete a **substantive and meaningful review** of your clinical research project submission, in accordance with the BRANY IRB standard operating procedures and the applicable regulations. In order to ensure an efficient review, it is essential that the application is accurate and complete. Please respond to each item on the application, or indicate not applicable if necessary. **NOTE: *Incomplete applications will result in delay of project review!***

The BRANY IRB office is available Monday-Friday, 9:00 AM – 5:00 PM (EDT), by calling (516) 470-6900, or by email (rhart@brany.com - Raffaella Hart, CIP, Director, IRB). Please contact the IRB staff for assistance.

IRBManager Access

To make and track submissions, generate study-specific documents, download IRB correspondence and view study status, you may request access to BRANY IRB's web portal, which is called *IRBManager*. Please specify individuals to receive *IRBManager* access information in Sections A & B below.

Education

All research personnel deemed as "key personnel" for any site must submit proof of human subject protections education. In your institution does not have a policy or requirement for mandatory training in human subject protections, BRANY IRB will accept: completion of the online NIH tutorial, available at <http://phrp.nihtraining.com/users/login.php>, Certification (Certified Principal Investigator or Certified Research Coordinator) from ACRP, CITI Course completion: minimum of Basic Biomedical Research Module (or equivalent). Alternative forms of training will be accepted on a case by case basis. Training should include topics such as federal research regulations, informed consent process, The Belmont Report, The Declaration of Helsinki, The Nuremberg Code, and Good Clinical Practice (E6).

Please note that IRB approval cannot be released for any site without proof of the Principal Investigator's completion of this training. If any other study personnel have not completed the training by the time a formal decision letter is ready to go out, the approval process would not be held up. We would release the formal letter with a caveat that certain named individuals cannot participate until proof of their training is received.

Contents

- A. Study Identifier Information
- B. Principal Investigator Information
- C. Research Staff Information
- D. Research Site Location(s)
- E. Site-specific Study Procedure Information
- F. The Recruiting and Enrolling Process
- G. Informed Consent Process
- H. Privacy and Confidentiality
- I. Local Research Context Evaluation
- J. PI Conflict of Interest Disclosure, Signatures, and Statement of Compliance

Attached Supplemental Forms

1. 01: Conflict Disclosure Statement (Required for all key study personnel)
2. 02: Conflict Report Form (Required for any "YES" disclosures on the statement.)
3. IRB Authorization Agreement
4. Additional Research Site Location Form (Optional – required only if the research will occur at multiple locations under the Principal Investigator's supervision.)

Supplemental Forms Available on <http://www.branyirb.com/forms-downloads>

5. Request for Waiver of Informed Consent/Documentation of Consent/Consent Elements (Optional)
6. Request for Waiver or Alteration to Release Protected Health Information (PHI) for Research Purposes [HIPAA Waiver] (Optional – not required if you will obtain written HIPAA authorization for all research and recruitment activity)
7. Data Use Agreement (Optional – required only if you are requesting access to a limited data set of Protected Health Information)



IRB STANDARD OPERATING PROCEDURES

A. Study Identifier Information

1) Sponsor: _____
 2) Protocol Version: _____
 3) Protocol No.: _____

4) Is this a multi-center research project? Yes No
 a) If YES – are you the lead PI (meaning you and your site/organization are responsible for coordinating all other sites involved in the research)? Yes No
 1. If YES – BRANY IRB expects that the lead PI/organization be responsible to obtain & manage the information obtained from the multi-center research that might be relevant to participant protections, including but not limited to:
 Unanticipated problems involving risks to participants or others
 Interim results
 Protocol modifications
Please provide a detailed plan for managing the above information (attach additional sheets as necessary): _____

B. Principal Investigator Information

5) Principal Investigator Contact Information

Name: _____ Email: _____
 Phone: (____) - _____ Fax: _____
 Address: _____
 City: _____ State: _____ ZIP/Postal Code: _____
 ← Check here to enable access to BRANY IRB's electronic portal: *IRBManager*. User may review status and access IRB documents. *Must have a valid & unique email address (users cannot share emails).
 ← Check here to schedule a brief demonstration for this contact.

6) Principal Investigator Qualifications

6.1) Has the Principal Investigator ever received any of the following? Yes No
 a) If YES, ***check all that apply*** and ***attach relevant documentation***, unless this information has previously been reported to BRANY IRB. Contact the IRB Director at 516-470-6909 with questions.
 Form FDA 483
 FDA warning letter
 OHRP warning letter
 NIDPOE letter

6.2) Licensing Information Not applicable
 Medical/clinical license #: _____ State: _____ Expiration Date: _____
 Medical/clinical license #: _____ State: _____ Expiration Date: _____
 Medical/clinical license #: _____ State: _____ Expiration Date: _____

6.3) Controlled Substances and DEA Information

a) Does this study involve controlled substances or narcotics? Yes No
 b) If YES, provide DEA registration # _____ Expiration date: _____

6.4) Massachusetts Researcher Registration Information

a) If this investigator will conduct research involving an investigational drug in the state of Massachusetts, provide the investigator's Massachusetts Researcher Registration #: _____
 Contact the Massachusetts department of public health at (617) 983-6712 or <http://www.mass.gov/dph/> to obtain information about registering to dispense investigational drugs. **You must obtain the appropriate registration before conducting research in the state of Massachusetts.**

6.5) Investigator Resources

The Investigator must ensure that adequate staffing and resources are available for each research project



IRB STANDARD OPERATING PROCEDURES

conducted, so that the rights and welfare of research subjects will be protected. Staff should have sufficient time to interact with subjects, as needed.

a) How may of the following does the Principal Investigator currently supervise?

- Open research studies: _____
- Locations: _____
- Physician sub-investigators: _____
- Research staff: _____
- Approximate # of active subjects: _____
- Approximate # of subjects to be enrolled in this study at your site(s): _____

6.6) Principal Investigator Training in Human Subject Protections

- a) Does your organization/institution have a requirement/policy for required training in human subject protections? Yes No
- b) If **YES**, describe (or attach) requirement/policy: _____
- c) If **YES**, attach documentation evidencing completion of the requirement
- d) If **NO**, attach documentation evidencing completion of one or more of the following:
- Online NIH tutorial, available at <http://phrp.nihtraining.com/users/login.php>.
 - CPI Certification (Certified Principal Investigator) issued by ACRP
 - CITI Course completion: Basic Biomedical Research Module (or equivalent)
 - Other (specify): _____ You must provide program/course description demonstrating that the following topics were covered: Federal research regulations, informed consent process, The Belmont Report, The Declaration of Helsinki, The Nuremberg Code.

6.6) Required Attachments for Principal Investigator

- FDA Form 1572 (signed & dated copy, **only if study involves investigational drug**)
- Statement of the Investigator (signed & dated copy, **only if study involves investigational device**)
- Evidence of training in human subject protections (see question above)
- CV (signed & dated within 2 years)
- Current medical/clinical license (*Upcoming expiration? Please submit updated info when available.*)

C. Research Staff Information

7) Primary Study Coordinator Contact Information

- Name: _____ Email: _____
 Phone: (____) - _____ Fax: _____
 Address: _____
 City: _____ State: _____ ZIP/Postal Code: _____
- ← Check here to enable access to BRANY IRB's electronic portal: *IRBManager*. User may review status and access IRB documents. **Must have a valid & unique email address (users cannot share emails).*
- ← Check here to schedule a brief demonstration for this contact.

8) Key Personnel Information

List all **key study personnel** and indicate those who will obtain consent. Staff should be sufficiently trained to administer the research protocol without impacting subject safety or data integrity. "Key personnel" are defined as individuals who are responsible for the design and conduct of a study.

Name	Role	Will obtain consent?	
_____	_____	<input type="checkbox"/> Yes	<input type="checkbox"/> No
_____	_____	<input type="checkbox"/> Yes	<input type="checkbox"/> No
_____	_____	<input type="checkbox"/> Yes	<input type="checkbox"/> No
_____	_____	<input type="checkbox"/> Yes	<input type="checkbox"/> No
_____	_____	<input type="checkbox"/> Yes	<input type="checkbox"/> No

9) Required Attachments for Each Research Staff Person

- Conflict Disclosure Statement** (BRANY IRB's form for declaring conflicts of interest, not the sponsor's financial disclosure form.)



IRB STANDARD OPERATING PROCEDURES

- Conflict Report Form (BRANY IRB's form for reporting details about declared conflicts of interest, not the sponsor's financial disclosure form.)
Evidence of training in human subject protections (see instructions page for more information)

D. Research Site Location(s)

Research Location #1 (Only include sites at which subjects will be seen.)

10) Institution/Organization Description

- a) Institution/Organization Name:
b) Phone:
c) Emergency (24 hour) phone:
d) Physical Address (must match box 3 of submitted Form FDA 1572, if applicable):
Address:
City: State: ZIP/Postal Code:
e) Should the phone and address in b) - d) above appear on the informed consent?
f) Institution/Organization Federalwide Assurance (FWA) Number:
g) Type of Facility: Medical office, Hospital, University, Psychiatric institution, Nursing home, Laboratory, Research Clinic, Dialysis center, Surgery Center, Other (specify):

Any changes to the information in item 10 above must be reported promptly to BRANY IRB.

11) Responsible Institutional Individual

Provide information about the appropriate institutional/organizational liaison in charge of research in order to facilitate reporting in the event of unanticipated problems involving risks to subjects or others, serious and/or continuing non-compliance, or other reportable issues (e.g., research director, institutional official, vice president for research, CEO)

- Check here if this individual is the same as the PI. If so, do not re-enter contact information.
Name: Title:
Phone: () - Email:
Address: Fax:
City: State: ZIP/Postal Code:

12) BRANY IRB Authorization Agreement

BRANY IRB requires a written IRB Authorization Agreement from the site before any submissions can be reviewed. Failure to provide an authorization agreement may results in a delay of IRB review.

- Complete the IRB Authorization Agreement and append to your application. This must be signed by a signatory official from your site (individual with authority to sign contracts).
Check here if you already have filed an IRB Authorization Agreement with BRANY IRB.
Date IRB Authorization was signed by your organization:

13) Additional Site-Required Reviews for BRANY IRB-Approved Research

- a) Does this investigator have an obligation to submit this study to another committee, or to obtain other organizational/institutional approval for conducting this study at this research site location? (Examples: radiation safety, protocol review committee, GCRC, CTSA, pharmacy, hospital/department approval, institution approval, etc.) Yes No



IRB STANDARD OPERATING PROCEDURES

b) If YES – It is the Principal Investigator's obligation to ensure other required approvals are in place before initiating BRANY IRB-approved research. PI Acknowledges

13.1) Does this investigator have an obligation to submit this study to another IRB, or to obtain other organizational/institutional approval for conducting this study at this research site location? Yes No

a) If YES – Provide documentation from the other IRB authorizing review by BRANY IRB. Contact BRANY IRB for further instruction: 516-470-6900 or rhart@brany.com. PI Acknowledges

14) Emergency Situations
 The investigator should ensure a plan is in place to have trained staff available to provide coverage in emergency situations.

a) Describe the emergency equipment available at this site (check all that apply):

Crash cart Emergency medications CPR trained staff
 Access to 911 Other (specify): _____ N/A – why? _____

b) Are research personnel available to subjects 24 hours a day? Yes No
 If **YES** – At which phone number are research personnel available 24 hours a day? (____) - _____
 If **NO** – explain how subjects can contact research personnel: _____

15) Additional Resources
 Describe any additional resources available to subjects:

Counseling services Certified medical interpreters
 Other: _____ NONE

16) Additional Site Locations Not applicable
 For each of your additional research locations, attach the *Additional Research Location Form* (see attachments).

E. Site-specific Study Procedure Information

17) Who will dispense the study drug? (Check appropriate box(es) below.)

A credentialed and/or licensed professional in accordance with my state's law
 A pharmacist
 Study personnel (in accordance with my state's law)
 Other (specify): _____

18) Where will the study drug be stored? _____

19) Optional – As needed, please provide other details explaining the study drug dispensation plan here: _____

F. The Recruiting and Enrolling Process

20) How do you intend to recruit research subjects? (Check all that apply)

My private patient population/database Physician referrals
 Research database obtained from a 3rd party Advertising
 Flyers Other (please specify): _____
 Clinical patient population at my institution (in accordance with applicable law and my institutional policies on protection of patient confidentiality)

← Check here if advertising/recruitment materials are attached for review, and list submitted items:

21) Will you be accessing records for patients other than your own for recruitment purposes (i.e. patients for whom you do not have the usual duty of care)? Yes No



IRB STANDARD OPERATING PROCEDURES

a) If **YES** – You will need to complete separate, applicable forms, which may include:
Request for Waiver or Alteration to Release Protected Health Information (PHI) for Research Purposes
 [HIPAA Waiver] → Go to: <http://www.branyirb.com/forms-downloads>
Data Use Agreement (Optional – required only if you are requesting access to a limited data set of
 Protected Health Information) → Go to: <http://www.branyirb.com/forms-downloads>

22) How will you determine if a potential subject is eligible (i.e., meets the inclusion/exclusion criteria) for participation in the research? (e.g., screening examination, review medical record/history)

23) Competing Study Information

Are you involved in any research projects that may involve the same subject population as this study? Yes No

a) If **YES** – How will you select which study subjects are offered participation in?
 (*NOTE: The investigator should not influence which project the potential subject participates in.)

24) What procedure will be provided for participants to ask questions and voice concerns or complaints to the investigator?

- Informed consent will include contact information for the research team (*see BRANY IRB's sample informed consent for language requirements)
- If no consent form will be used, how will subjects be instructed to contact the investigator for this purpose? _____
- Other: _____

25) Subject Compensation

25.1) Please provide subject payment information. The informed consent will be modified to reflect this information, if it not already included in the document

- Subjects will not be paid – *proceed to next question*
- Subjects will present receipts and be reimbursed for travel and or parking as follows: _____
- Subjects will be paid per completed visit as follows:
 Amount per completed visit: _____ Number of visits in the study: _____
 Any visits not paid: _____ Total payment: _____

25.2) When subjects will receive any form of payment, complete the following: Not applicable

- a) In what form can the subject expect to receive payment?
 Cash Check Other (specify): _____
- b) When can the subject expect to receive payment? (*Cannot be contingent upon completion of the study.*)

26) Demographics of Anticipated Subject Population

Approximate the ethnic makeup of the population to be recruited:

_____ % African American _____ % Middle Eastern _____ % Native American/First Nations
 _____ % Asian _____ % Caucasian
 _____ % Pacific Islander _____ % Hispanic _____ % Other (specify): _____

*NOTE: If you anticipate enrolling subjects with limited English proficiency (“LEP”) (e.g., the investigator’s practice is in an area with a known population of foreign-language speaking persons the investigator must obtain an informed consent form translated into the language(s) of the anticipated LEP population, with such translation being approved by BRANY IRB.

27) Protections Against Undue Influence

Subjects recruited must be free of any outside influences while deciding whether to participate. Even in the absence of overt coercive or inducing statements, an element of coercion may be introduced because of the relationship between the potential subject and the investigator.

Describe the steps taken to minimize the possibility of coercion or undue influence (check all that apply):



IRB STANDARD OPERATING PROCEDURES

Subjects will be given information during the informed consent process without bias or emphasis on potential risks or benefits
Subjects will be reassured that they will receive no penalty if they decide not to participate
Other: _____

G. Informed Consent Process

28) General Informed Consent Process
I will obtain informed consent from potential subjects prior to performing any study driven procedures.
Not applicable - This application requests a waiver of consent

29) Where will the consent process take place? _____ Not applicable

30) What opportunity will be afforded to the prospective subject (or the subject's legally authorized representative) to consider whether or not to participate? Check all that apply.
Schedule screening visits that allow for adequate discussion of the research and alternatives
Review informed consent form in detail with potential subject
Provide opportunity for subject to digest information and come back with questions at a later time
Mail consent document in advance of visit to allow extra time for review
Other (please specify): _____
N/A (only if consent waiver is requested)

31) How will it be determined that the subject (or the subject's legally authorized representative) understands what has been explained? (Check all that apply)
N/A (only if consent waiver is requested)
Have a conversation with the subject to assess understanding, and document this conversation in the subject's research record. *NOTE: Asking the subject if he/she understands in the form of yes/no questions is not sufficient.
Use the BRANY IRB Informed Consent Feedback Tool (available at www.branyirb.com)
Describe other method here: _____
Attach a copy of any relevant documentation templates or other tools you might use to make this assessment.

32) For long term studies (subject participation is greater than 1 year), how will you determine the ongoing consent of subjects?
Discussion reviewing informed consent details and reminding subject of their right to withdraw at any time. Select one:
via telephone contact with the subject
documented at a scheduled visit
Repeat the informed consent process (documented by obtaining a newly signed consent form)
N/A - This application does not apply to a long term study, or a consent waiver has been requested

33) Anticipated Study Populations
Indicate the anticipated population of subjects to be included in the research (check all that apply).
Males Females

33.1) Have members of minority groups have been included in the study population whenever possible and scientifically desirable? Yes No
a) If NO, please explain: _____

33.2) Do you anticipate that you will recruit/enroll individuals from any of the "vulnerable" populations listed below at your site? Yes No
a) If YES, check all that apply.
Mentally ill Mentally disabled Nursing home residents
Institutionalized Chronic condition Terminally ill
Incompetent adults Pregnant women Limited or non-readers
Hospitalized Those in emergent care settings Children
Poor/uninsured Children who are wards Emancipated minors
Prisoners Students of the PI/study staff



IRB STANDARD OPERATING PROCEDURES

- Students to be recruited in their educational settings (e.g., in class or at school)
Employees of the research site, PI, or Sponsor
Others vulnerable to coercion (specify):

b) If YES - what is the justification for including each "vulnerable" category of subjects indicated above?

c) If YES - are the safeguards afforded to all subjects in the protocol sufficient to protect the "vulnerable" subjects indicated above?

- Yes - If YES, what are they?
No - If NO, what are the safeguards in the protocol, & what additional safeguards are needed?

34) Languages and Translations

Do you anticipate enrolling subjects whose primary language is not English? Yes No

a) If YES, for which language(s) will you require translation?

- If YES, describe plan for conducting the consent discussion and ongoing communication with non-English speaking subjects:
Staff member fluent in foreign language
Use a certified medical interpreter
Other (specify):

35) Will you include adult individuals who may lack capacity to consent in this study at your site? Yes No

a) If YES, who will decide whether an individual subject is competent to consent?

b) If YES, how will this assessment be made?

c) If YES, will you obtain assent from adult participants who may lack the capacity to consent?

- No - if no, why not?
Yes - if so, what is the plan for obtaining the assent?
assent form - must be submitted for IRB review
documented assent discussion
other:

36) Do you plan to include adult individuals who require surrogate consent (consent by a legally authorized representative) in this study at your site? Yes No

a) If YES, does this study meet all of the following criteria? (Need all 5 for IRB approval)

- There is potential benefit over standard treatment; and
Standard treatment is not being withheld; and
There is no alternative standard treatment; and
Enrollment in the study is in the best interest of the patient; and
Participation in the research would not be contrary to the known wishes of the patient

b) Comments/further justification:

37) Do you plan to include incapacitated (mental or physical) patients in this study at your site? Yes No

a) If YES, the PI is responsible to ensure appropriate legal consultation is obtained to determine who is an appropriate authorized representative. PI acknowledges

38) Do you plan to include children in this study at your site? Yes No

a) If YES, the research involves children: ages of children:

b) If YES, are any of the children wards? Yes No

If yes, an advocate has been appointed for children who are wards

*Advocate's name & contact information:

If yes, and an advocate has not been appointed for children who are wards, please explain why:

c) Confirm that provisions will be made to solicit the consent of at least one parent or legal guardian (Note: BRANYIRB may, at its discretion, require permission of both parents). PI acknowledges

d) Will you obtain assent from all children? Yes No



IRB STANDARD OPERATING PROCEDURES

e) Will you obtain assent from **only some** children? Yes No
 If **yes**, from which? _____

f) How will assent be documented?
 assent form other (specify): _____ not obtaining assent

g) What **provisions** will be made **for soliciting the assent** of the children? (*check all that apply*)
 interview child without parents
 interview child with parents
 interview child with an impartial witness present (***required by BRANY**)
 other: _____

h) Will this research include any pregnancy testing for female minors of childbearing potential? Yes No
 If **yes**, parents/guardians will be informed of positive pregnancy test results at your site? *Please select the answer that is in accordance with your state law.* Yes No

39) Do you plan to include **women in labor** in this study at your site? Yes No

a) If **yes**, *check all that apply*:
 the pregnant woman in labor will be approached for her informed consent
 Efforts will be made to obtain informed consent during a prenatal visit, if possible.
 Other consent issues/safeguards: _____

b) If the **woman** will be in **active labor**, consent will also be asked of a second person, typically her husband, father of the baby, or woman's mother, or close relative accompanying her. PI acknowledges

40) Do you plan to include **surgical patients** in this study at your site? Yes No

a) If **yes**, *check all that apply*:
 efforts will be made to obtain written informed consent during pre-surgical testing visits, if possible
 consent will be obtained on the day of surgery, but prior to sedation
 Other consent issues/safeguards: _____

41) Do you plan to include **psychiatric patients** in this study at your site? Yes No

a) If **yes**, *check all that apply*:
 If the patient is hospitalized during enrollment, I agree to contact the subject's primary psychiatrist or other attending physician before recruiting the subject.
 I agree to tell patients that a research coordinator or other investigator in connection with the research will approach them.
 I agree to have a third party independent of the study assess the subject's capacity to consent to participate prior to enrolling subjects with psychiatric illness affecting competency in the study.
(*required by BRANY)

H. Privacy and Confidentiality

42) What precautions will be used to maintain the confidentiality of identifiable health information?
 Paper based records will be kept in a secured location & only accessible to personnel involved in study
 Computer based files will only be made available to personnel involved in the study through the use of access privileges & passwords.
 Prior access to any study-related information, personnel will be required to sign statements agreeing to protect the security and confidentiality of identifiable health information.
 Whenever feasible, identifiers will be removed from study-related information.
 Other (specify): _____

43) How will information about research participants be obtained? *Check all that apply*:
 Surveys Direct observation Other (specify): _____
 Questionnaires Performance of tests & procedures
 Interview



IRB STANDARD OPERATING PROCEDURES

44) What provisions are in place to protect the privacy interests of participants?

The IRB will assess the methods used to identify potential research subjects or to gather information about subjects in order to ensure that the privacy of individuals is not invaded.

Describe the methods in place to protect the privacy of participants (e.g., private interviews, use of barriers when subject is required to disrobe, private room for performing research interventions, consideration of whether teen subjects should be interviewed without parents when sensitive subject matter is involved):

Response: _____

45) How long will the research data be stored by the investigator?

_____ years after close of study (minimum 3 yrs after close or as specified by the sponsor, whichever is longer)

46) HIPAA Training (Check all that apply):

- I have training in the fundamental requirements imposed by the privacy rule (HIPAA).
- I will not enroll any subjects without first having them sign a research consent/authorization form that is compliant with the privacy rule (HIPAA)
- I will ensure that all patients and/or research subjects receive a privacy notice.

**If you left any of the 3 boxes above un-checked, please explain why here:* _____



IRB STANDARD OPERATING PROCEDURES

I. Local Research Context Evaluation

The IRB is responsible for understanding the community in which research occurs. Questions in this section are intended to provide a description of the community from which you will recruit your research subjects.

47) How would you describe your research setting? Check all that apply:
[] suburban [] urban (city) [] rural [] other: _____

48) Describe the setting of the study site(s). Check all that apply:
[] hospital [] university [] research facility [] private practice
[] nursing home [] clinic [] other: _____

49) Is any federally funded research conducted at your site(s)?
[] no [] yes

50) What is the overall attitude towards the conduct of research in your community?
[] neutral [] positive [] negative -> explain: _____

51) Are there any specific community attitudes relative to research (religious, ethical, ethnic, or economic) that the IRB should be aware of prior to the review of this research project?
[] no [] yes -> explain: _____

52) Has there been any recent media focus on research in your community?
[] no [] yes -> explain: _____

53) Are there any circumstances where certain subject populations in your community may feel coerced into participating in a research study? (e.g. poor and/or uninsured)
[] no [] yes v
If yes, how will you approach enrollment of subjects from such populations to avoid coercion?

54) What is the name of the nearest hospital or medical center (if the research is not taking place in a hospital/medical center)?
Name: _____ Approximately how many miles away? _____ [] N/A

55) Does this organization/institution have an institutional review board/ethics committee?
[] yes [] no [] unknown

56) Confirm that you are aware of applicable federal, state and local regulations/laws governing human subject research (e.g., 21CFR312, 21CFR812, 21 CFR 50, 54, 56, 45CFR46, state department of health regulations):
[] yes v [] no
Are you aware of any changes to such regulations/laws in the past year?
[] yes [] no [] unknown

57) Massachusetts sites: [] Not Massachusetts
Confirm you are registered with the Massachusetts department of public health to dispense investigational drugs. [] no [] yes

SECTION BELOW FOR BRANY IRB USE ONLY
PRINCIPAL INVESTIGATOR: Do not complete #58 or signature block on this page!

Consultant Review of Local Research Context | BRANY File #or Study ID: _____

Consultants to the IRB on this area should have personal knowledge of the local research context, such knowledge having been obtained through extended, direct experience with the research institution, its subject population and its surrounding community.

58) Do you concur with the description of the local research context provided above?
[] yes [] no -> If no, explain: _____
Printed name of consultant: _____
Signature of consultant: _____
Date: _____ ->->->Note: if the IRB reviewer is the consultant, please refer to the reviewer checklist in the IRB file for a response to this item.



IRB STANDARD OPERATING PROCEDURES

J. PI Conflict of Interest Disclosure, Signatures, and Statement of Compliance

59) PI Conflict of Interest in Research Disclosure Statement (FORM 01)

Definitions

“Financial Interest”

Anything of monetary value from a financially interested company, including but not limited to:

- Officer's/Director's fees
- Consulting fees
- Compensation for service on an Advisory Board (including scientific advisory boards)
- Honoraria for Lectures/Teaching;
- Gifts
- Other emoluments or "in kind" compensation such as travel and entertainment from a financially interested company (including those from a third party if the original source is a financially interested company), for any services not directly related to the reasonable costs of conducting the research as specified in the research agreement
- Compensation related to the research whose amount might be affected by the outcome of the research
- Equity interest of any kind and in any amount in a non-publicly or publicly traded Financially Interested Company (e.g., stocks, stock options, convertible notes, other ownership interests), including those for which the value cannot be determined through reference to publicly available prices, those for which the value may be affected by the outcome of the research, and those which represent a 5% or more interest in any one single entity
- Intellectual property related to the proposed research
- License fees, technology transfers, and/or current and future royalties from patents and copyrights
- Board or executive relationships related to the research (regardless of compensation)
- Paid/reimbursed travel, meaning the occurrence and value of any paid/sponsored (i.e., sponsored travel is that which is paid on behalf of the Investigator and not reimbursed to the Investigator so that the exact monetary value may not be readily available), and/or reimbursed travel, whether in connection with an outside position or for consulting, lecturing, or service on a scientific advisory board, data safety monitoring board, steering committee for a clinical trial, executive committee for a clinical trial, or other committee for an outside entity, or for any other purpose including the purpose of the trip, the identity of the sponsor/organizer, the destination and the duration

The term “Financial Interest” does *not* include:

- (i) Salary or other remuneration received from the institution/organization
- (ii) Grant support for salaries from the institution/organization
- (iii) Holdings in mutual funds or 401K/403B retirement funds
- (iv) De minimus gifts whose aggregate value does not exceed \$100 per annum; or reasonable business expenses.

“Financially Interested Company”

An entity whose financial interests could reasonably appear to be affected by the conduct or outcome of a research project. The term “entity” means any corporation, limited liability company, partnership, limited partnership, limited liability partnership, joint venture, business trust, or other business organization, and any not-for-profit organization, charity or foundation.

“Related Party”

Spouse, domestic partner, and dependent children, siblings, parents, or equivalents by marriage, or other individuals residing in the household.

“Significant Financial Interest”

A Financial Interest that is over \$5,000, or is less than \$5,000, and also involves a non-financial role in a Financially Interested Company, or is less than \$5,000, and the value cannot be determined through reference to publicly available prices, if the value will be affected by the outcome of the research, or the value represents 5% or more interest in any one single entity, and is determined by the COIC to be related to the research.

Instructions: The **Principal Investigator** is required to complete the questions below.



IRB STANDARD OPERATING PROCEDURES

a) Within the <i>last 12 months</i> , have you or, to the best of your knowledge, has any related party performed any work (<i>not directly related to the costs of conducting research</i>) <u>for a Financially Interested Company</u> ?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
b) Within the <i>last 12 months</i> , have you or, to the best of your knowledge, has any related party received compensation (<i>not directly related to the costs of conducting research</i>) <u>from a Financially Interested Company</u> ? Please answer Yes for paid/reimbursed travel (see definitions above).	<input type="checkbox"/> Yes	<input type="checkbox"/> No
c) Do you or, to the best of your knowledge, does any related party maintain any board or executive relationship related to the research, regardless of compensation ?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
d) Within the <i>next 12 months</i> , have you or, to the best of your knowledge, does any related party anticipate performing any work and/or receiving any compensation (<i>not directly related to the costs of conducting research</i>) <u>from a Financially Interested Company</u> ? Please answer Yes for paid/reimbursed travel (see definitions above).	<input type="checkbox"/> Yes	<input type="checkbox"/> No
e) Do you or, to the best of your knowledge, does any related party own stock, stock options or other forms of ownership in a <u>Financially Interested Company</u> ?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
f) Do you or, to the best of your knowledge, do any of your related parties have any intellectual property rights (e.g., named as an inventor in an issued patent or patent application, license fees, technology transfers, current or future royalties from patents and copyrights)?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
g) Does your department/institution/organization have a financial interest in the agent under investigation or in a company that could benefit from the study findings, or receive significant financial support from such a company?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
h) Do you want to voluntarily disclose anything else?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
For any YES answer to the above, complete and attach the <u>Conflict Report Form</u>.		
<i>Any change to the above responses must be promptly reported to BRANY IRB.</i>		
Any new significant financial interests must be reported within 30 days of acquisition or discovery.		

60) Person Completing This Form	
Name: _____	Title: _____
Signature: _____	Date (mm/dd/yyyy) _____
<input type="checkbox"/> Check here if this individual is the same as the PI, Primary Study Coordinator, or the Institutional Official. <i>If so, you do not need to re-enter contact information.</i>	
Phone: (____) - _____	Email: _____
Address: _____	Fax: _____
City: _____	State: _____ ZIP/Postal Code: _____

61) Principal Investigator's Statement of Compliance The proposed investigation involves the use of human subjects. I am submitting this form with a description of my project, prepared in accordance with organizational/institutional policy for the protection of human subjects participating in the research. I understand the BRANY IRB's policy concerning research involving human subjects and: I will not engage in any research involving human subjects without obtaining prior IRB approval; I agree that the BRANY IRB approved consent form must be the only consent form used in this study and must be used for every patient prior to enrollment; I agree to report to BRANY IRB any unanticipated effects on subjects that become apparent during the course or as a result of experimentation and the actions taken as a result; all serious adverse events must be reported to the IRB within 24 hours of discovery, and a written report must be submitted to the IRB within 5 days, unless otherwise agreed to by IRB administration; I agree to cooperate with members of BRANY IRB charged with the continuing review of this project and agree to submit continuing review applications in a timely fashion; I agree to obtain prior approval from BRANY IRB before amending or altering the scope of the project or



IRB STANDARD OPERATING PROCEDURES

implementing changes to the approved protocol or consent form;
I agree to maintain documentation of consent forms and continuing review applications;
I agree that all advertising must be approved by the IRB prior to submission to any agencies and before posting;
I agree to notify BRANY IRB of study termination and/or any change in the status of the study;
I agree to maintain records for a minimum of 3 years after closure, or as specified by the sponsor of the research, whichever is longer;
I will ensure that research subjects are given referrals for needed health care during the research or for follow-up after the research.
I have received and am familiar with the BRANY IRB's Standard Operating Procedures/Research Manual.

I further understand that:

Failure to comply with any of the above, with the BRANY IRB's Standard Operating Procedures, or with any applicable regulations may result in immediate closure of this study, which is reportable to my organization/institution, FDA and/or OHRP.

This research project will be subject to routine audits by BRANY QA department, and at the discretion of the BRANY Institutional Official, the results of such audits may be shared with appropriate Department Chairpersons, the Organization/Institutional Official, and/or the Sponsor.

NOTE: Investigators are referred to the BRANY IRB's Standard Operating Procedures for a complete statement of institutional policy and procedures regarding research and human subjects.

PI Signature:

Date (mm/dd/yyyy) _____



IRB STANDARD OPERATING PROCEDURES

Appendix 42 – BRANY IRB Standard Operating Procedures

Sponsor/CRO Research Application (CIRB)

Instructions

Thank you for selecting BRANY IRB. This application is designed to provide information necessary for BRANY IRB to complete a substantive and meaningful review of your research project submission, in accordance with BRANY IRB standard operating procedures and applicable regulations.

In order to ensure an efficient review, it is essential that the application is accurate and complete. Please respond to each item on the application, or indicate not applicable if necessary. **NOTE: Incomplete applications will result in delay of project review!**

The BRANY IRB office is available Monday-Friday, 9:00 AM – 5:00 PM (EDT), by calling (516) 470-6900, or by email (rhart@brany.com - Raffaella Hart, CIP, Director, IRB). Please contact the IRB staff for assistance.

Contents

- A. Sponsor and Protocol Information
- B. Billing Information
- C. Indemnification Agreement
- D. Sponsor/CRO Statement of Compliance

A. Sponsor and Protocol Information

1) Sponsor: _____
 2) Protocol Version: _____
 3) Protocol No.: _____
 4) Protocol Title: _____
 4.1) Will this study be registered on www.clinicaltrials.gov? Yes No

5) Who will serve as the contact for BRANY IRB? Sponsor Contact CRO Contact

6) Sponsor Contact Information

Name: _____ Email*: _____
 Phone: _____ Fax: _____
 Address: _____
 City: _____ State: _____ ZIP/Postal Code: _____

Any changes to the above must be reported promptly to BRANY IRB.

← Check here to assign this contact access to BRANY IRB's electronic portal: *IRBManager*. User may review status and access IRB documents.

**Must have a valid and unique email address (shared email addresses not permitted).*

← Check here to schedule a brief demonstration for this contact.

7) CRO Contact Information

N/A

Organization name: _____

Name: _____ Email*: _____
 Phone: _____ Fax: _____
 Address: _____
 City: _____ State: _____ ZIP/Postal Code: _____

Any changes to the above must be reported promptly to BRANY IRB.

← Check here to assign this contact access to BRANY IRB's electronic portal: *IRBManager*. User may review status and access IRB documents.

**Must have a valid and unique email address (shared email addresses not permitted).*

← Check here to schedule a brief demonstration for this contact.



IRB STANDARD OPERATING PROCEDURES

8) Party Responsible for Consent Form Review/Approval on the Sponsor's Behalf

Check one box at the right or fill in contact information below.

Sponsor Contact CRO Contact

Name: _____ Email*: _____

Phone: _____ Fax: _____

Address: _____

City: _____ State: _____ ZIP/Postal Code: _____

Any changes to the above must be reported promptly to BRANY IRB.

← Check here to assign this contact access to BRANY IRB's electronic portal: *IRBManager*. User may review status and access IRB documents.

*Must have a valid and unique email address (shared email addresses not permitted).

← Check here to schedule a brief demonstration for this contact.

9) Source of Funding (check all that apply)

Drug or medical device company

Not-for-profit sponsor

Federal government

a) Provide name of federal agency funding research: _____

b) Complete the FWA/Federal Funding Attachment

Other: _____

10) Federal Wide Assurance (FWA)

Is this study is being conducted under a FWA?

Yes

No

a) If **YES**, complete the FWA/Federal Funding Attachment

11) Study Type

11.1) Does this research involve an **investigational new drug, biologic**, or the **investigational use of a marketed drug or biologic**?

Yes

No

a) If **YES**, provide the IND number: _____

b) Documentation of the IND number is provided as follows (check all that apply):

IND number appears within the protocol

FDA correspondence confirming the assigned IND number for this investigation

Sponsor correspondence confirming the assigned IND number for this investigation

c) If the IND number is not available, explain why IND was not obtained:

11.2) Does this research involve a **device**?

Yes

No

a) If **YES**, the research sponsor classifies this devices as a (check one):

Significant risk device (SR) – see FDA definition at 21 CFR 812.3(m)

Non-significant risk device (NSR) – see FDA definition at 21 CFR 812.3(m)

b) For all device studies, provide one (1) of the following:

FDA letter granting an investigational device exemption for the proposed use

Letter from the sponsor stating that the study is a non-significant risk device study

Letter explaining why the investigation is exempt from the IDE requirements under 21 CFR 812.2(c) or otherwise exempt

11.3) If this research **does not** involve a drug or device as described above, how would you describe it? (check all that apply)

Retrospective chart review

Blood draw

Survey study

Data collection during routine clinical care

Other: _____

11.4) Does this research involve **any form of gene transfer or recombinant DNA**? Yes No

a) If **YES**, has it been submitted to the RAC (Recombinant DNA Advisory Committee)?

Yes → **Attach** a copy of the RAC correspondence

No

b) If **YES**, has there been institutional biosafety committee (IBC) review for any sites involved?

Yes → **Attach** IBC recommendations affecting the protocol and/or consent form



IRB STANDARD OPERATING PROCEDURES

No

c) If you would like information about BRANY's IBC services, please check here →

11.5) Has this study been submitted to, disapproved or terminated by another IRB prior to submission to BRANY IRB? Yes No

a) If **YES** → **Attach** the IRB decision, disapproval and/or termination letter, and/or other relevant correspondence

b) If **YES**, are you requesting a transfer of IRB oversight?

Yes → **Attach** Transfer of IRB Oversight form

No

12) Data Safety Monitoring Provisions

All clinical trials require safety monitoring, but not necessarily by a formal committee. Describe the provisions for safety monitoring for this project.

None – study is not a clinical trial or a study that requires safety monitoring (e.g., chart review)

A formal data monitoring committee has been established

a) **Attach** data monitoring plan, or **specify protocol pages/section** describing it:

A formal data monitoring committee has not been established

a) What mechanism is in place for safety monitoring?

13) Dispensing of Controlled Substances

Does this study involve the dispensing of a controlled substance? Yes No

a) If **YES**, name of controlled substance (brand and generic): _____

b) If **YES**, indicate classification of controlled substance:

Class I

Class II

Class III

Class IV

Class V

c) If **YES**, Does the sponsor/CRO agree to advise participating investigators to attach a photocopy of the DEA registration or controlled substance license for each investigator prescribing and/or dispensing the controlled substance. Yes

14) Sub-Study and/or Additional Research

Does this study involve a sub-study/additional research? Yes No

a) If **YES**, where is the sub-study/additional research described?

In the main protocol → Reference page/section: _____

In a separate document → **Attach**

Other → Explain: _____

b) If **YES**, is the sub-study/additional research optional for subjects? Yes No

c) If **YES**, how will subjects indicate consent for the sub-study/additional research?

With additional consent and HIPAA forms → **Attach**

Within the main study consent and HIPAA forms

Other → Explain: _____

d) If **YES**, **Attach** a list of participating sites to be submitted to BRANY IRB (if not all sites)

15) HIV Testing

Does this study involve HIV testing (either required by the protocol or allowed by protocol at investigator's discretion)? Yes No

a) If **YES**, Does the sponsor/CRO agree to advise each participating site that it is the Principal Investigator's responsibility to ensure compliance with state/local regulations/laws related to HIV testing? Yes

16) Research Location(s)

Indicate the type(s) of facility at which the research will take place (check all that apply):

Medical office

Hospital

University

Psychiatric institution

Nursing home

Laboratory

Research Clinic

Dialysis center

Surgery Center

Other (specify): _____



IRB STANDARD OPERATING PROCEDURES

17) Vulnerable Populations

Will this study recruit/enroll individuals from any of the vulnerable populations listed below? If **YES**, check all that apply Yes No

- | | | |
|---------------------------------------------------------------------------------------------------------------|----------------------------------------------------------|-------------------------------------------------|
| <input type="checkbox"/> Mentally ill | <input type="checkbox"/> Mentally disabled | <input type="checkbox"/> Nursing home residents |
| <input type="checkbox"/> Institutionalized | <input type="checkbox"/> Chronic condition | <input type="checkbox"/> Terminally ill |
| <input type="checkbox"/> Incompetent adults | <input type="checkbox"/> Pregnant women | <input type="checkbox"/> Limited or non-readers |
| <input type="checkbox"/> Hospitalized | <input type="checkbox"/> Those in emergent care settings | <input type="checkbox"/> Children |
| <input type="checkbox"/> Poor/uninsured | <input type="checkbox"/> Children who are wards | <input type="checkbox"/> Emancipated minors |
| <input type="checkbox"/> Prisoners | <input type="checkbox"/> Students of the PI/study staff | |
| <input type="checkbox"/> Students to be recruited in their educational settings (e.g., in class or at school) | | |
| <input type="checkbox"/> Employees of the research site, PI, or Sponsor | | |
| <input type="checkbox"/> Others vulnerable to coercion (specify): _____ | | |

18) Translations

Will the informed consent and/or other subject materials require translation? Yes No

a) If **YES**, what language(s): _____

b) If **YES**, who will provide translations? Sponsor/CRO BRANY IRB Vendor

19) Items Submitted for BRANY IRB Review

List each item for which you are seeking IRB review and acknowledgement/approval, or attach a separate document listing the items submitted.

- Include version and edition identifiers, as applicable.
- Include recruitment materials, and a description of any recruitment procedures not detailed in the protocol
- Include subject materials, and a description of any subject materials not detailed in the protocol
 1. Protocol and Exhibit A
 2. _____
 3. _____
 4. _____
 5. _____
 6. _____
 7. _____
 8. _____
 9. _____
 10. _____

B. Billing Information

20) Party Responsible for BRANY IRB Fees

Check one box or fill in contact information below.

Sponsor Contact listed in Section A.

CRO Contact listed in Section A.

Name: _____

Email: _____

Phone: _____

Fax: _____

Address: _____

City: _____

State: _____

ZIP/Postal Code: _____

C. Indemnification Agreement

BRANY IRB requests an *Indemnification Agreement* from the Sponsor for all protocols reviewed. Please contact BRANY IRB to obtain an agreement template. Failure to provide an indemnification agreement may result in a delay of IRB review.



IRB STANDARD OPERATING PROCEDURES

D. Statement of Compliance

1. The Sponsor/CRO will ensure that it selects qualified investigators;
2. The Sponsor/CRO will ensure proper monitoring of all sites conducting this study;
3. The Sponsor/CRO will report results and findings to BRANY IRB, including those that may directly affect subject safety, may affect the subject's willingness to continue participation in the research, influence the conduct of the study, or alter the IRB's approval to continue the study;
4. The Sponsor/CRO will ensure that contracts specify who will provide care for research-related injury and who is responsible to pay for such care. Applicable consent form text describing any compensation for research-related injury will be congruent with any applicable contracts;
5. The Sponsor/CRO will provide investigators with the information needed to conduct the research properly, including but not limited to all relevant safety information, data safety monitoring board reports, site specific monitoring reports, and interim study analysis;
6. If continuing review of this research is required, the Sponsor/CRO will provide BRANY IRB with a completed [Sponsor Supplement for Multi-Center Research Projects](#)
7. The Sponsor/CRO agrees to work with the designated BRANY IRB contact to outline a mutually agreed upon process for facilitating submissions to BRANY IRB.
8. The research protocol submitted to BRANY IRB for review is the final version, to the best of the Sponsor's/CRO's knowledge.
9. **Any changes to the contacts and/or roles of contact individuals specified in this application form will be reported to BRANY IRB promptly. For individuals for whom authorization/access to study information is no longer required/permitted, the Sponsor/CRO will notify BRANY IRB in writing within 3 business days.**

The designated Sponsor/CRO representative has reviewed the responses provided in this form and confirms that all responses are true and accurate to the best of his/her knowledge.

Printed Name

Signature

Date (mm/dd/yyyy)



IRB STANDARD OPERATING PROCEDURES

Appendix 43 – BRANY IRB Standard Operating Procedures

Request for Waiver of Authorization to Release PHI for Research Purposes

Form with fields: Sponsor Name and Protocol #, BRANY IRB File #, Principal Investigator, PI Phone, Name of person completing this form, Protocol Title, E-mail, Phone, Fax.

INSTRUCTIONS: An investigator may request a waiver of authorization for the release of protected health information (PHI) for research purposes. PHI is defined as individually identifiable health information. The Code of Federal Regulations Title 45, Part 164.512(i) permits the IRB to approve a waiver or alteration, if very specific criteria are met. Your request will be considered on a case-by-case basis by the IRB. To determine if your request meets these criteria, you must answer the following series of questions.

- 1) Describe the PHI that will be accessed. (See attached list of 18 identifiers for reference. Note: The standard is that only the minimum necessary information to conduct the research should be accessed.)
2) With whom will this PHI be disclosed (shared, transferred or otherwise given access to), and why?
3) Could this research be practicably conducted without access to and use of this PHI?
4) Why can't de-identified data or a limited data set be used, instead of asking for a waiver?
5) Could this research be practicably conducted without a waiver of authorization?
6) Does the research present more than minimal risk to the privacy of the subject?
7) Describe the plan to protect the identifiers (see attached list of 18 identifiers for reference) from improper use or disclosure:
a) Who at the site will have access to the PHI obtained?



IRB STANDARD OPERATING PROCEDURES

- b) Will the PHI obtained be kept on paper, such as a screening log?
 Yes No
 - i) If **yes**, will the paper documentation be stored in a **secure, locked area with limited access**?
 Yes No
 - ii) Specify where the secure, locked area is located:

- c) Will the PHI obtained be entered into an **electronic database** at this site?
 Yes No
 - i) If **yes**, will the PHI have **limited access** and **password protection**?
 Yes No
 - ii) Specify who has access to the electronic database:

d) Specify any **additional plans to protect the PHI from improper use/disclosure**:

- 8) What is the plan to **destroy the identifiers at the earliest opportunity consistent with the research**? (e.g., at the end of subject participation, after FDA approval, after specimen processing, after data analysis, etc.)
 - a) If the potential subject enters the study, will the PHI collected become **part of** the subject **source document**?
 Yes No - If **no**, what happens to the PHI? _____
 - b) Do you intend to ask **ineligible subjects** for **permission to retain the PHI** obtained under this waiver for research justification purposes (such as future study contact)?
 Yes No
 - c) If an eligible subject does NOT give permission for their PHI to be retained, will the plan to destroy the identifiers be to (check all that apply):
 - Shred the identifiers
 - Delete the identifiers from the computer database
 - Obliterate/black out the identifiers

Principal Investigator's Assurance (check each statement to attest to the following):

- The PHI will not be reused or disclosed to any other person or entity not listed on this form, except where required by law or for the oversight of this project.
- If at any time I want to reuse this PHI for other purposes or disclose it to other individuals or entities, I will seek approval from the IRB.

Signature of Principal Investigator Date



IRB STANDARD OPERATING PROCEDURES

REFERENCE PAGE

18 IDENTIFIERS:

1. Names
2. All geographic subdivisions smaller than a state, including street address, city, county, precinct, zip code and equivalent geocodes, except for the initial three digits of the zip code if according to the current publicly available information from the bureau of the census the initial three digits of the zip code for all geographic units contains more than 20,000 persons.
3. All elements of dates (except year) for dates directly related to an individual, including birth date, admission date, discharge date, date of death; and for all ages over 89 all elements of dates (including year) indicative of such age, except that such ages and elements may be aggregated into a single category of age 90 or older.
4. Telephone numbers
5. Fax numbers
6. Electronic mail addresses
7. Social security numbers
8. Medical records numbers
9. Health plan beneficiary numbers
10. Account numbers
11. Certificate/License numbers
12. Vehicle identifiers and serial numbers, including license plate numbers
13. Device identifiers and serial numbers
14. Web Universal Resource Locators (URL's)
15. Internet Protocol (IP) address numbers
16. Biometric identifiers, including finger and voice prints
17. Full face photographic images and any comparable images
18. Any other unique identifying number characteristic, or code, except a special re-identification code that cannot be shared with the investigator



IRB STANDARD OPERATING PROCEDURES

Appendix 44 – BRANY IRB Standard Operating Procedures

Data Use Agreement – 45 CFR 164.514 (e)

This Data Use Agreement (the "Agreement") is effective as of _____ (the "Effective Date") by and between _____ ("Covered Entity") and _____, the Limited Data Set recipient ("Recipient").

The Covered Entity is willing to provide Recipient with a Limited Data Set of Protected Health Information ("PHI") as defined by 45 CFR 164.514(e)(2) for research purposes; and

The Recipient warrants that it shall use or disclose the Limited Data Set exclusively for the purposes set forth herein:

- 1. Permitted Uses. Recipient agrees to use and disclose the Limited Data Set solely for the research protocol entitled:

Protocol Title:
Protocol No.: BRANY IRB File No.:

Additionally, Recipient agrees that it and all other "Permitted Users" of the Limited Data Set as defined in section 2, shall not use or further disclose the information other than as permitted by this Agreement or as required by law.

- 2. Permitted Users. In addition to the Recipient, the following individuals or class of individuals are permitted to use/receive the Limited Data Set:

- a.
b.
c.
d.
e.

- 3. Safeguards. Recipient and all Permitted Users shall use appropriate safeguards to prevent use or disclosure of the information other than as provided by this Agreement.

- 4. Reporting. Recipient agrees to report in writing to the Privacy Officer of the Covered Entity any unauthorized use or disclosure of the Limited Data Set that it becomes aware of within three (3) business days.

- 5. Agents and Subcontractors. Recipient ensures that its agents and subcontractors to whom it provides the Limited Data Set shall agree in writing, to adhere to the same restrictions and conditions herein regarding its use and disclosure.



IRB STANDARD OPERATING PROCEDURES

6. **Contact/Identification.** Recipient agrees and shall ensure that all Permitted Users shall agree not to identify the information in the Limited Data Set or contact the individual who is the subject of the Limited Data Set or his/her relatives, employers or household members.
7. **Indemnification.** Recipient shall indemnify, hold harmless and defend Covered Entity from and against any and all claims, losses, liabilities, costs and other expenses resulting from or relating to the acts or omissions of Recipient in connection with the representations, duties and obligations of Recipient under this Agreement.
8. **Term.** This Agreement shall become effective on the Effective Date of the Agreement and shall continue in effect until all obligations of the Parties have been met. The terms and conditions of this Agreement shall survive the expiration or termination of the Agreement.
9. **Termination.** Covered Entity may terminate this Agreement immediately in the event that Recipient is in material breach of its terms.
10. **No Third Party Beneficiaries.** Nothing express or implied in this Agreement is intended or shall be deemed to confer upon any person other than the Covered Entity and Recipient, and their respective successors and assigns, any rights, obligations, remedies or liabilities.

AGREED AND ACCEPTED:

Recipient:

By: (Name) _____

Title: _____

Signature: _____

Date: _____

Covered Entity:

By: (Name) _____

Title: _____

Signature: _____

Date: _____



IRB STANDARD OPERATING PROCEDURES

Appendix 45 – BRANY IRB Standard Operating Procedures

IND Determination Form

Determining Whether a Proposed Activity is Exempt from the Requirement to Submit an IND Application to the FDA	
Reviewer Assigned:	
Date of Meeting:	
BRANY Protocol #:	
PI Name:	

❖ *The BRANY IRB will consider research to be exempt from the requirement for an IND when either category one (I) or two (II) is satisfied:*

CATEGORY (I): When research involves the use of a drug other than the use of a marketed drug in the course of medical practice, the protocol must meet one of the FDA exemptions for the requirement to have an IND:

Exemption 1 (all of the following must be true)

- a) The drug product that is lawfully marketed in the United States.
- b) The investigation is not intended to be reported to FDA as a well-controlled study in support of a new indication for use nor intended to be used to support any other significant change in the labeling for the drug.
- c) If the drug that is undergoing investigation is lawfully marketed as a prescription drug product, the investigation is not intended to support a significant change in the advertising for the product;
- d) The investigation does not involve a route of administration or dosage level or use in a patient population or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product.
- e) The investigation is conducted in compliance with 21 CFR 50 and 21 CFR 56.
- f) The investigation is conducted in compliance with 21CFR312.7.

Exemption 2 (all of the following must be true)

- a) A clinical investigation is for an in vitro diagnostic biological product that involves one or more of the following:
 - b) blood grouping serum
 - c) reagent red blood cells, or
 - d) anti-human globulin,
- e) The diagnostic test is intended to be used in a diagnostic procedure that confirms the diagnosis made by another, medically established, diagnostic product or procedure.
- f) The diagnostic test is shipped in compliance with 21CFR312.160.

Exemption 3

- a) A clinical investigation involving use of a placebo if the investigation does not otherwise require submission of an IND.

OR

CATEGORY (II). The FDA has made a determination of exemption. (The research was already submitted to the FDA who determined in writing that an IND is not required. Such documentation must be included with the Research Application)

This research needs and IND (Satisfies **NONE** of the categories above)

This research does not need an IND (Satisfies **ONE** of the categories above)

X

Primary Reviewer: Printed Name

Signature

Date



IRB STANDARD OPERATING PROCEDURES

Appendix 46 – BRANY IRB Standard Operating Procedures

IDE Determination Form

Determining Whether a Proposed Activity is Exempt from the Requirement to Submit an IDE Application to the FDA

Reviewer Assigned:	
Date of Meeting:	
BRANY Protocol #:	
PI Name:	

BRANY IRB will consider research involving a medical device to not require an IDE if one of the following categories is satisfied:

- Category (1): The device is NOT a Significant Risk Device, and fulfills the requirements for an Abbreviated IDE, meaning all the following criteria MUST apply:**
 - The medical device is NOT intended as an implant that presents a potential for serious risk to the health, safety, or welfare of a subject.
 - The medical device is NOT purported or represented to be for a use in supporting or sustaining human life that presents a potential for serious risk to the health, safety, or welfare of a subject.
 - The medical device is NOT for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health that presents a potential for serious risk to the health, safety, or welfare of a subject.
 - The medical device does NOT otherwise present a potential for serious risk to the health, safety, or welfare of a subject.
 - The medical device is not banned.
 - The sponsor has presented the reviewing IRB with a brief explanation of why the medical device is not a significant risk device, and thereafter obtains and maintains IRB approval of the investigation.
 - Consent of subjects will be obtained as required by 21 CFR 50, and documented, unless documentation is waived.
 - The requirement for informed consent will not be waived.
 - The sponsor will comply with the requirements of §812.46 with respect to monitoring investigations.
 - The sponsor will maintain the records required under §812.140(b) (4) and (5) and makes the reports required under §812.150(b) (1) through (3) and (5) through (10);
 - The sponsor ensures that participating investigators maintain the records required by §812.140(a)(3)(i) and make the reports required under §812.150(a) (1), (2), (5), and (7); and
 - The sponsor will comply with the prohibitions in §812.7 against promotion and other practices.

- Category (2): Exemption (1). All of the following are true:**
 - The medical device was in commercial distribution immediately before May 28, 1976.
 - The FDA did not consider the medical device to be a new drug or an antibiotic drug before May 28, 1976.
 - The medical device is not a transitional device.
 - The medical device is being used or investigated in accordance with the indications in labeling in effect at that time of commercial distribution.

- Category (3): Exemption (2). All of the following are true:**
 - The medical device was introduced into commercial distribution on or after May 28, 1976.
 - The medical device is not a transitional device.
 - The FDA has determined the medical device to be substantially equivalent to a medical device in commercial distribution immediately before May 28, 1976
 - The FDA did not consider the medical device to be a new drug or an antibiotic drug before May 28, 1976.
 - The medical device is being used or investigated in accordance with the indications in the labeling FDA reviewed under subpart E of part 807 in determining substantial equivalence.



IRB STANDARD OPERATING PROCEDURES

- Category (4): Exemption (3).** *All of the following are true:*
- The medical device is a diagnostic device.
 - The sponsor will comply with applicable requirements in §809.10(c).
 - The testing is noninvasive.
 - The testing does not require an invasive sampling procedure that presents significant risk.
 - The testing does not by design or intention introduce energy into a subject.
 - The testing is not used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure.
- Category (5): Exemption (4).** *All of the following are true:*
- A medical device undergoing one of the following:
 - Consumer preference testing
 - Testing of a modification
 - Testing of a combination of two or more medical devices in commercial distribution
 - The testing is not for the purpose of determining safety or effectiveness and does not put subjects at risk.

Exemptions 5 and 6 are related to research in animals. BRANY does not review animal research.

- Category (6): Exemption (7).** *All of the following are true:*
- The medical device is a custom device meaning all of the following are true:
 - The medical device necessarily deviates from devices generally available or from an applicable performance standard or pre-market approval requirement in order to comply with the order of an individual physician or dentist.
 - The medical device is not generally available to, or generally used by, other physicians or dentists.
 - The medical device is not generally available in finished form for purchase or for dispensing upon prescription.
 - The medical device is not offered for commercial distribution through labeling or advertising.
 - The medical device is intended for use by an individual patient named in the order of a physician or dentist
 - One of the following is true:
 - The medical device is to be made in a specific form for that patient.
 - The medical device is intended to meet the special needs of the physician or dentist in the course of professional practice.
 - The medical device is NOT being used to determine safety or effectiveness for commercial distribution.

This research needs an IDE (Satisfies **NONE** of the categories above)

This research does not need an IDE (Satisfies **ONE** of the categories above)

X

Primary Reviewer: Printed Name

Signature

Date



IRB STANDARD OPERATING PROCEDURES

Appendix 47 – BRANY IRB Standard Operating Procedures

Change of Principal Investigator Form

CHANGE OF PRINCIPAL INVESTIGATOR (PI)	
<p>An investigator may not act as the Principal Investigator (PI) of a study without IRB approval. Change of PI requests should be submitted in a timely fashion to assure that the study has the proper oversight at all times. *All active subjects must be promptly notified that the PI has changed. This notification must be documented in the research record.</p>	
Sponsor Name and Protocol #:	BRANY IRB File #:
Title:	
Name of PI being Replaced:	Coordinator:
Please Indicate the Reason for the Change in PI:	

Please indicate the person replacing the current PI on the study below:

New PI name:	Phone:
Mailing Address:	Email:
Medical License Number:	State:
Expiration:	

INSTRUCTIONS: The New Investigator must answer each of the following questions. Any incomplete questions will delay your IRB review!

1. If the above referenced study involves narcotics, please provide the following information:

DEA Registration#: _____ Expiration Date: _____

2. Has the new Principal Investigator ever received an FDA warning letter that has not been previously submitted to BRANY? Yes No

3. Is the new Investigator already approved as a sub-investigator or key personnel?

Yes - If yes, please read below **No** - If no, go to question #4

If the newly proposed Principal Investigator is already approved by BRANY IRB to participate in the research as a sub-investigator or other key study personnel, then the request for change of Principal Investigator can be submitted as follows:

1. Submit the "Change in PI" form
2. Current CV and license
3. If appropriate, submit:
 - a. A revised informed consent document reflecting the change of PI and contact information
 - b. Any relevant subject materials reflecting the change of PI and contact information
 - c. A revised FDA Form 1572

4. If the new PI not currently approved as part of the research, the request for change of PI should include:

1. "Change of PI" form
2. Current CV and license



IRB STANDARD OPERATING PROCEDURES

- 3. Evidence of training in human subject projections for new PI
- 4. "Financial Conflict of Interest in Research Disclosure Form" completed by new PI
- 5. If appropriate, submit:
 - a. A revised informed consent document reflecting the change of PI and contact information.
 - b. A revised FDA Form 1572
 - c. Any relevant subject materials reflecting the change of PI and contact information

5. Is the coordinator remaining the same for this study?

- Yes** **No** – please provide name of new coordinator and attach the following:
- New Coordinator Name: _____
 - Revised Form FDA 1572 (if appropriate)
 - Evidence of training in human subject projections
 - Financial Conflict of Interest in Research Disclosure Form

6. Is there any change to the location where this research will take place?

- Yes** – If yes, please describe and attach a revised 1572 (if applicable) **No**

7. Please indicate the status of this study at your site.

- Study is actively enrolling subjects at this site
- Study is closed to enrollment at this site (subjects are active in the study and/or remain in follow-up)
 - Note: You will still be required to file for continuing approval if the study is not terminated prior to expiration of IRB approval.
- Study is closed at this site and only analysis of the data from this site remains.
 - Note: You will still be required to file for continuing approval if the study is not terminated prior to expiration of IRB approval

8. Please indicate the status of all subjects involved in this clinical research project below:

- a. _____ # subjects enrolled (defined as those who signed consent)
- b. _____ # subjects who were terminated early
- c. _____ # subjects completed
- d. _____ # subjects presently active, or still requiring follow-up (i.e., research continues)

9. The investigator must ensure that adequate staffing and resources are available for each research project conducted so that the rights and welfare of research subjects will be protected. Staff should have sufficient time available to interact with subjects as needed.

- How many of the following does the new PI currently supervise?



IRB STANDARD OPERATING PROCEDURES

- 1. Open Research Studies: _____
- 2. Locations: _____
- 3. Physician Sub-Investigators: _____
- 4. Research Staff: _____
- 5. Approx. # of Active Subjects: _____

- Are there any competing studies?

Yes - If **yes**, describe how enrollment will be determined below? **No**

10. The investigator should ensure a plan is in place to have trained staff available to provide coverage in emergency situations.

- Describe the emergency equipment available at your site:
 - Crash Cart Emergency Medications
 - Access to 911 CPR Trained Staff
 - Other _____

- Are research personnel available to subjects 24 hours a day?

Yes **No** - If no, describe how subjects may contact study personnel:



IRB STANDARD OPERATING PROCEDURES

Principal Investigator Statement of Compliance:
(to be read and signed by the new PI)

The proposed investigation involves the use of human subjects. I am submitting this change in PI form, prepared in accordance with institutional policy for the protection of human subjects participating in the research. I understand the Biomedical Research Alliance of New York's policy concerning research involving human subjects and:

1. I will not engage in any research involving human subjects without obtaining prior IRB approval.
2. **I agree that the IRB approved consent form must be the only consent form used in this study and must be used for every patient prior to enrollment;**
3. I agree to report to the BRANY IRB Committee any unanticipated effects on subjects that become apparent during the course or as a result of experimentation and the actions taken as a result; all serious adverse events must be reported to the IRB within 24 hours of discovery, and a written report must be submitted to the IRB within two (2) business days, unless otherwise agreed to by IRB administration;
4. I agree to cooperate with members of the Committee charged with the continuing review of this project;
5. I agree to obtain prior approval from the Committee before amending or altering the scope of the project or implementing changes in the approved consent form;
6. I agree to maintain documentation of consent forms and progress reports (continuing review applications);
7. I agree that all advertising must be approved by the IRB prior to submission to any agencies and before posting;
8. I agree to submit continuing review applications in a timely fashion;
9. I agree to notify the IRB of study termination and/or any change in the status of the study;
10. I agree to maintain records for a minimum of 3 years after closure, or as specified by the sponsor of the research, whichever is longer;
11. I will ensure that research subjects are given referrals for needed health care during the research or for follow-up after the research.
12. I have received and am familiar with the BRANY IRB's Standard Operating Procedures/Research Manual.

I further understand that:

1. Failure to comply with any of the above, with the BRANY IRB's Standard Operating Procedures, or with any applicable regulations may result in immediate closure of this study, which is reportable to my institution, FDA and/or OHRP.
2. This clinical research project will be subject to routine audits by BRANY, and at the discretion of the BRANY Institutional Official, the results of such audits may be shared with appropriate Department Chairpersons and/or the Institutional Official.

NOTE: Investigators are referred to the BRANY IRB's Standard Operating Procedures for a complete statement of institutional policy and procedures regarding research and human subjects.

I have reviewed the study and applicable documents and accept responsibility to serve as the PI on this study. I understand that as the PI of this study I am responsible for the conduct of the study and for leading the team of individuals coordinating the study

Principal Investigator (Print)	Signature of Principal Investigator	Date
--------------------------------	-------------------------------------	------

If the current PI of the study is available, please sign the statement below:

I am no longer able to serve as PI on the above study. _____ has the
(Name of new Principal Investigator)
appropriate knowledge and credentials to serve as PI on this study and I have provided him/her with all the necessary information and applicable documents for the study.

Signature of Current Principal Investigator _____
Date



IRB STANDARD OPERATING PROCEDURES

Appendix 48 – BRANY IRB Standard Operating Procedures

Conflict of Interest in Research Disclosure Forms (Form 01 & 02)

Name of individual completing this form: _____

Principal Investigator Name: _____

Sponsor Name: _____ **Protocol #/Identifier:** _____

Instructions: All key study personnel (i.e. individuals involved in the design, conduct, or reporting of the research) must disclose financial interests that require disclosure under regulation, including financial interests related to the research as defined below,

Definitions

“Financial Interest Related to the Research” – A financial interest in the sponsor, product, or service being tested, or anything of monetary value from a financially interested company, including but not limited to:

- Officer’s/Director’s fees
- Consulting fees
- Compensation for service on an Advisory Board (including scientific advisory boards)
- Honoraria for Lectures/Teaching;
- Gifts
- Other emoluments or "in kind" compensation such as travel and entertainment from a financially interested company (including those from a third party if the original source is a financially interested company), for any services not directly related to the reasonable costs of conducting the research as specified in the research agreement
- Compensation related to the research whose amount might be affected by the outcome of the research
- Equity interest of any kind and in any amount in a non-publicly or publicly traded Financially Interested Company (e.g., stocks, stock options, convertible notes, other ownership interests), including those for which the value cannot be determined through reference to publicly available prices, those for which the value may be affected by the outcome of the research, and those which represent a 5% or more interest in any one single entity
- Intellectual property related to the proposed research
- License fees, technology transfers, and/or current and future royalties from patents and copyrights
- Board or executive relationships related to the research (regardless of compensation)
- Paid/reimbursed travel, meaning the occurrence and value of any paid/sponsored (i.e., sponsored travel is that which is paid on behalf of the Investigator and not reimbursed to the Investigator so that the exact monetary value may not be readily available), and/or reimbursed travel, whether in connection with an outside position or for consulting, lecturing, or service on a scientific advisory board, data safety monitoring board, steering committee for a clinical trial, executive committee for a clinical trial, or other committee for an outside entity, or for any other purpose including the purpose of the trip, the identity of the sponsor/organizer, the destination and the duration

The term “Financial Interest” does *not* include:

- (i) Salary or other remuneration received from the institution/organization
- (ii) Grant support for salaries from the institution/organization
- (iii) Holdings in mutual funds or 401K/403B retirement funds
- (iv) *De minimus* gifts whose aggregate value does not exceed \$100 per annum; or reasonable business expenses.

“Financially Interested Company” – An entity whose financial interests could reasonably appear to be affected by the conduct or outcome of a research project. The term “entity” means any corporation, limited liability company, partnership, limited partnership, limited liability partnership, joint venture, business trust, or other business organization, and any not-for-profit organization, charity or foundation.

“Related Party” – Spouse, domestic partner, and dependent children, siblings, parents, or equivalents by marriage, or other individuals residing in the household.

“Significant Financial Interest” – A Financial Interest that is over \$5,000, or is less than \$5,000, and also involves a non-financial role in a Financially Interested Company, or is less than \$5,000, and the value cannot be determined through reference to publicly available prices, if the value will be affected by the outcome of the research, or the value represents 5% or more interest in any one single entity, and is determined by the COIC to be related to the research.



IRB STANDARD OPERATING PROCEDURES

Name of individual completing this form (Form 01): _____

Principal Investigator Name: _____

Sponsor Name: _____

Protocol #/Identifier: _____

a) Within the last 12 months, have you or, to the best of your knowledge, has any related party performed any work (not directly related to the costs of conducting research) for a Financially Interested Company? Yes No

b) Within the last 12 months, have you or, to the best of your knowledge, has any related party received compensation (not directly related to the costs of conducting research) from a Financially Interested Company? Please answer Yes for paid/reimbursed travel (see definitions above). Yes No

c) Do you or, to the best of your knowledge, does any related party maintain any board or executive relationship related to the research, regardless of compensation? Yes No

d) Within the next 12 months, have you or, to the best of your knowledge, does any related party anticipate performing any work and/or receiving any compensation (not directly related to the costs of conducting research) from a Financially Interested Company? Please answer Yes for paid/reimbursed travel (see definitions above). Yes No

e) Do you or, to the best of your knowledge, does any related party own stock, stock options or other forms of ownership in a Financially Interested Company? Yes No

f) Do you or, to the best of your knowledge, do any of your related parties have any intellectual property related to the proposed research (e.g., named as an inventor in an issued patent or patent application, license fees, technology transfers, current or future royalties from patents and copyrights)? Yes No

g) Does your department/institution/organization have a financial interest in the agent under investigation or in a company that could benefit from the study findings, or receive significant financial support from such a company? Yes No

h) Do you want to voluntarily disclose anything else? Yes No

For any YES answer to the above, complete and attach FORM 02: Conflict Report Form.

Any change to the above responses must be promptly reported to BRANY IRB.

Any new significant financial interests must be reported within 30 days of acquisition or discovery.

Signature: _____

Date (mm/dd/yyyy): _____



FORM 02: BRANY IRB – CONFLICT REPORT FORM

***Only complete this form if you answered YES on FORM 01.**

Principal Investigator Name: _____
Sponsor Name: _____ **Protocol #/Identifier:** _____

Name of individual/entity for whom interest is being reported: _____

Individual's relationship to study personnel:

- | | |
|----------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <input type="checkbox"/> Principal Investigator | <input type="checkbox"/> Related party (spouse, domestic partner, & dependent children, siblings, parents, or equivalents by marriage, or other individuals residing in the household) -- To whom is the party related? _____ |
| <input type="checkbox"/> Sub-investigator | |
| <input type="checkbox"/> Other study key personnel | <input type="checkbox"/> Other (specify): _____ |

Complete the questions below as they relate to the **study sponsor** or any **Financially Interested Company**. See relevant definitions on Form 01 or in BRANY IRB's policies.

a) Work performed within the last 12 months not directly related to the costs of conducting research:

- | | | | | | | | |
|-------------------------------------------------|-------|-------------------------------------------|-------|-----------------------------------------|-------|-------------------------------------------------|-------|
| <i>Check all that apply:</i> | | <i>Sponsor/entity name:</i> | | <i>Check all that apply:</i> | | <i>Sponsor/entity name:</i> | |
| <input type="checkbox"/> Consultant/advisor | _____ | <input type="checkbox"/> Officer/Director | _____ | <input type="checkbox"/> Fiduciary Role | _____ | <input type="checkbox"/> Other (Specify): _____ | _____ |
| <input type="checkbox"/> Employee | _____ | | | | | | |
| <input type="checkbox"/> Independent contractor | _____ | | | | | | |

b) Compensation received within the last 12 months not directly related to the costs of conducting research (check all that apply):

- | | | |
|---------------------------------------------------------------------|-----------------|----------------------------|
| <input type="checkbox"/> Consulting fees | Value: \$ _____ | Sponsor/entity name: _____ |
| <input type="checkbox"/> Honoraria (lectures, papers, teaching) | Value: \$ _____ | Sponsor/entity name: _____ |
| <input type="checkbox"/> Salaries | Value: \$ _____ | Sponsor/entity name: _____ |
| <input type="checkbox"/> Officer's / Director's fees | Value: \$ _____ | Sponsor/entity name: _____ |
| <input type="checkbox"/> Gifts / gratuities (>\$100) | Value: \$ _____ | Sponsor/entity name: _____ |
| <input type="checkbox"/> Compensation for service on advisory board | Value: \$ _____ | Sponsor/entity name: _____ |
| <input type="checkbox"/> Royalty payments | Value: \$ _____ | Sponsor/entity name: _____ |
| <input type="checkbox"/> Paid/Reimbursed Travel | Value: \$ _____ | Sponsor/entity name: _____ |
| <input type="checkbox"/> Other (specify): _____ | Value: \$ _____ | Sponsor/entity name: _____ |

c) Board or executive relationship related to the research, regardless of compensation:

- | | | | |
|-------------------------------------------------|-----------------|----------------------------|--|
| <i>Check all that apply:</i> | | | |
| <input type="checkbox"/> Board member | Value: \$ _____ | Sponsor/entity name: _____ | |
| <input type="checkbox"/> Director | Value: \$ _____ | Sponsor/entity name: _____ | |
| <input type="checkbox"/> Trustee | Value: \$ _____ | Sponsor/entity name: _____ | |
| <input type="checkbox"/> Other (specify): _____ | Value: \$ _____ | Sponsor/entity name: _____ | |

d) Describe anticipated work and/or receipt of compensation (within the next 12 months) not directly related to the costs of conducting research (specify any anticipated paid/reimbursed travel here):

Sponsor/entity name: _____ In what capacity? _____ Value: \$ _____



e) Stock, stock options or other forms of ownership: Please respond to the following for each entity, *including those for which the value cannot be determined through reference to publicly available prices, those for which the value may be affected by the outcome of the research, and those which represent a 5% or more interest in any one single entity.*

PUBLICLY TRADED			NON PUBLICLY TRADED			
	# shares	Entity name:	Value	% share	Entity name:	
<input type="checkbox"/> Stock	_____	_____	\$ _____	_____	_____	
<input type="checkbox"/> Stock options	_____	_____	\$ _____	_____	_____	
<input type="checkbox"/> Other (specify): _____	_____	_____	\$ _____	_____	_____	

f) Intellectual property Related to the Proposed Research (e.g., named as an inventor in an issued patent or patent application, license fees, technology transfers, current or future royalties from patents and copyrights):
Intellectual property: _____ Explain: _____ Value (if known): \$ _____

g) Department/institution/organization’s financial interest in the agent under investigation or in a company that could benefit from the study findings, or receipt of **significant financial support** from such a company:
Describe department/institution/organization: _____
Describe financial interest or support (include amount/\$ value if applicable): _____

h) Do you want to voluntarily disclose anything else?
 No
 Yes – describe: _____

i) Comments (optional): _____

Any change to the above responses must be promptly reported to BRANY IRB.

ATTESTATION: I certify that I have read the BRANY policy regarding Financial Conflict of Interest in Research (available in the current BRANY IRB Standard Operating Procedures). I hereby attest that with respect to the above clinical research project application that the above information is accurate and complete, **and that I will report any new significant financial interests within 30 days of acquisition or discovery.**

Printed Name _____ Signature _____ Date (mm/dd/yyyy) _____



IRB STANDARD OPERATING PROCEDURES

Appendix 49 – BRANY IRB Standard Operating Procedures

Change of Study Site/Institution Form

CHANGE OF INSTITUTION/STUDY SITE	
<p>The Principal Investigator (PI) must inform the IRB of any changes in the location where the study will be conducted. Change of study site requests must be submitted prior to initiating the research at the new location. *All active subjects must be promptly notified that the study site location has changed. This notification must be documented in the research record.</p>	
Sponsor Name and Protocol #:	BRANY IRB File #:
Title:	
Name of Prior Institution/Study Site	Coordinator:

Details of the new Institution/Study Site for this study:	
Name of New Institution/Study Site:	Phone:
Mailing Address:	Email:
	Fax:

INSTRUCTIONS: The Investigator must answer each of the following questions. Any incomplete questions will delay your IRB review!

1. Indicate the reason for the change of Institution/Study Site:

2. Review your study records and submit revised documents reflecting the change in study site location, as applicable.

Check all that apply:

- Updated CV for the PI reflecting the change of address/contact information is attached
- Revised informed consent document(s) and HIPAA authorization form (if applicable) reflecting the change of address and contact information is attached
- A revised FDA Form 1572, if applicable, is attached
- Relevant subject materials reflecting the change of address/contact information are attached



IRB STANDARD OPERATING PROCEDURES

3. Is the Research Coordinator remaining the same for this study?

- Yes** **No** – please provide name of new coordinator and attach the following:
- New Coordinator Name: _____
 - New Telephone Number: _____
 - New Fax Number: _____
 - Evidence of Training in Human Subject Protections
 - Financial Conflict of Interest in Research Disclosure Form

4. Indicate the status of all subjects involved in this research at the prior study site:

- a. _____ # subjects enrolled (defined as those who signed consent)
- b. _____ # subjects who were terminated early
- c. _____ # subjects completed
- d. _____ # subjects presently active, or still requiring follow-up (i.e., research continues)

5. Will study activity cease at the prior study site?

- Yes**
- No** – please explain: _____

6. Please indicate the status of this study at your new site.

- Study will be actively enrolling subjects at this site
- Study will be closed to enrollment at this site (subjects are active in the study and/or remain in follow-up)
- Note: You will still be required to file for continuing approval if the study is not terminated prior to expiration of IRB approval.
- Study will be closed at this site and only analysis of the data remains.
- Note: You will still be required to file for continuing approval if the study is not terminated prior to expiration of IRB approval

7. Specify whether any subjects who participated at the prior study site will be participating and/or followed at the new site.

- No** – subjects from the prior study site will not be participating/followed at the new study site
- Yes** – _____ # previously enrolled subjects participating/followed at the new study site

8. The investigator must ensure that adequate staffing and resources are available for each research project conducted so that the rights and welfare of research subjects will be protected. Staff should have sufficient time available to interact with subjects as needed.



IRB STANDARD OPERATING PROCEDURES

- How many of the following does the PI currently supervise at the new study site?
 1. Open Research Studies: _____
 2. Locations: _____
 3. Physician Sub-Investigators: _____
 4. Research Staff: _____
 5. Approx. # of Active Subjects: _____

- Are there any competing studies at the new study site?

No **Yes** - If **yes**, describe how enrollment will be determined below:

9. The investigator should ensure a plan is in place to have trained staff available to provide coverage in emergency situations.

- Describe the emergency equipment available at your new site:

<input type="checkbox"/> Crash Cart	<input type="checkbox"/> Emergency Medications
<input type="checkbox"/> Access to 911	<input type="checkbox"/> CPR Trained Staff
<input type="checkbox"/> Other _____	

- Are research personnel available to subjects 24 hours a day?

Yes **No** - If no, describe how subjects may contact study personnel:

Other considerations when changing study site location

- **Does this research include subjects that require consent by a legally authorized representative (LAR)?** If yes, contact BRANY IRB to ensure new location allows this type of consent.
- If your study included a **HIPAA waiver for recruitment, or a Data Use Agreement**, these may need to be amended to reflect the new study site location.
- **Your new study site location may have new requirements for conducting research**, such as submission to another institutional committee (e.g. radiation safety committee, institutional biosafety committee, GCRC, etc...). You must make sure you obtain any required additional approvals prior to initiating research activity at the new site.

Principal Investigator Signature:

Principal Investigator (Print) Signature of Principal Investigator Date



IRB STANDARD OPERATING PROCEDURES

Appendix 50 – BRANY IRB Standard Operating Procedures

Application for Transfer of IRB Oversight to BRANY IRB

PRINCIPAL INVESTIGATOR			
BRANY PROTOCOL #		Sponsor and Protocol #	
TITLE OF PROTOCOL:			
TO BE REVIEWED AT BRANY THE IRB MEETING OF:			

INSTRUCTIONS: Please complete all of the items in this form in order for your application to be considered.

1. (a) What is the status of this study?

- Actively enrolling
- Closed for subject entry but open for follow-up or for the collection of private identifiable information
- Open for data analysis only (i.e. no subject activity)

(b) When does the current IRB approval period expire? _

2. Please indicate the status of all subjects involved in this clinical research project below:

- a. _____ # subjects **enrolled (defined as those who signed consent)** →→→ **a. = b. + c. + d.**
- b. _____ # subjects who were **terminated early** →→→ **b. = i. + ii. + iii. + iv.**
 - i. _____ # **screen failures (of those that signed consent)**
 - ii. _____ # **withdrawn voluntarily**
 - iii. _____ # **withdrawn by the Principal Investigator**
 - iv. _____ # **lost to follow-up**
- c. _____ # subjects **completed**
- d. _____ # subjects **presently active, or still requiring follow-up** (i.e., research continues)

Describe **reason for ALL withdrawals:**

3. Please indicate the following gender classification and race/ethnic classification for all subjects entered into this clinical research project:

- Please provide the **gender classification** of all subjects entered into the study - i.e., # _____ female & # _____ male.
(NOTE: This question does not apply if the study is gender-specific)
- Please provide the **race/ethnic classification** of all subjects entered into the study:

_____ # AFRICAN-AMERICAN	_____ # MIDDLE EASTERN
_____ # CAUCASIAN	_____ # HISPANIC
_____ # PACIFIC ISLANDER	_____ # ASIAN
_____ # NATIVE AMERICAN/FIRST NATIONS	_____ # OTHER (SPECIFY): _____

4. SUBJECT EXPERIENCES AT YOUR SITE

- a. Have any subjects at your site benefited from participation in this study? **NO** **YES**



IRB STANDARD OPERATING PROCEDURES

If YES, describe benefit: _____

- b. Have there been any complaints from subjects at your site? [] NO [] YES
If YES, describe complaint and how it was resolved: _____

- c. ADVERSE EVENTS - Please provide a summary of adverse events since the last IRB review. Include description of the adverse event, the relationship to study agent, and whether the event was expected or unexpected. Attach additional sheets as necessary.

[Empty box for adverse events summary]

- d. SERIOUS ADVERSE EVENTS
At your site, have there been any Serious Adverse Events (SAEs)? [] NO [] YES
*Note: SAEs are defined as fatal or life threatening, permanently disabling or requiring hospitalization or prolongation of inpatient hospitalization or any other event the investigator considers significant

- If YES, have they been reported to the Sponsor? [] YES [] NO - If NO, report immediately.
• Were any events related to the drug/device?
[] YES - if related to drug/device, please describe event(s) below and explain relationship:
[] NO - the events were not related to the drug/device.

- 5. At your site, have there been any unanticipated problems involving risks to subjects or others? (e.g., pregnancy, loss of a laptop containing confidential study information, loss of study drug) [] YES [] NO

If YES, describe (attach separate sheet if necessary): _____

- 6. If this is a multi-center trial for which you are the lead PI, please attach any relevant multi-center trial reports.

- 7. Based on study results thus far, please provide a current risk-potential benefit assessment (attach a separate sheet as necessary):

[Empty box for risk-potential benefit assessment]

8. Site Performance Evaluation

- [] Attach the most recent monitoring report.

- 9. Please attach a copy of the two (2) most recently signed informed consent document(s) for this project. If no subjects have been enrolled, please attach a copy of the most recently approved consent form. []



IRB STANDARD OPERATING PROCEDURES

Please indicate below which items are being submitted for re-review

- Protocol (Version/Date: _____)
- Amendment(s) (Version/Date: _____)
- Informed Consent (1 hard copy and 1 electronic copy)
- Assent Form (1 hard copy and 1 electronic copy)
- Recruitment/Advertisement materials for the study (How Many? _____)
- Principal Investigator's Curriculum Vitae (CV), signed and dated
- Principal Investigator's Medical License and DEA certificate
- Research Application - signed & dated (also available for download at www.branyirb.com)
 - Note:** As per Question #22 of the Research Application, you are required to submit correspondence from the prior IRB of record, please include all IRB letters and any continuing review reports.
- Financial Conflict of Interest Disclosure Form for the principal investigator(s) & all study personnel
- Evidence of Training in Human Subject Protections for principal investigator(s) & anyone else authorized to obtain consent
- Other documents: (Specify) _____

FOR STUDIES OF DRUGS OR BIOLOGICS

- Investigator's Brochure
- Drug inserts or other documents relating to the study agent
- FDA Form 1572 with the BRANY IRB listed in Box 5, signed & dated, OR, if an IND has not been filed, then an explanation as to why

FOR STUDIES OF DEVICES

- Signed Investigator Agreement for protocols with an IDE (only for investigator initiated studies)
- One of the following:
 - FDA Letter granting the investigational device exemption (IDE); or
 - Letter from Sponsor stating that the study is a non-significant risk device study; or
 - Letter Explaining Why the Investigation Is Exempt from the IDE requirements under 21 CFR 812.2(c) or otherwise exempt

OTHER INSTITUTIONAL COMMITTEE REVIEWS, if applicable

- Radiation Safety Committee Approval
- Cancer Care Committee Approval
- Institutional Biosafety Committee (IBC) Approval (for recombinant DNA/gene transfer protocols only)
- Other: (specify) _____

WAIVERS

- HIPAA Waiver (**only** if your study requires a waiver of the requirement to obtain HIPAA authorization for screening/recruitment or enrollment)
- Data Use Agreement (**only** if you plan to share a limited data set of PHI without obtaining HIPAA authorization → must be accompanied by a HIPAA Waiver request)
- Consent Waiver/Alteration (**only** if your research requires a waiver or alteration of the requirement to obtain informed consent for screening/recruitment or enrollment)

PRINCIPAL INVESTIGATOR'S SIGNATURE:

Principal Investigator's Name

Principal Investigator's Signature

Date



IRB STANDARD OPERATING PROCEDURES

Appendix 51 – BRANY IRB Standard Operating Procedures

IRB SOP Document Control Checklist

Table of Contents

- Table of Contents is evaluated to ensure:
 - Section numbers are in correct chronological order and names are accurate
 - Page numbers accurately correspond to SOP content

Observations to be addressed:

Section Headings

- All section headings searched in SOP document and checked to ensure:
 - Section heading is appropriately numbered (per pre-determined convention) and the chronology is correct throughout the document
 - Section heading matches listing in table of contents

Observations to be addressed:

Check if none.

Regulatory References

- All regulatory references searched in SOP document and checked to ensure:
 - Regulation cited applies to SOP content
 - Regulation cited is correctly named

Observations to be addressed:

Check if none.

Appendix References

- All appendix references searched in SOP document and checked to ensure:
 - Appendix # matches number in appendix table of contents
 - Appendix document title in SOP text matches actual appendix document
 - Appendix document title name is correct in appendix table of contents

Observations to be addressed:

Check if none.

QA Review Comments/Recommendations to the SOP

Author:

Further Revisions Needed

No Further Revisions Needed

Review by: Print name:

Date of Review:

Sign name:

If any revisions are needed:

Response from SOP Author:

All observations addressed

Final Print name:

Date of Review:

Review by: Sign name:



IRB STANDARD OPERATING PROCEDURES

Appendix 52 – BRANY IRB Standard Operating Procedures

Additional Research Site Location(s) Form

FORM 04: Additional Research Site Location (location #)
(Only complete for additional sites not already described previously in this application, and only include sites at which subjects will be seen.)

1) Why are you adding this site location for this study?

2) Institution/Organization Description
a) Institution/Organization Name:
b) Phone: () -
c) Emergency (24 hour) phone: () -
d) Physical Address (must match box 3 of submitted Form FDA 1572, if applicable):
Address:
City: State: ZIP/Postal Code:
e) Check here if you have supplied a revised Form FDA 1572
f) Should the phone and address in b) - d) above appear on the informed consent?
g) Type of Facility
Medical office Hospital University
Psychiatric institution Nursing home Laboratory
Research Clinic Dialysis center Surgery Center
Other (specify):

3) Responsible Institutional Individual
Provide information about the appropriate institutional/organizational liaison in charge of research in order to facilitate reporting in the event of unanticipated problems involving risks to subjects or others, serious and/or continuing non-compliance, or other reportable issues (e.g., research director, institutional official, vice president for research, CEO)
Name: Title:
Phone: () - Email:
Address: Fax:
City: State: ZIP/Postal Code:

4) BRANY IRB Authorization Agreement
BRANY IRB requires a written IRB Authorization Agreement from the site before any submissions can be reviewed. Failure to provide an indemnification agreement may results in a delay of IRB review.
Complete the IRB Authorization Agreement and append to your application. This must be signed by a signatory official from your site (individual with authority to sign contracts).
Check here if agreement for location #1 covers this location.
Check here if you already have filed an IRB Authorization Agreement with BRANY IRB.
Date IRB Authorization was signed by your organization:

5) Additional Site-Required Reviews for BRANY IRB-Approved Research



IRB STANDARD OPERATING PROCEDURES

a) Does this investigator have an obligation to submit this study to another committee, or to obtain other organizational/institutional approval for conducting this study at this research site location? (Examples: radiation safety, protocol review committee, GCRC, CTSA, pharmacy, hospital/department approval, institution approval, etc.) Yes No

b) If **YES** – It is the Principal Investigator’s obligation to ensure other required approvals are in place before initiating BRANY IRB-approved research. PI Acknowledges

5.1) Does this investigator have an obligation to submit this study to another IRB, or to obtain other organizational/institutional approval for conducting this study at this research site location? Yes No

a) If **YES** – Provide documentation from the other IRB authorizing review by BRANY IRB. Contact BRANY IRB for further instruction: 516-470-6900 or rhart@brany.com. PI Acknowledges

7) Study Procedures

a) Is this location appropriate for all study related procedures, including storage/administration of the study product (if applicable)? Yes No

If **NO** – explain why and indicate the study related procedures that will NOT be done at this site location: _____

6) Emergency Situations

The investigator should ensure a plan is in place to have trained staff available to provide coverage in emergency situations.

a) Describe the emergency equipment available at this site (check all that apply):

Crash cart Emergency medications CPR trained staff
 Access to 911 Other (specify): _____ N/A – why? _____

b) Are research personnel available to subjects 24 hours a day? Yes No

If **YES** – what is the phone number at which research personnel are available 24 hours a day? (____) - _____

If **NO** – explain how subjects can contact research personnel: _____

7) Additional Resources

Describe any additional resources available to subjects:

Counseling services Certified medical interpreters Other: _____

8) Research Staff Information for this Site Location

a) Will the primary study coordinator for this site location be the same as for the original site location? Yes No

If **NO**, provide **primary study coordinator contact information for this site location** below:

Name: _____ **Email:** _____
Phone: (____) - _____ **Fax:** _____
Address: _____
City: _____ **State:** _____ **ZIP/Postal Code:** _____

b) Key Personnel Information for this Site Location

List all **key study personnel for this site location, indicate those that are *NEW*, and specify any staff who will obtain consent**. Staff should be sufficiently trained to administer the research protocol without impacting subject safety or data integrity. “Key personnel” are defined as individuals who are responsible for the design and conduct of a study.

Name	Role	Will obtain consent?		New to this study?	
_____	_____	<input type="checkbox"/> Yes	<input type="checkbox"/> No	<input type="checkbox"/> Yes	<input type="checkbox"/> No
_____	_____	<input type="checkbox"/> Yes	<input type="checkbox"/> No	<input type="checkbox"/> Yes	<input type="checkbox"/> No
_____	_____	<input type="checkbox"/> Yes	<input type="checkbox"/> No	<input type="checkbox"/> Yes	<input type="checkbox"/> No
_____	_____	<input type="checkbox"/> Yes	<input type="checkbox"/> No	<input type="checkbox"/> Yes	<input type="checkbox"/> No
_____	_____	<input type="checkbox"/> Yes	<input type="checkbox"/> No	<input type="checkbox"/> Yes	<input type="checkbox"/> No



IRB STANDARD OPERATING PROCEDURES

c) Required Attachments for each *NEW* Research Staff Person

- Conflict Disclosure Statement (BRANY IRB's form for declaring conflicts of interest, not the sponsor's financial disclosure form.)
 - If a conflict is reported on the Conflict Disclosure Statement, you must provide a completed Conflict Report Form.
- Evidence of training in human subject protections (see instructions page for more information)

9) Changes to the Protocol or Consent

- a) Describe any needed changes to the protocol or consent form as a result of adding this site location (e.g., add address or phone #, add site-specific procedure instructions, add site-specific research coordinator contact information, etc.): _____ Not applicable

10) Additional Site Locations

For each of your additional research locations please complete another Additional Research Location Form. Not applicable

PI Signature: _____

Date (mm/dd/yyyy) _____



IRB STANDARD OPERATING PROCEDURES

Appendix 53 – BRANY IRB Standard Operating Procedures

IRB Member Evaluation Questionnaire

BRANY IRB policy and our accreditation with AAHRPP require our Human Research Protection Program (“HRPP”) to have procedures for the ongoing review and maintenance of committee membership, including development of procedures for evaluation of IRB members.

To this end, the BRANY IRB Member Task Force was established. The IRB Member Task Force has been charged with addressing concerns and complaints about IRB members, reviewing IRB member performance (e.g., contributions during IRB meetings; ability to perform a substantive and meaningful review; accuracy and completeness of required documentation), and developing and administering an evaluation of IRB members.

The survey you’re about to complete is a self evaluation. Please think about your performance as an IRB member. The question text represents the standard BRANY IRB expects its members to meet, and below each question, we ask you to rate yourself with relation to the particular standard.

Your completed survey will be sent to both chairs for review and comment. The chairs or BRANY IRB administrative staff will contact you with the results, which we hope to make available at the beginning of the second quarter. Please contact the BRANY IRB team with any questions.

1. Please print your name: _____

Knowledge and Abilities

2. Maintains adequate knowledge of BRANY IRB SOPs, FDA and OHRP Regulations and Guidelines, and Ethical Principles

- Exceeds Standard
- Meets Standard
- Needs Improvement
- Standard Unmet

3. IRB Manager- Maintains adequate ability to navigate system to find study records, assigned reviews, and initiate correct xForm checklists

- Exceeds Standard
- Meets Standard
- Needs Improvement
- Standard Unmet

Education

4. Participates in continuing education discussions and meetings

- Exceeds Standard
- Meets Standard
- Needs Improvement
- Standard Unmet



IRB STANDARD OPERATING PROCEDURES

5. Attends training classes provided by IRB staff (e.g., IRBManager tutorial)

- Exceeds Standard
- Meets Standard
- Needs Improvement
- Standard Unmet

6. Continuing Education Needs: About which topic do you feel you need additional education (e.g., review

of particular BRANY IRB SOPs or regulations)?

Preparedness

7. Provides complete and accurate reviews of assigned items

- Exceeds Standard
- Meets Standard
- Needs Improvement
- Standard Unmet

8. Contacts staff within 24 hours of receiving the agenda when he/she has a conflict with any item on the agenda

- Exceeds Standard
- Meets Standard
- Needs Improvement
- Standard Unmet

9. Contacts site/sponsor/IRB staff more than 24 hours prior to meeting to address concerns/questions

- Exceeds Standard
- Meets Standard
- Needs Improvement
- Standard Unmet

10. Provides input based on his/her experience during convened meetings

- Exceeds Standard
- Meets Standard
- Needs Improvement
- Standard Unmet

11. Completes checklist prior to the meeting (NOTE: The checklist is intended to serve as a tool to prompt reviewers to ensure they are considering the regulatory criteria for approval. Thus, this question presupposes that you *fill-in* the checklist prior to the meeting to guide you in presenting your review, though we recognize you may not actually *submit* the checklist prior to the meeting in the event you want to change responses as a result of discussion during the meeting.)

- Exceeds Standard
- Meets Standard
- Needs Improvement
- Standard Unmet



IRB STANDARD OPERATING PROCEDURES

12. Submits checklists no later than 24 hours after the meeting

- Exceeds Standard
- Meets Standard
- Needs Improvement
- Standard Unmet

Attendance

13. Has flexibility in attending meetings and has minimal changes in schedule once agreeing to a meeting

- Exceeds Standard
- Meets Standard
- Needs Improvement
- Standard Unmet

Additional Comments

14. Please provide any additional comments here.

Thank you! Your completed survey will be sent to both chairs for review and comment. The chairs or BRANY IRB administrative staff will contact you with the results, which we hope to make available at the beginning of the second quarter. Please contact the BRANY IRB team with any questions.



Appendix 54 – BRANY IRB Standard Operating Procedures

Minor Protocol Deviation Log

Minor Protocol Deviation Log

INSTRUCTIONS: Use this form to record minor protocol deviations, which are defined as any temporary alteration/modification to the IRB-approved protocol that do not affect subject safety, rights, welfare, or data integrity. This may include administrative and minor departures from the IRB approved protocol that do not affect the scientific soundness of the research plan.

Submit this form by attaching it to the Application for Continuing Approval xForm in *IRBManager*. Append supporting documentation as needed.

Sites should track deviations, evaluate any trends and implement corrective and preventive actions (CAPAs) as appropriate. A single CAPA can be used to address multiple deviations. Append appropriate CAPAs as needed.

PI Name:				BRANY IRB File #			
Title:				Sponsor Name and Protocol #			
Date of Deviation	Patient ID (No PHI please)	Associated Visit (e.g., Baseline, V1, W1)	Deviation Type	Description of Deviation	Action Taken	If Applicable, Sponsor Notification Date (required for IND/IDE studies)	
			Select one				
			Select one				
			Select one				
			Select one				
			Select one				
			Select one				
			Select one				



IRB STANDARD OPERATING PROCEDURES

Appendix 55-199 – BRANY IRB Standard Operating Procedures

Reserved



IRB STANDARD OPERATING PROCEDURES

Appendix 200 – BRANY IRB Standard Operating Procedures

Jun 2011 IRB SOP Change Summary

Revision Summary and Rationale: The BRANY IRB Standard Operating Procedures (“SOPs”) have been revised primarily to enact changes based on observations identified during a pharmaceutical sponsor’s central IRB vendor qualification audit.

Major changes include:

- Addition of an SOP [No. REC01] describing BRANY IRB’s use of the *IRBManager* electronic records system and compliance with 21 CFR Part 11, which establishes the requirements for electronic records and electronic signatures to be trustworthy, reliable, and essentially equivalent to paper records and handwritten signatures.
- Addition of a Records Room SOP [No. REC02], which describes a new check-in/check-out procedure and method of electronically tracking records retrieved by staff.
- The “section” symbol (“§”) was removed from regulatory references throughout the document, except where appropriate. All regulatory references were revised for consistent formatting.
- References to the terms “IRB Record” or “Project file” were clarified and made consistent throughout the document.
- Additional changes have been made in response to internal assessments by the IRB Director and BRANY’s QA Division of IRB procedures and regulatory guidance/revisions.
- Grammatical modifications were made throughout the entire document to improve/enhance readability, and to clarify statements as needed.
- BRANY IRB’s two-part Research Application for central IRB clients has been added to the appendix of forms.

Specific SOP Revisions

1. Section I.2.a.1., “Quality Assurance,” was reworded to indicate that BRANY QA Division will maintain its own SOPs separately, and that the IRB SOP describes BRANY IRB procedures relative to processing of QA reports.
2. Section I.2.a.2., “Vetting Investigators,” was revised to accurately refer to Appendix 35 as the “Investigator Database Information Form.”
3. Section I.2.a.4., “Finance,” was revised to remove the last paragraph, which referred to procedures undertaken by the separate BRANY Finance department that functions independently from the IRB department.
4. Section I.2.a.5., “BRANY’s Institute for Research Education,” was revised to add a description of the Institute’s education modules that are mandatory for all BRANY staff.



IRB STANDARD OPERATING PROCEDURES

5. Section II.2.b., “BRANY IRB Definition of Human Subject Research,” reference to Appendix 9 was revised to accurately refer to the form name as “Checklist – Human Research.”
6. Section II.3.i., “Initial Training, Continuing Education, and Professional Development of IRB Members,” has been revised to include applicable FDA regulations that IRB members receive as part of new member training.
7. Section II.4.d., “Initial Training, Continuing Education, and Professional Development of IRB Staff ,” has been revised to include applicable FDA regulations that IRB staff receive as part of new member training.
8. Section II.5.a., “Record Retention”, was revised (see underlined sections in excerpt below) to discern on-site vs. off-site record retention timelines, to clarify the total retention period, and to specify that document destruction occurs only after consultation with the appropriate party.

“In accordance with federal regulations (45 CFR 46.115(b), and 21 CFR 56.115) the IRB will retain research records for at least 3 years after the completion, early termination or cancellation of the research with which the research record is associated regardless of whether or not subjects were enrolled in the project. Records for studies with active BRANY IRB approval remain in the records room on site at the BRANY IRB facility. Records will be maintained on site 6 months after the study has been reported closed to BRANY IRB, and will then be sent to an external storage facility. IRB Staff will follow instructions outlined on the Document Retention Schedule (see Appendix 33). All documents will be prepared for storage as directed by the storage facility and in accordance with the Document Retention Schedule. Internal Logs will be maintained with tracking numbers for easy access to files. After the retention period ends, the records are destroyed only after consultation with the study sponsor (or sponsor’s representative) or the PI for non-sponsored research.”

9. Section II.5.b., “Access to IRB Records,” has been revised to indicate the revised procedure for accessing IRB records. The revised policy is excerpted below:

“II.5.b. Access to IRB Records:

To protect the confidentiality of subject information all IRB records will be kept secure in a locked records room. Secure electronic records shall be maintained in accordance with BRANY’s policies for *IRBManager* access and 21 CFR Part 11. Access to IRB records is controlled by a designated IRB staff member. IRB records will only be released to the Chairpersons and members of the IRB, the administrative staff of the IRB, approved research site personnel, officials of Federal and state regulatory agencies, including OHRP, FDA, and ORCA, and individuals who are authorized to audit the research records on behalf of BRANY or the sponsor.”

10. Section II.5.c., “IRB Records,” was updated to reflect that COI forms collected are no longer kept in a separate location. They are kept with the IRB record (binder) in the locked records room.



IRB STANDARD OPERATING PROCEDURES

11. Section II.5.e., “Education and Training Records:” was revised to specify the records required to be on file for IRB members and IRB staff, and is excerpted below:

“II.5.e. Education and Training Records:

The IRB Director, with assistance from the BRANY Human Resources Department, will maintain an accurate record of all IRB staff, IRB members, investigators, coordinators and others who are considered to be “key personnel” who have fulfilled the human subject protection initial and continuing training requirements.

IRB Staff training records will be maintained in accordance with BRANY’s Human Resources employee training policy, and shall include:

- New employee training schedule, checklist and evaluation form
- Documentation of completed human subject protection training
- Documentation of applicable continuing education activities
- Documentation of applicable certifications (e.g. CIP, CIM)

IRB member training records will be maintained in the member’s file, and shall include:

- Documentation of completed human subject protection training
- Documentation of completion of OHRP assurance module
- Membership acceptance statement, which documents training on BRANY IRB’s SOPs and applicable regulations and guidance (for IRB members added to the committee in 2004 or later)

Documentation of training for investigators, coordinators and “key personnel” will be maintained in each research project’s file, and shall include:

- Documentation of completed human subject protection training in accordance with section II.6.a. of this policy”

12. Section VI.1.b. “Reporting of Financial Interests” was revised to clarify COI disclosure form processing and IRB review of COI committee determinations. Specific revisions are as follows (see text that is underlined or stricken):

In the event there is no Conflict of Interest Committee at the Investigator’s facility, the Financial Interest will be initially screened by the Director of the IRB. If the Financial Interest is less than \$10,000 and the Investigator has no other non-financial roles, the Director will inform the IRB and Investigator that the Conflict of Interest Committee has determined that a significant conflict does not exist, that a disclosure statement must be added to the informed consent document (when the study includes ~~a consent document~~s), and that the Committee has recommended no further action for the reported item. The Chairperson of the Conflict of Interest Committee will be notified of this ~~situation before the study begins~~ determination. This recommendation and the resulting revised consent(s) shall be provided to the IRB for review.



IRB STANDARD OPERATING PROCEDURES

If:

- the Financial Interest is over \$10,000, or,
- the Financial Interest is less than \$10,000, and also involves a non-financial role in the financially interested company, or,
- the Financial Interest is less than \$10,000, and the value cannot be determined through reference to publicly available prices, if the value will be affected by the outcome of the research, or the value represents 5% or more interest in any one single entity, then,

it will be reviewed by the BRANY Conflict of Interest Committee to determine whether a conflict exists, and if so, how the conflict can be eliminated, reduced, or otherwise managed.

If the Conflict of Interest Committee determines that no significant conflict exists on no management plan is required, the resulting determination shall be reported to the IRB at a subsequent meeting.

If it is determined that a conflict exists, and the resulting recommendation is to add a disclosure statement to the informed consent(s) (when the study includes consent documents), this recommendation and the resulting revised consent(s) shall be provided to the IRB for review.

If it is determined that a conflict exists, and the resulting recommendation is to require a management plan other than or in addition to adding a disclosure statement to the informed consent(s) (when the study includes consent documents), such recommendation will be provided presented to the IRB for at the meeting at which the research is to be reviewed, or at the next convened meetingreview.

If the reviewed disclosure is from the Principal Investigator, the COIC's determination must be reviewed by the IRB before a final IRB approval can be granted. If the disclosure is from study personnel other than the Principal Investigator, BRANY IRB may grant approval for the research prior to receiving the outcome of the COIC review of the study personnel disclosure, only if the IRB's approval specifies that such personnel are not approved to participate in the research and that the personnel's participation will be reconsidered when the determination from the COIC is available for IRB review.

Wherever possible, conflicts...

...The IRB has final authority to decide whether the interest and its management, if any, allows the research to be approved."

13. Section VI.1.h. "Organization Officials" was revised to add the following statement: "Individuals responsible for the IRB's business development are prohibited from serving as members on the IRB and from carrying out day-to-day operations of the review process."



IRB STANDARD OPERATING PROCEDURES

Section VI.1.I. "Providing for Protection of Privacy of Individual's Financial Information Except as Needed to Manage Conflict of Interest:" was revised to clarify that IRB members will disclose potential conflicts of interest using the IRB's disclosure form upon being accepted onto the IRB, rather than on an annual basis.

IRB members are reminded at each meeting to verify that no conflict exists concerning the protocols being reviewed. If a member has a conflict or a potential conflict, the member shall disclose it prior to discussion of the protocol in question. If the IRB agrees that a conflict exists, or if there is any disagreement or question as to whether a conflict exists, the member shall be excused from the meeting for voting on the protocol in question. Any new conflicts reported are noted by the IRB Director in order to aid in protocol review assignments and to ensure proper voting procedures, since no member may be present for voting on a protocol in which the member has a Financial Interest. Therefore annual disclosures are not required.

This section was also updated to reflect that Conflict of Interest forms become part of the IRB's records for the research in question, and that access to IRB records shall be controlled in keeping with Section II.5.b of the IRB policy.



IRB STANDARD OPERATING PROCEDURES

Appendix 201 – BRANY IRB Standard Operating Procedures

Dec 2011 IRB SOP Change Summary

Revision Summary and Rationale: The BRANY IRB Standard Operating Procedures (“SOPs”) have been revised primarily to reflect procedural changes related to operational efficiencies (e.g., electronic document flow), update sections relative to new/updated regulations, and address procedural changes for central IRB processing.

Major changes include:

- Required elements of informed consent were revised to include the new requirement under 21 CFR Part 50.25(c) for applicable consents to include specific language relating to a trial’s registration on www.clinicaltrials.gov.
- Procedures and definitions related to reporting of serious adverse events were revised to reflect the updated definitions and requirements at 21 CFR Part 312.32, which changed adverse event terminology (e.g., adverse reaction = adverse event caused by the drug, suspected adverse reaction = adverse event for which there is evidence to suggest a causal relationship between the drug and the adverse event). Adverse reactions that also represent study endpoints will now fall outside of the reporting requirement.
- The conflict of interest section was revised to reflect the new guidelines provided by PHS, reducing the threshold for financial holdings constituting a conflict from \$10,000 to \$5,000, and including changes to definitions.
- Policy revised to reflect circumstances in which use of short form consents is permitted, in accordance with FDA guidance.
- Clarification of items categorized as qualifying “Administrative Review”
- Additional changes have been made in response to internal assessments of IRB procedures and regulatory guidance/revisions by the IRB Director and BRANY’s QA Division.
- Grammatical modifications were made throughout the entire document to improve/enhance readability, and to clarify statements as needed.
- All application/submission forms that have been updated since the last SOP revision were updated in the SOP Appendix.

Specific SOP Revisions

- 14.** Section IV.1.j., “Additional Elements of Informed Consent“ was updated to include the requirement to add the following statement to the informed consent, when applicable:

“A description of this clinical trial will be available on <http://www.ClinicalTrials.gov>, as required by U.S. Law. This Web site will not include information that can



IRB STANDARD OPERATING PROCEDURES

identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.”

1. This will apply to *applicable clinical trials*, as defined in 42 U.S.C. 282(j)(1)(A), such as:

- Trials of Drugs and Biologics: controlled clinical investigations, other than Phase 1 investigations, of a product subject to FDA regulation (not generics)
- Trials of Devices: Controlled trials with health outcomes of devices subject to FDA regulation, other than small feasibility studies, and pediatric postmarket surveillance

15. Section IV.3.d., “When Investigator Encounters a Non-English Speaking Subject Whose Primary Language Was Not Anticipated (e.g., rarely-encountered foreign languages):” was revised to add the following text related to use of short form consents (added as third paragraph):

“If investigators enroll subjects without a BRANY IRB approved written translation, a “short form” written consent document, in a language the subject understands, should be used to document that the elements of informed consent required by 21 CFR 50.25 were presented orally to the subject or the subject’s legally authorized representative. When this method is used, there shall be a witness to the oral presentation. Also, the IRB shall approve a written summary of what is to be said to the subject or the representative. Only the short form itself is to be signed by the subject or the representative. However, the witness shall sign both the short form and a copy of the summary, and the person actually obtaining the consent shall sign a copy of the summary. A copy of the summary shall be given to the subject or the representative in addition to a copy of the short form.”

16. Section III.1.h. “Administrative Review”, was revised to clarify types of submissions qualifying for administrative review.

“To be conducted by the Director of the IRB or the designated IRB staff member ONLY for the following:

- (8) Typographical and grammatical error correction
- (9) Administrative and formatting changes such as contact names/numbers and study/sponsor identifier information
- (10) Addition/substitution of investigators, sub investigators, and study personnel (provided that there is no increase in risk). This will include acknowledgement of receipt of any applicable required forms (e.g., evidence of training in human subject protections, financial conflict of interest disclosure forms).
- (11) When applicable, the addition/removal of witness signature lines to satisfy individual Institutional policy requirements
- (12) Addition of Lay language from the section of these standard operating procedures entitled “Glossary of Lay Terms for Use in Preparing Informed Consent Documents” (see Appendix 5)
- (13) Changes in advertisement format when content (including text and images) has been previously approved (e.g., using approved internet ad text as a flyer), or verification of final format of advertisement after conditional approval”



IRB STANDARD OPERATING PROCEDURES

17. Section VI.1.b. "Reporting of Financial Interests" was revised to clarify COI disclosure form processing and IRB review of COI committee determinations. Specific revisions are as follows (see text that is underlined or stricken):

In the event there is no Conflict of Interest Committee at the Investigator's facility, the Financial Interest will be initially screened by the Director of the IRB. If the Financial Interest is less than ~~\$10,000~~ \$5,000 and the Investigator has no other non-financial roles, the Director will inform the IRB and Investigator that the Conflict of Interest Committee has determined that a significant conflict does not exist, that a disclosure statement must be added to the informed consent document (when the study includes ~~a consent document~~s), and that the Committee has recommended no further action for the reported item. The Chairperson of the Conflict of Interest Committee will be notified of this determination. This recommendation and the resulting revised consent(s) shall be provided to the IRB for review.

If:

- the Financial Interest is over ~~\$10,000~~ \$5,000, or,
- the Financial Interest is less than ~~\$10,000~~ \$5,000, and also involves a non-financial role in the financially interested company, or,
- the Financial Interest is less than ~~\$10,000~~ \$5,000, and the value cannot be determined through reference to publicly available prices, if the value will be affected by the outcome of the research, or the value represents 5% or more interest in any one single entity, then,



IRB STANDARD OPERATING PROCEDURES

Appendix 202 – BRANY IRB Standard Operating Procedures

Aug 2012 IRB SOP Change Summary

Revision Summary and Rationale: The BRANY IRB Standard Operating Procedures (“SOPs”) have been revised primarily to reflect procedural changes related to operational efficiencies (e.g., electronic document flow), update sections relative to new/updated regulations, reflect revised procedure for audits of IRB minutes, add a policy and procedure for IRB review of Exception From Informed Consent (EFIC) for Planned Emergency Research, and to address additional procedural changes for central IRB processing.

Major changes include:

- Addition of a policy and procedure for IRB review of Exception From Informed Consent (EFIC) for Planned Emergency Research
- Revision to procedure for audits of IRB minutes.

Minor changes include:

- Revisions to reflect use of “xForm” submissions, as applicable.
- Revisions to reflect changes in procedures for processing Central IRB submissions, including:
 1. Revised administrative procedures for processing CIRB site and sponsor applications
 2. Criteria that would prompt review of additional site applications by the convened IRB rather than via expedited review (e.g., compliance history, FDA 483)
 3. Submission forms for use by CIRB sites and sponsors
- Additional changes have been made in response to internal assessments of IRB procedures and regulatory guidance/revisions by the IRB Director and BRANY’s QA Division. (e.g., change to guidelines for IRB to recommend approval periods less than 12 months)
- Grammatical modifications were made throughout the entire document to improve/enhance readability, and to clarify statements as needed.
- Application/submission forms that have been updated since the last SOP revision were updated in the SOP Appendix.

Drafts Appended

1. Exception From Informed Consent (EFIC) for Planned Emergency Research
2. REC02_BRANY IRB Meeting Minutes Quality Assurance Review Procedure
3. REC02_QA Checklist for IRB Meeting Minutes



IRB STANDARD OPERATING PROCEDURES

Appendix 203 – BRANY IRB Standard Operating Procedures

Dec 2012 IRB SOP Change Summary

Revision Summary and Rationale: The BRANY IRB Standard Operating Procedures (“SOPs”) have been revised primarily to reflect procedural changes related to removing the requirement for IRB staff to use “wet signatures” for official IRB correspondence, including IRB determination letters.

Major changes include:

- Revisions to remove references to wet signatures.

Minor changes include:

- Grammatical modifications were made throughout the entire document to improve/enhance readability, and to clarify statements as needed.

Specific SOP Revisions (underlined text represents additions; strikethrough for deletions)

18. Section II.1., “Purpose of the IRB” was revised to correct grammar:

- a. To hold regularly scheduled meetings in order to review all research proposals ~~that involve~~involving human subjects.

19. Section II.3.e., “IRB Chairperson’s Responsibilities,” item (16) was revised as follows:

- (16) The Chairperson or designee(s) will ~~sign~~compose official IRB correspondence.

20. Section II.5.f., “IRB Correspondence“ was updated to specify that IRB decision letters will no longer include a “wet signature.”

II.5.f. IRB Correspondence:

The IRB administrative staff will be responsible for maintaining records of all correspondence to or from the IRB (45 CFR 46.115(a)(4), and 21 CFR 56.115(a)(4)). Correspondence to or from investigators that relate to a specific research project will be maintained in the file for the specific project.

IRB Correspondence will not reflect a “wet signature” of the author. BRANY IRB correspondence shall be considered valid when:

1. It is sent directly from a valid BRANY email address by an actively employed and designated BRANY staff member,



IRB STANDARD OPERATING PROCEDURES

2. The letter is attached to BRANY's electronic research protocol tracking system by an actively employed and designated BRANY staff member,

Valid copies of BRANY IRB correspondence can be downloaded by research staff via the electronic research protocol tracking system.

21. Section III.1., "Actions Taken by the IRB," was updated to specify that IRB decision letters will no longer include a "wet signature."

...The Chairperson(s) of the committee or the administrative staff of the IRB, as designated by the Chairperson(s), may ~~sign~~ compose and send IRB approval notices...

22. Section III.1.j.3., "IND Safety Reports (Off site adverse events)," was updated to correct spelling:

Investigators should also report:

- Findings from other studies (Such as ~~epidemiological~~ epidemiological studies...)

23. Section III.1.o., "Reporting Procedures for Unanticipated Problems Involving Risks to Subjects or Others, Non-Compliance, or Suspension or Termination of IRB Approval," was updated to reflect that reports will no longer include a wet signature.

The IRB Director will ~~sign~~ compose the letter and copies will be sent to:

24. Section VII.3.e., "Waiver of Authorization" was revised to specify that the required signature of the IRB Chairman or authorized member will be available via the completed IRB Reviewer Checklist.

5. Signature of the IRB Chairman or authorized member (available via the completed Reviewer Checklist).



IRB STANDARD OPERATING PROCEDURES

Appendix 204 – BRANY IRB Standard Operating Procedures

Jun 2013 IRB SOP Change Summary

Revision Summary and Rationale: The BRANY IRB Standard Operating Procedures (“SOPs”) have been revised primarily to reflect procedural changes related to processing of protocol deviations and to incorporate guidelines for informing investigators of re-consent requirements.

Major changes include:

- The policy for reporting protocol deviations has been revised to include definitions of major and minor protocol deviations. Major deviations are required to be reported upon discovery and in no case later than 10 days after discovery. Minor deviations will be recorded on a deviation log and supplied to the IRB with applications for continuing review, or if the study is closed prior to continuing review, with the notification of study closure.
- The policy regarding principal investigator responsibilities specific to informed consent has been revised to include guidelines for when a revision to the informed consent warrants re-consenting of subjects. IRB correspondence will specify when re-consent is required.

Minor changes include:

- Revision to the procedure for conducting evaluation of IRB members.
- Clarification that a protocol summary may not always be applicable and that it will only be part of IRB records as a separate item when it is applicable.
- Clarification of the role of a designated IRB reviewer in reviewing reports of unanticipated problems involving risks to subjects or others.
- Clarification of requirements for reporting to regulatory agencies when a reported event that is external to the site(s) operating under BRANY IRB approval meets criteria for unanticipated problems involving risks to subjects or others, or serious and/or continuing non-compliance.
- Clarification that research involving vulnerable populations may qualify for review by the expedited procedure.
- Grammatical modifications were made throughout the entire document to improve/enhance readability, and to clarify statements as needed.

Specific SOP Revisions (underlined text represents additions; strikethrough for deletions)

25. Section I.2.1.2., “Vetting Investigators” – correction of typographical error:



IRB STANDARD OPERATING PROCEDURES

...BRANY conducts an in depth interview of the prospective investigator and their staff. This process includes the completion of ~~an~~ Investigator Database Information Form (See Appendix 35.)...

26. Section I.2.a.4, "Finance" – correction of typographical error:

...Together they analyze the prior year's budget, assess the organization's assumptions for growth, and review various financial reports such as balance sheets, profit and loss statements as well as other key performance indicators. Several factors...

27. Section II.1., "Purpose of the IRB" – correction of typographical error is item (a):

To hold regularly scheduled meetings in order to review all research proposals ~~that involve~~ involving human subjects.

28. Section II.3.e. – Added section header "Evaluation of IRB Chairpersons" above existing text describing this process.

- a. Subsequent section headers were updated accordingly.

29. Section II.3.f – Added section clarifying procedures for evaluation of IRB members.

II.3.f. Evaluation of IRB Members

The performance of IRB members will be evaluated biannually. IRB administrative staff will provide the IRB members with the "IRB Member Self-Evaluation Form" (Appendix 53). The evaluation form captures key information that will assist in determining if the member is effective in his/her role. The IRB Director or designee will tabulate the results and provide a report to the IRB Chairperson(s) to evaluate. Together, they will determine whether a change in the membership is warranted based on the evaluation, and will provide feedback to the IRB members. If the IRB member fails to adequately fulfill membership responsibilities, or if circumstances arise that in the opinion of the Chairperson(s) or IRB administrative team, warrant the IRB member's removal, the member will be removed from the IRB. The appointment process may be activated at any time to fill vacancy and/or to ensure the effective operation of the IRB.

30. Section II.3.e., "IRB Chairperson's Responsibilities," is now Section II.3.g.

31. Section II.3.f., "Consultants," is now Section II.3.h.

32. Section II.3.g., "Guests," is now Section II.3.i.



IRB STANDARD OPERATING PROCEDURES

33. Section II.3.h., “IRB Committees,” is now Section II.3.j.
34. Section II.3.i., “Initial Training, Continuing Education, and Professional Development of IRB Members,” is now Section II.3.k.
35. Section II.4.c., “IRB Staff Responsibilities” item 2) was revised to indicate that a protocol summary will be transmitted when it is applicable.
36. Section II.5.c., “IRB Records” item (7) was revised to indicate that a protocol summary will be included in the project file when it is applicable.
37. Section II.6., “Principal Investigator (PI) Responsibilities,”
 - a. Item 14.) was updated to specify that major protocol deviations must be reported in accordance with section III.1.k. of the policy
 - b. Item 17.) was updated to reflect that unanticipated problems involving risks to subjects or others, or any instance of noncompliance with the Federal regulations or the requirements or determinations of the IRB in keeping with sections III.1.i. and III.1.L.
 - c. Item 32.) was updated to refer to the need for the PI to refer to BRANY IRB policy as well as applicable regulations with regard to required reporting.
38. Section II.8., “Sponsor Responsibilities” – Grammatical corrections under the section “For Central IRB projects” as follows:

For Central IRB projects the Sponsor will ensure that the Investigators selected to conduct the clinical trial; ~~that~~ are able to use the services provided by a Central IRB, and receive all the appropriate BRANY IRB submission documents.

39. Section II.9.a, “Organization and Responsibilities”
 - a. Item (c) was updated to specify that periodic reports will also be provided to the HRPP Committee.
40. Section III.1.b.1., “Initial Review by the Convened IRB” was revised to specify that IRB reviewers will receive a protocol summary only when it is applicable.

Prior to distribution of the materials, a primary and secondary reviewer will be assigned to review each project. Reviewers will receive copies of:

- the completed Research Application, including (if applicable): form FDA 1572, or IDE form, or other IND/IDE correspondence
- the full protocol,
- the investigator’s brochure and safety reports, DSMB; DMC reports, drug/device inserts or other documents relating to the investigator brochure (when applicable),
- the Curriculum Vitae of the Principal Investigator (or other documentation evidencing qualifications),
- the protocol summary, when applicable (e.g., when not already contained within the protocol, or when protocol is brief and summary is not required),
- the informed consent form and...



IRB STANDARD OPERATING PROCEDURES

41. Section III.1.b.1.1., “Primary and Secondary Reviewer System,” paragraph following first bulleted list, the expiration date example was revised to change expiration time from midnight to 11:59 PM, to be consistent with the time listed in the continuing review policy.

“...the project will expire at ~~midnight~~ 11:59 PM on January 27, 2007.”

42. Section III.1.c.1., “Continuing Reviewer’s Responsibilities”
- a. Item (h) was revised to specify that a minor deviation log will be provided at continuing review in keeping with section III.1.k. of the policy.
 - (h) Protocol Deviation reports, if any (i.e., major protocol deviations not previously reported to the IRB, and minor protocol deviation log – see SOP III.1.k.)

43. Section III.1.c.4., “Reinstatement of a Terminated Research Project” was revised to indicate the reinstatement application must be received within 30 days of expiration.

44. Section III.1.d., “Expedited Review of Research”

- a. Second paragraph was revised to indicate that designated IRB staff member(s), not just the IRB Director, will determine with concurrence from the IRB reviewer that a submission qualifies for expedited review.
- b. Fifth paragraph was revised to refer to the Reviewer Checklist (Appendix 6) and eliminate reference to the Addendum Checklist for Expedited Review (Appendix 43), because the latter has been integrated into the former.

45. Section III.1.f.1., “Amendment Review,” item (c) has been updated to refer to the Reviewer Checklist (Appendix 6) and eliminate reference to the Addendum Checklist for Expedited Review (Appendix 43), because the latter has been integrated into the former.

46. Section III.1.i., “Review of Reports of Unanticipated Problems Involving Risks to Subjects or Others”

- a. Throughout the subsections 2-6, revisions were made to indicate that the IRB Chair or designated IRB reviewer is responsible for review and consideration of reports of unanticipated problems involving risks to subjects or others.

The main procedural clarification was specified as follows:

If assigned to a ~~The~~ Chairperson for review, the Chair will also determine whether immediate suspension or other action needs to be taken to eliminate apparent immediate harm to subjects until the convened committee can consider the matter. If assigned to a designated reviewer for consideration, and the designated reviewer feels that immediate suspension or other action needs to be taken to eliminate apparent immediate harm to subjects, the report will be referred to the



IRB STANDARD OPERATING PROCEDURES

IRB Chair immediately for such determination. The IRB staff ~~places~~ adds the event on the agenda of the next available IRB meeting for review.

- b. In 2 locations, the definition of unexpected was updated in accordance with applicable guidance from OHRP.

Unexpected: An event is “unexpected” when its specificity and severity are not accurately reflected in the informed consent document or other protocol-related documents, and the characteristics of the population being studied.

- c. Item 8. Under “Principal investigators must report,” was revised to replace references to the term “protocol violation” with terminology consistent with the revised protocol deviation reporting policy.

~~Protocol violation~~ deviation (meaning an accidental or unintentional change to the IRB-approved protocol) that placed one or more participants at increased risk, or has the potential to occur again (see SOP III.k.).

47. Section III.1.j.2., “Reporting Procedures for SAEs,” the second paragraph was revised to add the word serious to the following sentence:

Investigators are also required to report promptly to the IRB any serious adverse event that is reported to the FDA or the Study sponsor in accordance with FDA requirements.

48. Section III.1.k., “Deviations, Exceptions, and Violations,” was revised as follows:

III.1.k. Deviations, Exceptions, and Violations:

Definitions:

Protocol Deviation: Any temporary alteration/modification to the IRB-approved protocol. The protocol may ~~includes~~ the detailed protocol, protocol summary, consent form, recruitment materials, questionnaires, and any other information relating to the research study. Deviations can be major or minor.

Major Protocol Deviation: A deviation that affects subject safety, rights, welfare, or data integrity.

Examples of major protocol deviations include (but are not limited to):

- Failure to obtain informed consent (i.e., no documentation of informed consent, consent obtained after study procedures were initiated)
- Enrolling subject who does not meet inclusion/exclusion criteria
- Use of study procedures not approved by the IRB



IRB STANDARD OPERATING PROCEDURES

- Failure to report serious adverse events to the IRB and/or sponsor (per applicable requirements)
- Failure of subject to show up for a study appointment that results in missing treatment
- Failure to perform a required study procedure or lab test that could affect subject safety or integrity of study data (e.g., procedure or lab test results needed to determine eligibility for the research)
- Error in dispensing or dosing of drug/study medication, whether committed by subject or study team
- Error involving use of device
- Study visit conducted outside of required timeframe, only if it affects subject safety
- Failure to follow safety monitoring plan
- Enrollment of subjects after IRB-approval of study expired

Minor Protocol Deviation: A deviation that does not affect subject safety, rights, welfare, or data integrity.

Examples of minor protocol deviations include (but are not limited to):

- Missing original signed and dated consent form (only photocopy available)
- Inappropriate documentation of informed consent, including:
 - Copy not given to the person signing the consent form
 - Someone other than the subjects dated the consent form
 - Expired consent used, but the version letter is identical to the currently approved consent form.
- Deviations from the approved study procedure that do not affect subject safety or data integrity
- Study procedure conducted out of sequence
- Omitting an approved portion of the protocol
- Failure to perform a required lab test
- Missing lab results
- Study visit conducted outside of required timeframe
- Failure of subject to return study medication

Protocol Exception: A deviation that has been submitted to the IRB for review, and has been approved by the IRB prior to initiation.

Protocol Violation: A deviation that has been implemented without IRB approval.

- III.1.k.1. **Procedure for Reporting Protocol Deviations to BRANY IRB:**
It is the responsibility of the PI to determine if a deviation is major or minor. Reports of protocol deviations should also be submitted to the sponsor according to the sponsor's protocol.



IRB STANDARD OPERATING PROCEDURES

Major Protocol Deviations

Major protocol deviations must be reported to the IRB within ten (10) working days of discovery using the Reportable Event Form (Appendix 13).

The IRB Chairperson or designee will review the major protocol deviation, and the following actions may result:

- a. If the IRB chairperson or designee, after consideration of the major protocol deviation, does not have concerns about human subject safety, the investigator will receive written notification indicating that a major protocol deviation has been reviewed by the IRB and no additional action is required at this time. Such deviations will be reported promptly to the IRB committee in the agenda of a subsequent IRB meeting.
- b. If the IRB Chairperson or designee determines that the major protocol deviation does not qualify for expedited review or raises new concerns about risks to subjects, the reviewer will forward the item to the full board for review at an IRB meeting. The Chairperson or designee may initiate further inquiry or review, depending on the major protocol deviation. The IRB may then acknowledge the major protocol deviation, require additional information, request remedial action, or suspend or terminate IRB approval.

Major protocol deviation may also be considered unanticipated problems involving risks to participants or others, and will be processed in accordance with BRANY IRB SOP III.1.i. Numerous major protocol deviations may reflect non-compliance by the investigator and will be processed in accordance with BRANY IRB SOP III.1.i Reports of Non-Compliance.

Minor Protocol Deviations

Minor protocol deviations should be reported in aggregate to the IRB at continuing review or with notification of study closure, using a protocol deviation log (see Appendix 54).

The designated IRB reviewer will review the minor protocol deviation log in conjunction with the materials provided in the application for continuing approval or the notification of study closure. Logs processed with applications for continuing approval will be processed in accordance with BRANY IRB SOP III.1.c Continuing Review; acknowledgement of IRB review will appear on the IRB decision notice. Logs provided with notification of study closure will be processed in accordance with the BRANY IRB SOP III.1.d.3. Expedited Review of Minor Changes in Previously Approved Research; acknowledgement of IRB review will appear on the IRB notification acknowledging receipt of the notification of study closure.

Deviation Report Contents

All reports of protocol deviations submitted to the IRB should include:

- A detailed description of the incident
- Indication as to whether the deviation placed any subject at risk



IRB STANDARD OPERATING PROCEDURES

- Indication as to whether the deviation affected the integrity of the study data
- A description of any changes to the protocol or other corrective actions that have been taken or are proposed in response to the deviation
- Information regarding changes implemented by the study team to ensure that such deviations will not occur in the future.

III.1.k.2. Procedure for Requesting Approval of Protocol Exceptions from BRANY IRB:

If the investigator wishes to deviate from the IRB-approved protocol, he or she must submit such a request using the Reportable Event Form (Appendix 13) to the IRB for review and approval prior to initiation of such deviation. The IRB Chairperson or designee will review the deviation. The following actions may result:

- (a) If the IRB approves the temporary change to the IRB-approved protocol, the investigator will receive written notification indicating that a **protocol exception** has been approved by the IRB.
- (b) If the IRB Chairperson or designee determines that the temporary change in the IRB-approved protocol does not qualify for expedited review or raises new concerns about risks to subjects, the reviewer will forward the item to the full board for review at an IRB meeting. The IRB may then approve, require modification to, or disapprove the requested protocol exception.

49. Section III.1.l., “Reports of Non-Compliance,” the definition of serious non-compliance, item 3. was updated to refer to failure to report major protocol deviations as an example:

Examples of serious non-compliance include, but are not limited to:

- (7) Failure to obtain IRB approval prior to initiation of research project;
- (8) Continuation of research activities when the IRB approval for the research protocol has expired (i.e., failed to file for continuing review);
- (9) Failure to notify the IRB of changes in ongoing research (e.g., major protocol deviations, amendments, SAEs);
- (10) Failure to obtain informed consent;
- (11) Failure to document informed consent; or
- (12) Failure to properly document the research and research procedures.

50. Section III.1.m., “Suspension/Termination of IRB Approval,” first paragraph was updated to include major protocol deviations as a potential reason for suspension or termination of IRB approval.

51. Section III.1.n.11., “Recruitment of Subjects” – grammatical correction to the following sentence in the second paragraph:

...Even in the absence of overt coercive or inducing statements, ~~an element of coercion may be introduced because of~~ the relationship between the potential subject and the



IRB STANDARD OPERATING PROCEDURES

investigator can introduce latent influence. Patients may feel obliged to agree because their physicians have asked them....

- 52.** Section III.1.o., “Reporting Procedures for Unanticipated Problems Involving Risks to Subjects or Others, Non-Compliance, or Suspension or Termination of IRB Approval,” the penultimate paragraph was updated to specify that reporting of external events determined to be unanticipated problems involving risks to subjects or others is not required for multicenter research projects:

For multicenter research projects, only the institution at which the subject(s) experienced an adverse event determined to be an unanticipated problem (or the institution at which any other type of unanticipated problem occurred) must report the event to the supporting agency head (or designee) and OHRP (45 CFR 46.103(b)(5)). Reporting to a regulatory agency FDA is not required if the event occurred at a site that was not subject to the direct oversight of the institution/organization, and the agency has been notified of the event by the investigator, sponsor, another organization, or other mechanisms.

- 53.** Section III.3.a., “Justifying External Factors” – grammatical correction to the last sentence in the paragraph:

...Since almost any amount of such payment could be considered an an coercive-undue inducement in certain circumstances, the IRB recognizes that such payments must be reasonable and not excessive.

- 54.** Section III.3.b., “Review of Compensation for Reasonableness” – grammatical correction to the following sentence:

... However, excessive compensation should not be offered as it might coerce-unduly influence a subject to participate....

- 55.** Section III.3.c., “Compensation in Pediatric Research” – grammatical correction to the last sentence in the paragraph:

... Reimbursements must not be coercive-unduly influence either to the parents or the children, and must be reasonable in relation to the visits and discomfort involved in the research.

- 56.** Section III.4., “Certificates of Confidentiality,” the URLs for the OHRP guidance and NIH web site with information about certificates of confidentiality was updated to reflect the current, active URLs.

- 57.** Section III.8.b., “Implementation of IRB requirements in accordance with 21CFR50.24(a)(7) [Section (7) above],” item (1), grammatical correction:

“...the community representatives the PI haves met or will be meeting with (e.g. community board president), and the setting and frequency in which the PI haves met or



IRB STANDARD OPERATING PROCEDURES

will be meeting with the community representatives (e.g. monthly at community board meetings)....”

58. Section III.8.b., “Implementation of IRB requirements in accordance with 21CFR50.24(a)(7) [Section (7) above],” item (2), grammatical correction at end of 2nd paragraph:

“...This report must be reviewed and approved, in addition to the remainder of the protocol, prior to study ~~implantation~~ implementation by the PI.”

59. Section IV.1.d., “Principal Investigator’s Responsibilities” [under section IV.1., “Informed Consent”] has been updated to include guidelines for re-consenting as follows:

IV.1.d. Principal Investigator’s Responsibilities:

When any research project or clinical investigation is undertaken that involves human subjects, the Principal Investigator is required to observe the following:

1. The BRANY IRB must review the research prior to initiation. Refer to the Research Application (Appendix 11) for submission instructions.
2. When BRANY IRB has not approved a waiver of the requirement to obtain consent, ~~written~~ informed consent as approved by the BRANY IRB will be obtained from the human subject (or the subject’s legally authorized representative, if consent by a legally authorized representative has been approved by the IRB).
3. The written informed consent form and any other written information to be provided to subjects should be revised whenever important new information becomes available that may be relevant to the subject’s consent, including new information that may affect the risks or benefits to subjects or a subject’s willingness to continue participation in the research. Any revised written informed consent form or other revised written information to be provided to subjects should receive the IRB’s approval in advance of use.

The subject or the subject’s legally authorized representative should be informed in a timely manner if new information becomes available that may be relevant to the subject’s willingness to continue participation in the trial. The communication of this information should be documented.

IV.1.d.1. Re-Consent

Subjects may need to be re-consented due to changes in their status (i.e., previously enrolled by proxy and now able to consent on their own behalf) or due to changes in the protocol and/or consent form as follows:

- The protocol and/or consent form has been modified since the subject enrolled and the changes are more than administrative (i.e. the information which has

IRB STANDARD OPERATING PROCEDURES

been added/deleted may have an impact on risk to subjects or their willingness to participate).

- The subject was initially enrolled in a study by parents, a legally authorized representative or a research proxy because:
 - The subject was a minor at the time of entry into a study and has since reached the age of 18 and can now consent on his/her own behalf, or
 - The subject was incapacitated at the time of enrollment and has regained capacity to consent on his/her own behalf.

IV.1.d.1.a. Re-consent due to modifications:

If the modifications are minor (see III.1.d.3. Expedited Review of Minor Changes in Previously Approved Research), including typographical errors or basic reformatting, re-consent is most likely not needed or re-consent may be accomplished by verbally informing subjects of the change with documentation in the medical record/study subject record that such notification took place.

If the modifications are more than minor and/or could affect the subject's willingness to continue participation, the IRB requires that research subjects be re-consented. It may be appropriate to provide the subject with an addendum to the original consent form that provides the new information, or to revise the full consent form. If an addendum is used, it must clearly state that the information in the original consent form is still current and valid, and that the information in the addendum is supplementary.

IRB approval letters will indicate whether or not re-consent is necessary and the method that should be used for re-consent. This information will also be documented in the IRB record.

60. Section IV.1.f., "Consent Form Criteria" – addition of omitted phrase "undue influence" in the sixth paragraph:

...The "deliberate objection" of a child subject should be construed as a veto of the consent of a parent or guardian, whether that objection is verbal or non-verbal. In order to be valid, consent must be freely given - that means free from all coercion or undue influence. However, in rare instances...

61. Section VI.1., "Potentially Vulnerable Subject Groups," the third paragraph has been updated to provide clarification that qualifying research involving vulnerable populations may be eligible for review via the expedited procedure:

The IRB is also required to ensure that it has adequate representation on the Board to consider research involving these vulnerable populations in a satisfactory manner. When the IRB reviews a project involving vulnerable populations, the IRB Coordinator(s) will ensure that one or more individuals who are knowledgeable about or experienced in



IRB STANDARD OPERATING PROCEDURES

working with such participants will be present at the IRB meeting, or will be available to provide consultation to the designated IRB reviewer when the submission qualifies for expedited review. When necessary the IRB will seek legal counsel for guidance on the definitions below when state and/or local laws may apply. For research involving potentially vulnerable subject groups, determinations of exempt status will be made by the BRANY IRB according to Section II.2.c of this policy.

62. Section V.1.b.5., “Requirements for Permission by Parents or Guardians and for Assent by Children” – addition of omitted phrase “undue influence” in item (a)(ii):

...When applicable, an Assent form (see Appendix 20: Sample Assent Form and Preparation Guidelines) must be completed to document that assent was freely obtained and without any coercion or undue influence....

63. Section V.1.b.9., “Proposed Reimbursement for Child Subjects,” a grammatical correction was inserted as follows:

In reviewing pediatric research, the IRB must consider the appropriateness of the payment to the parents/guardian, as well as to the child, if any. Reimbursements must not ~~be coercive~~ represent an undue influence either to the parents or the children, and must be reasonable in relation to the visits involved in the research.

64. Appendices

- a. Appendix 19 (Sample Informed Consent Form) was updated with a new version of BRANY IRB’s sample consent form. Embedded guidance further directs users on elements required for submission to the IRB.
- b. Appendices 53-56 (IRB SOP Change Summaries) reassigned to Appendices 200-203
- c. Appendix 53 is now the IRB Member Evaluation Questionnaire
- d. Appendix 54 is now the Minor Protocol Deviation Log
- e. Appendices 55-199 remain reserved for future use



IRB STANDARD OPERATING PROCEDURES

Appendix 205 – BRANY IRB Standard Operating Procedures

Dec 2013 IRB SOP Change Summary

Revision Summary and Rationale: The BRANY IRB Standard Operating Procedures (“SOPs”) have been revised primarily to reflect procedural changes related to processing of protocol deviations and to incorporate guidelines for informing investigators of re-consent requirements.

Major changes include:

- Removal of requirement for researchers to submit IND Safety Reports to the IRB.
- Addition of requirements for research supported by the Department of Defense
- Update to method for determining IRB approval dates for conditional approvals/approval with modifications.
- Update to definitions and procedures related identification and management of conflicts of interest.

Minor changes include:

- Grammatical modifications were made throughout the entire document to improve/enhance readability, and to clarify statements as needed.
- Hyperlinks to regulatory resources available on the Internet were updated throughout the document.
- General formatting changes were made for readability.

Specific SOP Revisions

1. Section I1.2.a. “Definition of Terms” – Added definitions of “minimal risk,” “experimental subject” and “research involving a human being as an experimental subject” for research supported by the Department of Defense
2. Section II.2.c. “Exemptions” – Added qualifier indicating that research must be no greater than minimal risk to qualify for determination of exempt status. Clarification that IRB will also consider measures to protect subject privacy for exempt applications.
3. Section II.3.a. “IRB Membership Requirements” – Clarified that IRB considers non-scientific members to represent the general perspective of participants. Added membership requirements for classified research subject to the requirements of the Department of Defense.



IRB STANDARD OPERATING PROCEDURES

4. Section II.3.g.1. – Added section describing the Vice-Chair role and Responsibilities.
5. Section II.3.f – Added section clarifying procedures for evaluation of IRB members.
6. Section II.3.j. “IRB Committees” – Updated to reflect twice weekly meeting frequency.
7. Section II.5.a. “Record Retention” – Added clarification of record format pre-2013 (paper) and post-2013 (electronic).
8. Section II.5.b. “Access to IRB Records” – Added statement specifying accessibility of applicable records to relevant Department of Defense personnel.
9. Section II.5.c. “IRB Records” – Clarified that IRB may also consider scientific evaluations provided by an entity other than the IRB, which will become part of the IRB records for the research. Listed the following as additional items that will be part of the IRB records for the research, when applicable: recruitment materials, data and safety monitoring reports, documentation regarding any non-compliance or unanticipated problem determinations, copies of correspondence between the IRB and the researchers. Added listing of record components when a project is considered for determination of exempt status.
10. Section II.5.g. “Electronic Research Protocol Tracking System” – Added detail regarding how records are maintained, accessed, and used by IRB members and staff via the *IRBManager* portal.
11. Section II.5.h. “IRB Minutes” – Added specification that each action will have its own separate deliberation documented. Added more explicit specification that in the case an IRB member exits a meeting due to a conflict of interest, it is explicitly stated in the minutes.
12. Section II.8. “Sponsor Responsibilities” – Clarified parties between whom agreement must be in place prior to enrollment. Removed reference to IND Safety Reports and attendant reporting form.
13. Section II.9.b.1. “Auditing Process” – Removed reference to IND Safety Reports.
14. Section II.9.b.2. “Selection of Trials to be Audited” – Added requirements for notifying appropriate Department of Defense Human Research protection Officer in the event of a for-cause audit by a Federal department, agency, or national organization.
15. Section II.10.e. “Review of Protocol-Specific IRB Records” – Removed reference to IND Safety Reports.
16. Section III.1. “Actions Taken by the IRB” – Clarified that IRB actions are communicated in writing to the investigator, as well as designated institutional liaisons. Specified that when the IRB requests substantive clarifications or modifications directly relevant to the determinations required by the IRB, the protocol will return to the convened IRB for reconsideration and will not be approved by the expedited procedure. Added clarification of IRB’s procedure for determining approval dates.



IRB STANDARD OPERATING PROCEDURES

17. Section III.1.b. "Types of IRB Review" – Removed redundant language regarding quorum requirements and cross-referenced the section of the policy already containing this information.
18. Section III.1.c. "Continuing Review" – Clarified language with regard to determining approval periods. Added requirement to notify the DoD Human Research Protection Officer of the results of continuing review for research supported by the Department of Defense.
19. Section III.1.d.1, "Categories...Expedited Review Procedure" – Added note indicating that non-exempt classified research is not eligible for expedited review.
20. Section III.1.f.2. "Amendment Approval/Rejection" – Removed reference to IND Safety Reports and attendant reporting form.
21. Section III.1.g. "Full Board Review..." – Added requirement to notify the DoD Human Research Protection Officer of the substantive changes to research supported by the Department of Defense.
22. Section III.1.i. "Review of Reports of Unanticipated Problems Involving Risks to Subjects or Others" – Added reportable event types formerly listed under the IND Safety Report section of the policy.
23. Section III.1.i.1. "Processing reports of unanticipated problems involving risks to subjects or others" – Added the option to refer matters to other organizational entities in the actions considered by the IRB.
24. Section III.1.j.2. "Reporting Procedures for SAEs" – Removed references to IND Safety Reports.
25. Section III.1.j.3 Title changed from "IND Safety Reports" to "External Adverse Events." Added clarification that external adverse events are only reportable when they meeting the criteria for an unanticipated problem involving risks to participants or others. Clarified reporting requirements and timelines.
26. Section III.1.j.4. "Possible Actions..." – Removed references to IND Safety Reports.
27. Section III.1.l.1. "Investigation and Processing of Allegations of Non-compliance" – Clarified that IRB will consider whether allegations of non-compliance is based on fact.
28. Section III.1.n.1. "Levels of Risk" – Added clarification of definition of minimal risk and requirements for a research monitor independent of the team conducting the research for research supported by the Department of Defense.



IRB STANDARD OPERATING PROCEDURES

29. Section III.1.n.4. "Equitable Selection of Subjects" – Added clarification of requirements for research involving military personnel for research subject to the requirements of the Department of Defense.
30. Section III.1.n.o. "Reporting Procedures for Unanticipated Problems Involving Risks to Subjects or Others, Non-Compliance, or Suspension or Termination of IRB Approval" – Noted that other sites involved in the research might be notified of relevant BRANY IRB determinations, when appropriate. Added timeline for notifying the Human Research Protections Officer for research supported by the Department of Defense.
31. Section III.1.b. "Review of Compensation for Reasonableness" – Added requirements for considering compensation for research supported by the Department of Defense.
32. Section III.8. "Exception From Informed Consent (EFIC) for Planned Emergency Research" – Added qualifier that when research is subject to requirements of the **Department of Defense**, an exception from consent in emergency medicine research is prohibited unless a waiver is obtained from the Secretary of Defense.
33. Section III.8.a. "Requirements" – Added clarification of requirements for obtaining consent from a legally acceptable representative for planned emergency research.
34. Section III.8.b. "Implementation of IRB requirements..." – Clarified that exception from informed consent for planned emergency research is prohibited for DoD protocols without a waiver from the Secretary of Defense.
35. Section III.8.c. "References" – Added regulatory reference for DHHS.
36. Section IV.1.a. "Informed Consent" – For research subject to DoD requirements, specified that disclosures in the consent form related to compensation for injury must follow the requirements of the DoD component.
37. Section IV.1.j. "Additional Elements of Informed Consent" – Added elements for classified research subject to DoD requirements.
38. Section IV.2.a. "Waiver or Alteration of Informed Consent Requirements/Minimal Risk Research" – Added exclusion for classified research subject to DoD requirements.
39. Section IV.2.c. "Waiver of Informed Consent for Department of Defense Supported Research" – Section added to address DoD supported research.
40. Section V.1.d. "Prisoners" – Clarified research involving prisoners must be reviewed by the convened IRB. Specified that DoD supported research involving prisoners of war is prohibited. Added requirements for DoD supported research involving prisoners.
41. Section V.1.f.2. "Assessment of Capacity" – Clarified that proxy consent for research is not applicable for research supported by DoD.
42. Section VI. "Conflicts of Interest" and Appendix 48 – Updated definitions and procedures related to identification and management of conflicts of interest.



IRB STANDARD OPERATING PROCEDURES

43. Archived Appendix 15 – IND Safety Report Submission Form
44. Archived Appendix 30 – Access to PHI in Preparation of Research Form
45. Archived Appendix 33 – Document Retention Schedule (Now maintained as a separate SOP by BRANY administration because it was not limited to IRB document retention.)
46. Archived Appendix 40 – CIRB IND Safety Report Submission Form
47. Appendix 4 “Glossary” – Added definitions for “experimental subject” and “human subjects”
48. Updated the following appendices with current working versions:
 - a. 17 – Reviewer Checklist
 - b. 10 – Sample IRB Approval Letter
 - c. 11 – Research Application
 - d. 13 – Reportable Event Form
 - e. 15 – Request for IRB Review of Modification
 - f. 19 – Sample Informed Consent Form
 - g. 27 – Application for Determination of Exempt Status
 - h. 32 – Binder Organization List
 - i. 48 – Conflict of Interest Disclosure Forms
 - j. 50 – Application for Transfer of IRB Oversight to BRANY IRB



IRB STANDARD OPERATING PROCEDURES

Appendix 206 – BRANY IRB Standard Operating Procedures

Mar 2014 IRB SOP Change Summary

Revision Summary and Rationale: The BRANY IRB Standard Operating Procedures (“SOPs”) have been revised primarily to reflect changes recommended by AAHRPP during Step 1 of the re-accreditation process.

Major changes include:

- Clarification of additional requirements for Department of Defense supported research throughout the policy
- Updates to IND and IDE exemption category listings and attendant forms
- Updates to definitions in the conflict of interest policy (“financial interest related to the research” and attendant form (Form 01)
- Specification of IRB staff responsible for ensuring various required IRB determinations are appropriately made and documented

Minor changes include:

- Grammatical modifications were made throughout the entire document to improve/enhance readability, and to clarify statements as needed.
- General formatting changes were made for readability.

Specific SOP Revisions

1. Section I.2. “Mandate to Protect Human Subjects” – Added text describing how resources are provided for BRANY’s HRPP.
2. Section II.1. “Purpose of the IRB” – Clarified the terms “institutional official” or “institutional liaison” refer to officials of the organization where the research is taking place.
3. Section II.2.a. “Definition of Terms” – Added definition of “Generalizable Knowledge” and “Systematic Investigation.”
4. Section II.3.3. “Evaluation of IRB Chairpersons” – Clarified method for providing evaluation results to the chairpersons.
5. Section II.3.k. “Initial Training, Continuing Education, and Professional Development of IRB Members” – Clarified IRB Director or a designee is responsible for providing continuing education relative to current DoD requirements at a convened IRB meeting.



IRB STANDARD OPERATING PROCEDURES

6. Section II.4.3. "Initial Training, Continuing Education, and Professional Development of IRB Staff" – Clarified IRB Director or a designee is responsible for providing continuing education relative to current DoD requirements at IRB Team meetings.
7. Section II.3.f – Added section clarifying procedures for evaluation of IRB members.
8. Section II.3.j. "IRB Committees" – Updated to reflect twice weekly meeting frequency.
9. Section II.5.a. "Record Retention" – Added "and all other records required to be kept by the IRB" to allude to records kept by the IRB in addition to protocol-specific records.
10. Section II.5.b. "Access to IRB Records" – Clarified statement indicating records are made accessible for inspection and copying by authorized representatives of federal agencies or departments.
11. Section II.5.c. "IRB Records" – Added statement: "IRB records document determinations required by laws, regulations, codes, and guidance."
12. Section II.5.h. "IRB Minutes" – Added explicit statement indicating the approval period will be documented for initial and continuing reviews. Added reference to participants with diminished capacity to list of vulnerable populations requiring protocol-specific findings to be described in the minutes.
13. Section II.5.i. "Creation, Review, Maintenance, Revision and Archive of BRANY IRB Standard Operating Procedures (SOPs)" Clarified method of distribution of new information to researchers and/or their staff, IRB members, and the IRB staff (via email and postings on the www.branyirb.com website). Eliminated reference to "research manual" that is no longer in use. Specified each researcher is provided the SOP manual with each new study approval.
14. Section II.5.j. "Quorum Requirements" – Added items (6)-(8):
 - (6) At least one unaffiliated member will be present at each meeting.
 - (7) At least one member who represents the general perspective of participants will be present at convened meetings.
 - (8) When the IRB reviews research that involves subject populations vulnerable to coercion or undue influence, one or more individuals who are knowledgeable about or experienced in working with such participants will be present.Note that the unaffiliated member, the member representing the general perspective of subjects, and the non-scientific member may be the same person or they may be represented by two or three different persons.

Added explicit statement indicating that no votes can be taken in the absence of quorum.
15. Section II.6. "Principal Investigator (PI) Responsibilities" – Added responsibility of PI to inform the IRB if a study is prematurely completed or suspended or terminated by any other entity (item #23).



IRB STANDARD OPERATING PROCEDURES

16. Section II.6.a. “Investigator (and Key Personnel) Human Subject Protection Education Requirement” – Added statement:

“Evidence of training in the specific requirements of the applicable DoD component must be provided with each DoD supported research project application that is submitted to BRANY IRB for review (e.g., CITI Training Module for DON-Supported Extramural Performers, as per the Department of the Navy Training and Education Guidance issued April 15, 2011)”

17. Section III.1. “Actions Taken by the IRB” – Clarified that the researcher may also provide written responses to address the IRB’s requested modifications, and noted that if the research expires before the conditions are reviewed and approved by the IRB, all research activities must stop until IRB approval is obtained (item B). Clarified that any response to a disapproval provided by the investigator will be considered by the IRB at a subsequent convened meeting (item D).
18. Section III.1.b.2. “Primary and Secondary Reviewer System” – Added statement that the IRB may rely on outside experts to provide an evaluation of scientific merit. Noted that the IRB considers scientific merit for non-exempt research.
19. Section III.1.d.1, “Categories...Expedited Review Procedure” – Added to category (7):

(NOTE 2: For Department of Defense (DoD) supported research that involves surveys being performed on Department of Defense personnel, the investigator must submit to, and ensure review and approval by the Department of Defense after the research protocol is reviewed and approved by the IRB.)

20. Section III.1.d.3. “Expedited Review of Minor Changes in Previously Approved Research” – Specified that expedited reviewer will apply same considerations for IRB review of new applications to IRB expedited review of modifications to previously approved research *when the modification affects a criterion for approval.*
21. Section III.1.3. “Modifications to Previously Approved Research” – Specified that the IRB reviewer will apply same considerations for IRB review of new applications to IRB review of modifications to previously approved research *when the modification affects a criterion for approval.* Specified Investigators sign a Request for IRB Review form and are provided with notification of receipt stating that IRB review is not complete until the PI receives the IRB’s determination in writing for the submission.
22. Section III.1.g. “Full Board Review...” – Added to item (13) that the IRB will consider the need for notification to subjects when the review relates to significant new findings that may affect the participant’s willingness to continue participation.
23. Section III.1.i. “Review of reports of unanticipated problems involving risks to subjects or others” – Added:

The review process will be the same for all unanticipated problems involving risk to subjects or others, regardless of risk level.



IRB STANDARD OPERATING PROCEDURES

- 24.** Section III.1.k.1. “Procedure for Reporting Protocol Deviations to BRANY IRB” Added that the IRB may determine a reported deviation to be minor non-compliance (scenario (a) under “Major Protocol Deviations”) or serious and/or continuing non-compliance (scenario (b) under “Major Protocol Deviations”). Added that the designated IRB reviewer will consider whether the reported deviations represent serious and/or continuing non-compliance, and if so will forward to the convened IRB for review.
- 25.** Section III.1.m. “Suspension/Termination of IRB Approval” – Added references to suspensions/terminations by persons/entities other than the IRB, and noted these are reportable by the PI to the IRB.
- 26.** Section III.5. “Compliance with All Applicable State and Local Law” – Added statement: “When federal regulations and other applicable laws conflict, BRANY IRB will adhere to the stricter regulation.”
- 27.** Section III.6. “Emergency Use of a Test Article Without IRB Review” – Added text to specify procedures for contacting manufacturers of drugs or biologics, as well as requests for authorization from FDA to ship test articles in these circumstances.
- 28.** Section III.8.a. “Requirements [for EFIC studies]” – Added specific text clarifying procedures to be followed to meet requirements for studies involving exception from informed consent (planned emergency research).
- 29.** Section III.9.i.2. “Responsibilities for a Lead Investigator in a Multi-Site Study” – Added statement relative to requirements for a formal agreement between organizations for DoD regulated multi-site research.
- 30.** Section IV.1.f. “Consent Form Criteria” – Added text describing requirements when a participant withdraws for the interventional portion of a study and does not consent to continued follow-up.
- 31.** Section IV.1.h. “Waiver of Documentation of Consent” – Added statement to explicitly indicate the IRB will consider whether the researcher will be required to provide participants with a written statement regarding the research when considering a waiver of documentation of consent.
- 32.** Section IV.3.c. “When Investigator Anticipates a Limited English Proficient Population” – Added caveat allowing use of short form when the language was anticipated but the translated consent document is in progress but unavailable at the time a potential participant presents.
- 33.** Section IV.3.d. “When Investigator Encounters a Non-English Speaking Subject Whose Primary Language Was Not Anticipated” – Added clarification to IRB determinations that will be required in order to permit use of short form consents.



IRB STANDARD OPERATING PROCEDURES

34. Section V.1. "Potentially Vulnerable Subject Groups" – Added explicit statements that IRB will follow Subparts B, D when the research involves pregnant women/fetuses/neonates and children, respectively. Added statement indicating that the IRB will consider additional safeguards that may be required when the research involves adults unable to consent.
35. Section V.1.b. "Research Involving Children – Special Considerations" Add explicit statement that IRB will follow Subpart D for research involving children. Noted the IRB Coordinator as the individual responsible for ensuring the IRB makes and documents these required determinations.
36. Section V.1.b.2. "Degrees of Risk" – Clarified language under category (c) per the regulatory criterion.
37. Section V.1.n.3. "Children Who Are Wards of the State or Other Agency, Institution, or Entity" – clarified text relating to appointed advocate and the IRB's requirements for research involving wards. Noted the IRB Coordinator as the individual responsible for ensuring the IRB makes and documents these required determinations.
38. Section V.1.c.2. "Research Involving Pregnant Women or Fetuses" – Added item (d): "The consent of the mother is obtained in accordance with the regulations." Noted the IRB Coordinator as the individual responsible for ensuring the IRB makes and documents these required determinations.
39. Section V.1.c.3. "Research Involving Neonates" – Added item (d) to specify requirements for consent of either parent of the neonate to be obtained in accordance with the regulations. Noted the IRB Coordinator as the individual responsible for ensuring the IRB makes and documents these required determinations.
40. Section V.1.c.3.2. "Neonates of Uncertain Viability" – Removed unnecessary text: "covered by this subpart." Noted the IRB Coordinator as the individual responsible for ensuring the IRB makes and documents these required determinations.
41. Section V.1.c.3.3. "Nonviable Neonates" – Noted the IRB Coordinator as the individual responsible for ensuring the IRB makes and documents these required determinations.
42. Section V.1.d. "Prisoners" – Added specific requirements for prisoner representative responsibilities. Noted the IRB Coordinator as the individual responsible for ensuring the IRB makes and documents these required determinations. Clarified the definition of "minimal risk" for research involving prisoners. Added statement that IRB will permit epidemiological research involving prisoners only when prisoners are not a particular focus of the research, among other listed criteria. Specified the IRB Director or designee will send required communications to OHRP for prisoner research that is federally funded.
43. Section VI. "Conflicts of Interest" – Added definitions of "Financial Interest Related to the Research." Repeated definition of key personnel in Section VI.1.b. Added consultants to Section VI.1.e. and specified how IRB reviewer/consultant conflicts of interest are



IRB STANDARD OPERATING PROCEDURES

captured. Clarified Section VI.1.g. regarding what relationships the Organization prohibits, thus avoiding organizational conflicts of interest.

- 44.** Section VIII.1.b."Research Involving Investigational FDA Regulated Test Articles" – Revised policy to provide specifics on IND processing, and to specify IND exemptions more clearly. Specified BRANY IRB will not release a final IRB approval determination without confirmation that a valid IND is in effect, when applicable. Revised policy to provide specifics on requirements for Abbreviated IDEs, and noted categories of exemptions for investigational devices.
- 45.** Appendix 8 – Application for Continuing Approval – Revised instructions for reporting subject accrual status. Revised follow-up questions for on-going studies. Added question to solicit information from PI regarding whether translations continue to be required. Added question to identify whether study agent was administered during the approval period. Clarified UPIRTSO terminology. Clarified wording in question about DSMB to elicit more accurate responses. Made submission of PI license a required question. Improved questions related to informed consent to allow for proper "skip patterns" when the study was approved allowing a waiver of consent. Enhanced question choices for consent modifications to be submitted with continuing review applications.
- 46.** Appendix 11 – Research Application – Added description of requirements for protocol document contents to ensure adequate information is provided to the IRB for review. Improved question wording for requests for waiver/alteration of informed consent to allow for more accurate responses. Moved questions related to compensation for research related injury to the end of the form.
- 47.** Appendix 19 – Sample Informed Consent Form – Added "or requests for information" to the required language provided to subjects regarding whom to contact.
- 48.** Appendix 45 – IND Determination Form – Revised to match IND exemption categories that were revised in the SOP.
- 49.** Appendix 46 – IDE Determination Form – Revised to match Abbreviated IDE requirements and IDE exemption categories that were revised in the SOP.
- 50.** Appendix 48 – Forms 01 & 02 – Updated Form 01 to reflect definitions from revised Conflict of Interest policy in SOP.



IRB STANDARD OPERATING PROCEDURES

Appendix 207 – BRANY IRB Standard Operating Procedures

Sept 2014 IRB SOP Change Summary

Revision Summary and Rationale: The BRANY IRB Standard Operating Procedures (“SOPs”) have been revised primarily to reflect changes in response to observations made by AAHRPP as a result of the re-accreditation site visit that occurred August 5-6, 2014.

Major changes include:

- Clarification of policy to better reflect existing procedures related to review of non-compliance
 1. Review of IRB non-compliance by BRANY’s HRPP Committee
 2. Review of allegations of non-compliance by IRB Chair or designated IRB reviewer
- Clarification that expirations or lapses in IRB approval will be considered by the convened IRB for a non-compliance determination

Minor changes include:

- Grammatical modifications and correction of typographical errors were made throughout the entire document to improve/enhance readability, and to clarify statements as needed.
- General formatting changes were made for readability.

Specific SOP Revisions (added text is underlined, deleted text marked with strikethrough)

1. Pg. 5, TOC, changed section title for III.1.c.4. to “Reinstatement of a Terminated or Lapsed Research Project”
2. Changed “noncompliance” to “non-compliance” throughout the document for consistency.
3. Changed “Institution Official” to “Institutional Official” throughout the document for consistency.
4. Pg. 61, Section II.10. Quality Improvement Activities to Monitor Institutional Review Board Functions and HRPP Effectiveness, added the following paragraphs after paragraph #4

At its regularly scheduled meetings, the HRPP Committee will review any observed deficiencies and attendant improvement plans to consider whether the observations represent IRB non-compliance, and if so, whether such non-compliance was serious or continuing.



IRB STANDARD OPERATING PROCEDURES

In the event that the potential IRB non-compliance involves potential risks to a subject's rights or welfare, an ad-hoc meeting of the HRPP committee will be scheduled within one week to review to the observation for IRB non-compliance, and if so, whether such non-compliance was serious or continuing.

If the HRPP Committee determines that IRB non-compliance is serious or continuing, it will report such determination in accordance with section III.1.o. of this policy.

5. Pg. 76, Section III.1.c.2. Study Termination, revised as follows:

III.1.c.2. Study Termination

The BRANY IRB requires that a Notification of Study Termination Form be submitted at the completion of every IRB approved study (exempt research is not applicable). Termination forms should be filed promptly and prior to expiration of IRB approval. If no termination form is received by the expiration date, the IRB will issue an Expiration Letter, informing the investigator that no research activity may continue, and that the investigator has failed to meet continuing review obligations. Investigators who fail to file final reports may be subject to sanctions including, but not limited to, required additional education and training or suspension of investigator privileges. **Failure to submit a Notification of Study Termination or a request for reinstatement of IRB approval post-expiration will be reported to the convened IRB for consideration of whether such failure represents minor, serious, or continuing non-compliance.**

It is the responsibility of the Investigator to ensure that the report is accurate and submitted in a timely fashion.

6. Pg. 77, Section III.1.c.4. Reinstatement of a Terminated or Lapsed Research Project, revised as follows:

III.1.c.4. Reinstatement of a Terminated or Lapsed Research Project

A project that has been terminated, for any reason, **or for which IRB approval has lapsed**, cannot be reinstated unless it is re-reviewed and approved at a convened meeting of the IRB. Within 30 days of expiration, the investigator must re-submit the project for review at a convened meeting of the BRANY IRB. **A PI's failure to submit a Notification of Study Termination or submit a request for reinstatement of IRB approval within 30 days will be reported to the convened IRB for consideration of whether such failure represents minor, serious, or continuing non-compliance.**

Reinstatement and approval of a research project requires that the IRB review and approve the following at a convened meeting of the IRB:

- (1) A completed Application for Continuing Approval ([Appendix 8](#)).
- (2) A memo to the IRB that incorporates the following information:
 - (a) An explanation of the circumstances that led to failure to submit the application at the appropriate time, and a corrective action plan detailing measures to prevent future occurrences;



IRB STANDARD OPERATING PROCEDURES

- (b) A statement indicating whether patients were enrolled during the period that the project was not IRB approved; and
- (c) A statement indicating if there were any subjects maintained on a therapeutic intervention after the expiration date of IRB approval, the number maintained on therapy and why abrupt cessation of that therapy would have been detrimental to each patient's health.

The convened IRB will review the final report and provide acknowledgement to the investigator. **The IRB will also determine whether the lapse in IRB approval represents serious or continuing non-compliance in accordance with the definitions in section III.1.I. of this policy, and if so, report such determination in accordance with section III.1.o. of this policy.**

7. Pgs. 103-105, Section III.1.I.1. Investigation and Processing of Allegations of Non-compliance, revised as follows:

III.1.I.1. Investigation and Processing of Allegations of Non-compliance

- (1) The IRB Director and Quality Assurance Manager will initially review all allegations of non-compliance to determine if the allegation is truly non-compliance. When necessary additional information may be sought from the Investigator, research staff or other appropriate parties. If the IRB Director and Quality Assurance Manager deem that there is merit to the allegation it will be forwarded to the IRB Chair **or designated IRB reviewer** for further evaluation.
- (2) Allegations of non-compliance will be forwarded to the IRB Chairperson or **designated IRB reviewer** to determine if the non-compliance is serious or continuing. If it is determined that the allegation is neither serious nor continuing, the IRB will provide documentation to the investigator indicating this determination. The IRB Chairperson **or designated IRB** reviewer will determine an appropriate corrective action plan, **if applicable**, to prevent future non-compliance. The IRB Director and/or Quality Assurance Manager will be responsible for ensuring ~~the~~**such** corrective action plan has been enacted. The QA Department may conduct a subsequent audit to confirm the corrective action plan.
- (3) If the IRB Chairperson **or designated IRB reviewer** determines that the allegation of non-compliance might be serious or continuing, the QA Department will conduct an audit to investigate the allegation, **unless the allegation resulted from an observation during a BRANY QA audit.** If the **IRB Chairperson determines the** allegation appears to place subjects at risk, the Chairperson may call for immediate suspension or termination of the research project. **If the designated IRB reviewer determines the allegation appears to place subjects at risk, he/she will immediately notify the IRB Chairperson, and the IRB Chairperson may call for immediate suspension or termination of the research project.**
- (4) Audit findings will be presented to the Institutional Official, IRB Chair(s) and the item will be reviewed by the IRB at a convened meeting.



IRB STANDARD OPERATING PROCEDURES

- (5) All IRB members scheduled to attend the IRB meeting will be sent the relevant materials for review, including a synopsis of the event, audit report results and any other information deemed pertinent.
- (6) The IRB Chair **or designated IRB reviewer** will be assigned the primary review of the item and will present the review to the convened IRB. In addition to the materials referenced above, the Chair will receive the currently IRB approved protocol and consent document, any other reports of unanticipated problems involving risks to subjects or others and the Investigator Drug/Device Brochure, if applicable. **If possible,** the QA auditor who conducted the initial investigation will also be in attendance at the meeting to assist in the presentation of the issues and address any additional questions or concerns pertaining to the matter.
- (7) The IRB will consider whether the allegation of non-compliance is based on fact and decide, by vote, whether or not the allegations represent non-compliance. If so, the IRB will further determine if the non-compliance is serious or continuing.
- (8) When the IRB determines that serious or continuing non-compliance has occurred, the committee must further determine one or more of the following:
 - (a) Is suspension or termination of the research warranted (if so policy III.1.m Suspension/Termination of IRB Approval, will be followed)?
 - (b) Is additional investigation of the Investigator warranted?
 - (c) Is a corrective action plan required and if so will the IRB require:
 - (i) Modification to the research protocol
 - (ii) Modification to the informed consent document
 - (iii) Subjects to be re-consented
 - (iv) Earlier continuing review of the project
 - (v) Monitoring of the consent process
 - (vi) Increased monitoring of the research
- (9) The Investigator will be informed of the IRB's findings in writing from the IRB Director. The letter will be drafted by the IRB director, or designee, and will be reviewed by the QA Manager and the IRB Chair. The letter will include:
 - (a) a summary of the IRB's findings,
 - (b) actions required by the IRB;
 - (c) a request for the Investigator to provide a corrective action plan
 - (d) a deadline by which the Investigator must respond
 - (e) a date when the information will be considered by the full board

Prior to distribution the letter will be approved by the IRB Chair(s) and the Institutional Official.
- (10) The Investigator must address the IRB's findings in writing within the specified timeline assigned by the IRB. The Investigator may, upon request, make a presentation directly to the IRB at a convened meeting. If any part of the corrective action plan requires more than minor modifications to the research,



IRB STANDARD OPERATING PROCEDURES

such changes must be submitted for full board review by the IRB. The IRB may allow changes that do not involve more than minor modifications to be reviewed by Expedited Review.

- (11) The Investigator's response will be reviewed by the IRB at a convened meeting. All members scheduled to attend the meeting will be provided with the response and any other relevant materials. The IRB Chair will be assigned as the primary reviewer.
- (12) The IRB may:
 - (a) Accept the Investigator's response and report that the issue was satisfactorily resolved and no further action is needed.
 - (b) Request additional information from the Investigator (which will also be submitted to the IRB in accordance with the procedures described above)
 - (c) Suspend and/or terminate the research
- (13) Vote counts and determinations made by the IRB will be documented in the IRB meeting minutes. All documentation will be maintained in the IRB Record.

In addition, BRANY IRB SOP III.1.o. Reporting Procedures will be followed as appropriate.

8. Pgs. 118-120, Section III.1.o. Reporting Procedures for Unanticipated Problems Involving Risks to Subjects or Others, Non-Compliance, or Suspension or Termination of IRB Approval, revised as follows:

III.1.o. Reporting Procedures for Unanticipated Problems Involving Risks to Subjects or Others, Non-Compliance, or Suspension or Termination of IRB Approval

Reports of: a) unanticipated problems involving risk to subjects or others, b) serious or continuing non-compliance, and/or c) suspension or termination of approved research, must be promptly reported to the IRB, the Institutional Official, sponsor, the appropriate institutional liaison, and the appropriate regulatory agencies.

The BRANY IRB will comply with all applicable local, state, and federal regulations concerning the conduct of research.

Once the BRANY IRB has taken any of the following actions:

- Determined that an event represents an unanticipated problem involving risks to subjects or others
- Determined that non-compliance was serious or continuing
- Suspended or terminated approval of research.

Or, once the HRPP Committee has determined that IRB non-compliance was serious or continuing, then the IRB Director or designated staff will prepare a letter including the following information, **as applicable**:

- the nature of the event (~~U~~unanticipated problem involving risks to subjects or others, serious or continuing non-compliance, suspension or termination of approval of research),



IRB STANDARD OPERATING PROCEDURES

- the name of the institution conducting the research,
- title of the research project in which the problem occurred,
- name of the principal investigator on the protocol,
- the BRANY IRB file number,
- a detailed description of the problem including the findings and the reasons for the ~~IRB's decision determination~~,
- actions the organization/institution is taking or plans to take to address the problem the (e.g., revise the protocol, suspend subject enrollment, terminate the research, revise the informed consent document, inform enrolled subjects, increase monitoring of subjects, corrective and preventative actions, etc.), and
- any plans to send a follow-up or final report by the earlier of a) a specific date or b) when an investigation is completed or a corrective action plan has been implemented

The IRB Chair(s) and the Institutional Official will review such correspondence and recommend modifications as necessary.

The IRB Director will compose the letter and copies will be sent to:

- Principal Investigator
- The Institutional Official
- Institutional Liaison
- Sponsor, ~~if appropriate and~~/or CRO (Contract Research Organization), if applicable
- OHRP, if the study is subject to DHHS regulations or subject to a DHHS Federalwide Assurance
- FDA, if the study is subject to FDA regulations.
- Other sites involved in the research, when appropriate.
- If the study is conducted or funded by any Federal Agency other than DHHS that is subject to "The Common Rule" such as:
 - (xix) Agency for International Development (22 CFR 225)
 - (xx) Central Intelligence Agency (Executive order)
 - (xxi) Consumer Products Safety Commission (16 CFR 1028)
 - (xxii) Department of Agriculture (7 CFR 1c)
 - (xxiii) Department of Commerce (15 CFR 27)
 - (xxiv) Department of Defense (32 CFR 219)
 - (xxv) Department of Education (34 CFR 97)
 - (xxvi) Department of Energy (10 CFR 745)
 - (xxvii) Department of Homeland Security (Public law 108-458 Sec. 8306)
 - (xxviii) Department of Justice (28 CFR 46)



IRB STANDARD OPERATING PROCEDURES

- (xxix) Department of Transportation (49 CFR 11)
- (xxx) Department of Veterans' Affairs (38 CFR 16)
- (xxxix) Environmental Protection Agency (40 CFR 26)
- (xxxixii) Housing and Urban Development (24 CFR 60)
- (xxxixiii) National Aeronautics and Space Administration (14 CFR 1230)
- (xxxixiv) National Science Foundation (45 CFR 690)
- (xxxixv) Office of Science and Technology Policy (Adoption of policy)
- (xxxixvi) Social Security Administration (Public law 7.5.26)

The report is sent to OHRP or the head of the agency as required by the agency.

- If the event involves unauthorized use, loss, or disclosure of PHI, the Privacy Officer should be sent a copy of the letter.
- **If the event involves serious or continuing non-compliance by the IRB, OHRP and/or FDA, will be notified as applicable.**

For multicenter research projects, only the institution at which the subject(s) experienced an adverse event determined to be an unanticipated problem (or the institution at which any other type of unanticipated problem occurred) must report the event to the supporting agency head (or designee) and OHRP (45 CFR 46.103(b)(5)). Reporting to FDA is not required if the event occurred at a site that was not subject to the direct oversight of the institution/organization, and the agency has been notified of the event by the investigator, sponsor, another organization, or other mechanisms.

The IRB Director will ensure that such reporting is completed within 30 days after the IRB's **or HRPP Committee's** determination has been made. Whenever possible and in the event of more serious actions, the IRB Director will expedite this process.

For research supported by the **Department of Defense** (DoD), prompt reporting (no longer than within 30 days) to the DoD human research protection officer.



IRB STANDARD OPERATING PROCEDURES

Appendix 208 – BRANY IRB Standard Operating Procedures

Apr 2015 IRB SOP Change Summary

Revision Summary and Rationale: The BRANY IRB Standard Operating Procedures (“SOPs”) have been revised primarily to reflect eliminate restrictions on the exempt and expedited review procedures that are not required by regulation.

Major changes include:

- Clarification of policy to permit qualifying research involving genetic testing to be reviewed by the expedited review procedure.
- Clarification of policy to permit the BRANY IRB Chairperson to make determinations of exempt status for qualifying research involving pregnant women, fetuses, or in vitro fertilization.

Minor changes include:

- Modifications to forms and appendices necessitated by the changes noted above.
- Grammatical modifications and correction of typographical errors were made throughout the entire document to improve/enhance readability, and to clarify statements as needed.
- General formatting changes were made for readability.

Specific SOP Revisions (added text is underlined, deleted text marked with strikethrough)

1. Changed “multicenter” and “multi-site” to “multi-center” throughout the document for consistency.
2. Pg. 26, Section II.2.c. Exemptions, deleted the following phrase:
 - BRANY IRB will not make determinations of exempt status for research involving prisoners, ~~pregnant women, fetuses, and *In vitro* fertilization.~~
3. Pg. 60, Section II.10. Quality Improvement Activities to Monitor Institutional Review Board Functions and HRPP Effectiveness, first paragraph revised as follows:

BRANY maintains a Quality Assurance (QA) Department, reporting to Senior Administration. This department is responsible for assuring compliance by the various departments ~~involved in clinical development~~ with the applicable regulations...
4. Pg. 73, Section III.1.c. Continuing Review, revised as follows:



IRB STANDARD OPERATING PROCEDURES

If BRANY IRB performs continuing review more than 30 days before the IRB approval period expires, the anniversary date will not be retained. The date by which the next continuing review must occur will be changed to reflect a time period (no greater than 365 days) ~~beginning with~~ **based upon** the date of the IRB meeting at which continuing review occurred (or the date that continuing review qualifying for expedited review was completed by the IRB Chair or designee). **The date of IRB approval will be the date the IRB determines the conditions of approval have been satisfied.**

5. Pg. 87, Section III.1.g. Full Board Review (More than Minor Modifications to Previously Approved Research), revised as follows:

Modifications that may NOT be reviewed via the mechanism of expedited review and will require full board review include:

- (1) Addition of a new drug
- (2) Addition of a new device
- (3) Addition of an invasive procedure
- (4) Increase in medication dose or a decrease in dose that may increase the risk
- (5) Addition of vulnerable subjects as a study population
- (6) Prolongation of the patient's participation in the study other than for observational purpose
- (7) Change in the inclusion/exclusion criteria which may involve incorporation of populations at greater risk
- (8) Identification of new, potentially significant risks
- (9) Collection of additional blood samples that exceed the limits set in expedited category 2.) (Section III.1.d.1.)
- (10) Unanticipated problems which caused harm (or placed person at increased risk of harm), were related to the research and was unforeseen
- ~~(11) Research involving genetic testing (See Section V.5.b. of this policy)~~
- (11)** ~~(12)~~ Substantial changes in the level of risks, the research design or methodology, the number of subjects enrolled in the research, the qualifications of the research team, the facilities available to support the safe conduct of the research
- (12)** ~~(13)~~ Any item deemed to warrant full board review by the Chair or designee

6. Pg. 120, Section III.1.p. Reporting and Procedures for AAHRPP Accreditation, revised as follows:

In accordance with the requirements of its accreditation and timelines specified by AAHRPP, BRANY HRPP will submit annual reports to AAHRPP. BRANY HRPP will also re-apply for accreditation ~~every three years~~ **at intervals determined by the accrediting organization**, and will fulfill other interim reporting requirements, including:

7. Pg. 177, Section V.5.a. Definitions [Genetic Research and Tissue Banking], revised as follows:



IRB STANDARD OPERATING PROCEDURES

...In contrast to the types of risks (often physical) that are presented by many biomedical research protocols that the IRB considers, the risks associated with genetic research may include social and psychological harm rather than physical injury.

In genetic research and research using stored tissue samples, there are potential health, societal, emotional and legal issues to consider. Many subjects may be naive to these issues and it is therefore necessary for the IRB to evaluate the protocols and consent forms for such studies with great care. As this new science develops and laws evolve, it is important to continuously rethink and refine the issues and the way in which they are presented to subjects. ~~These studies that generate information about individuals' personal health risks can provoke anxiety and confusion, damage familial relationships, and compromise the individuals' employment opportunities and insurability. Thus, the IRB does not consider genetic studies to fall in the category of minimal risk even though they may only entail obtaining a family history and blood drawing. These studies require review and approval at the convened meeting of the IRB.~~

8. Pg. 178, Section V.5.b. Issues in Genetic Research, revised as follows:

...Information obtained through genetic research may also have serious repercussions for the subject's family members. Consequently, **for** these studies **the IRB will consider these potential risks, and will** ~~should not be considered to present no risk or minimal risk. Thus, if~~ **take into account whether** a biological sample can be linked back to a subject, directly or indirectly, ~~that research will require full board review at a convened meeting of the IRB.~~

~~Modifications to genetic research (or to the genetic testing component of research) that was previously reviewed and approved via full board review will be processed in accordance with Section III.1.e.~~