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SUNY DOWNSTATE HEALTH SCIENCES UNIVERSITY
HUMAN RESEARCH PROTECTIONS PROGRAM
POLICY AND PROCEDURES

Subject:

Human Research Protections Program Policies and Procedures

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POLICY AND PURPOSE

This policy and procedures manual includes procedures for the preparation and submission of research protocols, including informed consent documents, for review by the State University of New York (SUNY) Health Science Center at Brooklyn Downstate Institutional Review Board (IRB) and Privacy Board (Downstate IRB). This policy outlines the responsibilities of investigators and key personnel during the conduct of human research and after a study is closed.
Downstate has a Federal Wide Assurance (FWA00003624) with the US Department of Health and Human Services, Office for Human Research Protections (OHRP). This policy ensures compliance with the terms of Federal Wide Assurance. The FWA applies whenever this Downstate becomes engaged in human research conducted or supported by any U.S. federal department or agency that has adopted the U.S. Federal Policy for the Protection of Human Subjects (also known as the Common Rule), unless the research is otherwise exempt from the requirements of the Common Rule or the department or agency conducting or supporting the research determines that the research shall be conducted under a separate assurance.
Downstate may also conduct research covered by a separate assurance issued by another US federal department or agency. The FWA held by Downstate indicates Downstate applies the Common Rule only to federally conducted or supported research. To meet NY state requirements, Downstate also applies the Common Rule, Subpart A of 45 CFR 46) to any human research that is not subject to Federal requirements (i.e., research not regulated by FDA or HIPAA), regardless of funding source. Downstate attests to the New York State Department of Health that it follows federal regulations for all human research.

The Downstate IRB registration with OHRP is IORG#0000064 and serves as the primary IRB for Downstate research. External (reviewing) IRBs with oversight of Downstate research must be registered with OHRP.

Activities requiring IRB review must have IRB approval and meet all other applicable requirements before they begin. This policy ensures compliance with policies, regulations, and laws pertaining to human research, including the requirements of the local jurisdiction where research takes place or the local jurisdiction for the source of specimens or data.
When the Downstate IRB approves research with investigators or key personal from an external site, such investigators or key personal must follow Downstate policies and the policies of their own institution and must be covered under an IRB Reliance Agreement or Individual Investigator Agreement with Downstate.

When regulations or policies conflict with one another, Downstate generally abides by the most stringent rule to allow the most protection to research participants and maintain regulatory compliance. Investigators who face a conflict about which regulation or policy to apply are directed to consult with the IRB to determine how to proceed.

Copies of any referenced documents or forms are available on the Downstate IRB Website.
When this policy does not address a situation, investigators should review IRB guidance materials or contact the IRB Office at IRB@downstate.edu to seek guidance on the specific situation.

The use of the word “must” in this policy means something is required under this policy or is a regulatory requirement. The use of the words “in general” or “should” in this policy, mean that something is recommended, suggested, or is a best practice, but not always required. An investigator may use an alternative approach if the approach satisfies the policy or regulatory

requirement. The IRB is available to discuss alternative approaches by e-mail at IRB@downstate.edu.

IRB POLICY AND PROCEDURES REVIEW CYCLE

The Executive Director or delegate creates IRB policies and procedures with input from relevant parties. Starting December 2025, these policies must be reviewed at least every two years to stay current. All policies require IRB Committee approval before being activated.

APPLICABILITY OF SPECIFIC REGULATIONS AND POLICIES

KEY REGULATIONS

Use the table below to determine which key regulations apply to a specific human research study:

Guidelines:	Key Regulations:
Downstate certifies the following to the NYS Department of Health: • Downstate conducts human research that is subject to policies and regulations promulgated by any agency of the federal government for the protection of human research participants. • Downstate conducts or proposes to conduct or authorize human research that is not subject to any policies and regulations promulgated by any agency of the federal government for the protection of human participants. • Downstate complies with policies and regulations promulgated by any agency of the federal government for the protection of human participants; and Downstate does or shall comply with such policies and regulations promulgated by any agency of the federal government for the protection of human participants in carrying out its human research activities, whether subject to the Federal Human Research Protection Regulations or not.	NYS Article 24A.
Effective January 21, 2019, Downstate applies the July 19, 2018, Common Rule (45 CFR 46) to all human research conducted, supported, or otherwise subject to regulations by any federal department or agency. Downstate also applies subpart A, as a minimum to non-FDA regulated and non-HIPAA regulated studies to comply with NYS Article 24A. Downstate does not apply exemption category 7 or 8 to research. Downstate does not have a policy for the use of Broad Consent under these exemption categories.	Common Rule (July 19, 2018, edition of 45 CFR 46) (45 CFR 46, Subpart A). The U.S. Department of Health and Human Services and fifteen other Federal Departments and Agencies' published revisions to the Federal Policy for the Protection of Human Subjects (the Common Rule) on July 19, 2018. Refer to the OHRP

Federal Expedited review categories apply, when applicable to Common Rule regulated research. Subparts B, C, D, and E apply when applicable, as indicated within the regulations. Research approved prior to January 21, 2019 is grandfathered under the Pre-2018 Common Rule requirements. However, when there is a compelling reason to transition the research, the IRB or an investigator may amend the research to comply with this version of the policy on or after January 21, 2019. *Note: The 2018 Common Rule does not apply to FDA-regulated and DOJ-supported research. Common Rule Exemptions (categories 1-6) might not necessarily apply to research regulated by the FDA or DOJ.*	website regarding the Revised Common Rule for additional information.
U.S. Department of Justice (DOJ) regulated research.	The DOJ is not a signatory to the July 21, 2018, Common Rule. Follow the Pre-2018 Common Rule and policies of the National Institute of Justice (NIJ) for NIJ funded studies.
Investigational studies involving research participants (including specimens) and FDA regulated articles (e.g., drugs including biologics, food or color additives, and medical devices), including bioavailability and bioequivalence studies. FDA exemptions apply to FDA regulated clinical investigations, when applicable. Federal Expedited review categories apply, when applicable to FDA regulated research.	Applicable FDA regulations apply to the research as defined by the FDA (e.g., clinical investigations that must comply with 21 CFR 50, 56, 312, 320, 812, 814, etc.)
Research conducted or supported by a Federal Department or Agency.	Apply any additional requirements from Federal Departments or Agencies, when they fund or conduct the research.
HIPAA Privacy and Security Rules.	The HIPAA Privacy & Security Rules (45 CFR Parts 160, 162, and 164) applies to any research involving Protected Health Information (PHI), also known as Individually Identifiable Health Information (IHII).
Multi-site research requires Single IRB (sIRB) review as required by Federal Regulations, as follows: 1) *NIH* funded non-exempt research that uses a single protocol to conduct research at multiple sites 2) Other studies as required by other *Federal Department/Agency* (contact funding Department/Agency for determination)	*For sIRB requirements & exceptions, see:* · Single IRB for Multi-Site or Cooperative Research · NOT-OD-16-094: Final NIH Policy on the Use of

3) Multiple sites are *engaged* (as determined by where the investigator is an employee or agent, per OHRP guidance) in non-exempt federally funded Human Research 4) *FDA* regulated Clinical Investigation with multiple US site participation *(pending FDA implementation, included here for planning purposes)*	a Single Institutional Review Board for Multi-Site Research · Single IRB Exception Determinations | HHS.gov · Engagement of Institutions in Human Subjects Research (2008) · FDA Proposed Rules for Harmonization and sIRB (pending FDA implementation).

OTHER REGULATIONS AND POLICY

Regardless of the key regulations that apply to the research described above, other regulations, standards, and policy may apply as noted below:

- When a clinical investigation follows Good Clinical Practices (GCP), or when a study meets the definition of a clinical trial by NIH, or when required by a sponsor, investigators must follow the GCP principles when conducting the research.
- The IRB and investigators must comply with this policy and all other applicable Downstate policies pertaining to research, including those of the Downstate Office of Compliance and Audit Services (OCAS).
- Principal Investigators (PI) and *investigators for the purposes of conflict of interest (COI)*, as determined by the PI, must follow the NIH regulations on financial Conflicts of Interest, as outlined in Downstate Conflict of Interest Policy. Investigators who are not employees of Downstate must comply with their institution's COI policy. For additional information, please see the IRB guidance regarding training and COI Disclosures, available within the IRB Guidance for Investigators, on the IRB's Policies and Guidance website.
- Downstate follows law passed by the official governing body of an American Indian or Alaska Native tribe and any foreign law or regulation when applicable to the research that provide additional protections for research participants.
- Downstate applies foreign regulations, when applicable. For international research, investigators may need to:
    - Follow host country ethical and legal standards, including local IRB or ethics board approval or their equivalent approval.
    - Comply with foreign data protection laws when handling personally identifiable data, referencing specific host country rules.
    - Use Data Transfer Agreements (DTA) or similar instruments for secure, lawful cross-border data exchange.
- Prior to commencing any international collaboration, investigators must consult the Downstate IRB to ensure adherence to both U.S. and foreign regulations and to determine if supplemental documentation, such as local site letters of support, foreign IRB approvals, or translated consent forms, is required. The Downstate IRB will consult with Downstate OCAS or General Counsel, when necessary to provide guidance to investigators.
- Downstate applies additional regulations, which may be applicable to certain research, as determined by the IRB, Sponsor, OCAS, or General Counsel.

HHS FUNDED OR SUPPORTED RESEARCH INVOLVING FDA REGULATED PRODUCTS

Based on our assurance (FWA) Downstate must comply with both the HHS and FDA regulations.[1,2] Where the regulations differ, the regulations that offer the greater protection in research participants should be followed.[3] The FDA is not a Common Rule agency. When an HHS funded study is regulated by the FDA, the FDA has a regulatory oversight jurisdiction of the research; however, the funding requirements of HHS also apply. In other words, the human research review and approval are based on the applicable FDA regulations; however, other funding requirements are still applicable. If a clinical investigation is conducted or supported by HHS and involves an FDA-regulated product, the study is subject to both the Common Rule and the FDA regulations pertaining to IRB review and Informed consent requirements. Both the investigators and the IRB should understand the impact of certain provisions of the Common Rule and FDA regulated clinical investigations to ensure compliance. For example, for research that is eligible for expedited review, FDA requires the IRB must determine that the research is no greater than minimal risk and the IRB must conduct continuing review of the research at intervals appropriate to the degree of risk, but not less than once per year. In addition, both the FDA and the HHS requirements for informed consent must be followed.[4]

ETHICAL PRINCIPLES IN HUMAN RESEARCH

As a standard practice, the Downstate IRB applies to the ethical principles set forth in the Belmont Report to all research, as created by the National Commission for the Protection of Research Participants of Biomedical and Behavioral research. The three quintessential requirements for the ethical conduct of Human research are:

- **Respect for persons:** Recognition of the personal dignity and autonomy of individuals, and special protection of those persons with diminished autonomy.
- **Beneficence**: Obligation to do no harm and to protect persons from harm by maximizing the anticipated benefits and minimizing possible risks.
- **Justice**: Distribute the benefits and burdens of research fairly.

The principles of the Belmont Report are the foundation for the development of the US Federal regulations. When applicable, the principles of the Nuremburg Code or the Declaration of Helsinki may also apply to the research, particularly for transnational research.

All Downstate staff must follow the Downstate Code of Ethics and Business Conduct. In addition, research professionals follow the ethical principles of their scientific and professional disciplines.

SCOPE

This policy and procedures within apply to investigators and staff reviewed and subject to review by the Downstate IRB, including those investigators covered by an IRB Reliance Agreement or an Individual Investigator Agreement with Downstate.

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1 FDA Information Sheet: IRB FAQs
2 FDA GCP Educational Materials: Comparison of FDA and HHS Human Subject Protection Regulations
3 FDA Guidance Document: Informed Consent (August 2023)
4 Impact of Certain Provisions of the Revised Common Rule on FDA-Regulated Clinical Investigations | FDA (October 2018)

This policy and procedures within apply to all research conducted by the Downstate workforce (regardless of whether compensation is received) while on Downstate time, utilizing Downstate resources (e.g., equipment), or Downstate property (including space leased or used by the Downstate).

This policy applies to the following:

- All activities which make Downstate engaged in human research,
- All FDA regulated investigational studies (clinical trials) involving research participants (or any human specimens, including de-identified specimens) and FDA regulated articles (e.g., drugs including biologics, food or color additives, and medical devices),
- All activities for which an IRB determination is made by the Downstate IRB,
- Any activity overseen by the Downstate IRB, including research non-compliance, research audits, and IRB review of investigational agents (including HUDs) for treatment purposes, and,
- Preparatory to research activities.

Investigators who are not members of the Downstate workforce should consult with their institution's policies.

This document contains both policies and procedures, which will be separated into individual documents as the IRB launches new processes with the MyResearch IRB Module replacing IRBNet. Once established, the latest approved procedure or policy will supersede prior documentation.

DEFINITIONS

This policy describes relevant definitions within specific sections as applicable to this policy. The IRB follows any additional definitions described pertinent or applicable regulations.

DETERMINING WHETHER IRB APPROVAL IS REQUIRED

In addition to meeting other applicable requirements, a PI or Clinical Investigator (CI) must obtain IRB approval before beginning any activity that requires IRB review.

ACTIVITIES REQUIRING IRB REVIEW

FDA REGULATED RESEARCH

This section describes FDA definitions and regulated research that is subject to IRB review under FDA regulations.

FDA DEFINITIONS

Human Subject (Drugs, Biologics, General FDA): A human subject is an individual who is or becomes a participant in research, either as a recipient of the test article or as a control.[5]

5 21 CFR 50.3(g)

Human Subject (Medical Devices): A subject is a human who participates in an investigation, either as an individual on whom or on whose specimen an investigational device is used or as a control.[6]

Clinical Investigation (Drugs, Biologics, General FDA): Any experiment that involves a test article and one or more human subjects that is subject to FDA submission requirements or intended to support FDA applications.[7]

Clinical Investigation (IRB Regulations): Any experiment involving a test article and one or more human subjects that must meet requirements for prior submission to FDA or whose results are intended to be submitted to FDA.[8]

FDA REGULATED ACTIVITIES REQUIRE IRB REVIEW UNDER FDA REGULATORY FRAMEWORK

Any Downstate activity meeting the FDA definition of a clinical investigation involving human subjects must be reviewed and approved by the Downstate IRB before initiation, except as permitted under emergency exceptions[9] or limited exemptions.[10]

Emergency exceptions and limited exemptions, which are described elsewhere in this policy and on the Downstate IRB website, include:

- One-time emergency use of a test article, provided that such emergency use is reported to the Downstate IRB within 5 working days. Subsequent use of the test article requires IRB review.
- Taste and food quality evaluations and consumer acceptance studies, if wholesome foods without additives are consumed or 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. This activity must be submitted to the Downstate IRB with an Exempt application.
- Specific in vitro diagnostic uses of leftover, de-identified specimens.[11] These activities should be submitted to the Downstate IRB for review. In general, these activities will qualify for an IRB Determination.

Downstate Research must be reviewed by the Downstate IRB under FDA regulations, if:

- It involves an FDA-regulated test article (e.g., drug, device, biologic, food additive, electronic product);

6 21 CFR 812.3(p)
7 21 CFR 50.3(c)
8 21 CFR 56.102(c)
9 21 CFR 50.23 and 50.24
10 21 CFR 56.104
11 FDA Guidance: Guidance on Informed Consent for In Vitro Diagnostic Device Studies Using Leftover Human Specimens that are Not Individually Identifiable

- Data will be submitted to or held for inspection by the FDA as part of a research or marketing application OR the activity requires an IND[12,13,14] or IDE.[15,16,17] Investigators may propose an exemption; however, the IRB or IRB Office, or FDA must confirm regulatory status.

Research involving human subjects (as defined by FDA) that is exempt from IND or IDE requirements is still to be subject to FDA oversight and must be reviewed by the IRB in accordance with applicable FDA regulations, including 21 CFR Parts 50 and 56. Such research must also comply with institutional policies, HIPAA requirements (when applicable), and all other federal, state, and local laws.

At Downstate, human subjects research that is not regulated by the FDA is reviewed under the Common Rule and associated institutional policies.

EXAMPLES:

FDA-regulated research includes:

- Drug trials needing an IND
- Medical device studies needing an IDE, including those with an NSR determinations
- Research on investigational devices with specimens
- Studies of marketed products aimed at labeling changes

Activities that are generally not classified as FDA-regulated research include:

- Basic scientific investigations conducted without the intention of supporting FDA submissions
- Utilization of secondary data that does not involve a test article
- Non-clinical laboratory studies (i.e., studies governed by Good Laboratory Practice [GLP] standards)

FDA REGULATED NON-RESEARCH ACTIVITY

FDA regulations also require the IRB to have oversight of some non-research activities, including Humanitarian Use Devices and Expanded Access (compassionate use). The activities must also be submitted to the Downstate IRB.

These activities are discussed in more detail in this policy and on the IRB website.

NON-FDA REGULATED HUMAN RESEARCH (COMMON RULE RESEARCH)

12 21 CFR 312
13 FDA Guidance Document: INDs – Determining Whether Human Research Studies Can Be Conducted Without an IND
14 IRB Responsibilities for Reviewing the Qualifications of Investigators, Adequacy of Research Sites, and the Determination of Whether an IND/IDE is Needed
15 21 CFR 812
16 SR and NSR Device Studies
17 IRB Responsibilities for Reviewing the Qualifications of Investigators, Adequacy of Research Sites, and the Determination of Whether an IND/IDE is Needed

For a non-FDA regulated activity to be considered research under the Common Rule(45 CFR 46)[18], and for human research that is funded or supported by Common Rule Departments and Agencies[19], it must be both 1) a systematic investigation (including research development, testing, and evaluation) and 2) be designed to develop or contribute to generalizable knowledge. Some demonstration and service programs may include research activities. In order for research to be considered *human research (and thus requiring IRB approval before the study begins)*, the research must involve *living* individuals *about whom* an investigator (whether professional or student) conducting research either 1) obtains information or biospecimens through *intervention* or *interaction* with the individual, and uses, studies, or analyzes the information or biospecimens; or 2) obtains, uses, studies, analyzes, or generates *identifiable private information* or *identifiable biospecimens.*

The following **federal definitions** in the Common Rule (45 CFR 46) provide clarity when making the determination as to whether IRB approval is required:

> ***Intervention*** includes both physical procedures by which information or biospecimens are gathered (e.g., venipuncture) and manipulations of the research participant or the research participant's environment that are performed for research purposes.
>
> Examples of interventions include:
> - Physical procedures through which data are gathered.
> - Collecting blood
> - Obtaining vital signs
> - Behavioral interventions
> - Evaluating an unknown psychotherapy procedure
> - Manipulation of research participants' environment
> - Playing music in the operating room to determine the impact on patient outcomes.
>
> *CAUTION: In general, the scientific definition of an intervention is the act of purposefully intervening, interfering or interceding with the intent of modifying some outcome. The above regulatory definition, which applies to determining when IRB approval is required, is much broader than the scientific definition of an intervention.*
>
> ***Interaction*** includes communication or interpersonal contact between an investigator and a research participant.
>
> Examples of interactions include:
> - Communication
> - Face-to-face
> - Electronic (including online surveys without identifiers)
> - Interpersonal contact
> - Observations
> - Interviews
>
> ***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

18 45 CFR 46
19 Common Rule Departments and Agencies

information that has been provided for specific purposes by an individual and that the individual can reasonably expect will not be made public (e.g., a medical record).

Identifiable private information is private information for which the identity of the research participant is or may readily be ascertained by the investigator or associated with the information.

> ***TIP:***
>
> ***Private information*** *must be* ***individually identifiable*** *for obtaining the information to constitute human research. For example, if an investigator is collecting information associated with a medical record number, the investigator is collecting individually identifiable private information.*

An ***identifiable biospecimen*** is a biospecimen for which the identity of the research participant is or may readily be ascertained by the investigator or associated with the biospecimen.

Note: On a periodic basis, federal departments or agencies implementing the Common Rule will reexamine the meaning of identifiable private information *and* identifiable biospecimen *and review analytic technologies or techniques that may generate identifiable private information. The Downstate IRB plans to adopt any new regulatory provisions for these definitions, once available in the Federal Register.*

SYSTEMATIC INVESTIGATION

For this policy, a ***systematic investigation*** is generally an activity that is planned, orderly, methodical, and uses data collection and analysis to answer a question, even if the activity is limited to the following:

- development, testing, evaluation of future research (including a pilot study)
- internal training or educational activity
- oral history, ethnography, or journalism,
- performance or quality improvement or similar healthcare operations activity

Although research must include ***systematic investigation***, non-research operations activities also include *systematic investigation* to ensure reliable outcomes. A ***systematic investigation*** does not, in and of itself, define research.

GENERALIZABLE KNOWLEDGE

For the purposes of this policy, activities designed to develop or contribute to ***Generalizable knowledge*** are those designed to draw general conclusions or inform policy (i.e., knowledge gained from a study may be applied to populations outside of the specific study population). Conclusions must be disseminated for research purposes (or be part of a program of investigation that will be disseminated) to be generalizable. A useful definition of dissemination is that the material includes sharing beyond the local setting.

- Obvious examples of dissemination are publication in a scholarly journal, presentation at a professional conference, or placement of a report in a library.

- Examples that are not dissemination include oral presentation to a Downstate Department in fulfillment of a Downstate requirement, sharing of results with an agency that cooperated in information collection, or internal presentation for utilization and review purposes.

Examples of generalizable knowledge:

- Applying the findings from the activity involving a patient population at Downstate to a population outside of Downstate.
- Applying the findings from a population within a Downstate healthcare network to a population outside of the Downstate network.
- Applying the findings of a Downstate student research project to other students in another school.
- When the outcomes are generalizable to other organizations, programs, or services.
- If the activity is limited to oral history, ethnographic, or journalism, it is generalizable when the project involves stories that will or may draw broad conclusions about the population, cultures, norms, and practices, even if no research hypothesis is being tested or validated.

IRB applications are not required for quality improvement activities conducted by one or more institutions whose purposes are limited to: (a) implementing a practice to improve the quality of patient care, and (b) collecting patient or provider data regarding the implementation of the practice for clinical, practical, or administrative purposes. For more information on quality improvement activities, see HHS/OHRP FAQs on Quality Improvement Activities.

Intent to publish is an insufficient criterion for determining whether a quality improvement activity involves research. Planning to publish an account of a quality improvement project does not necessarily mean that the project fits the definition of research; people seek to publish descriptions of non-research activities for a variety of reasons, if they believe, others may be interested in learning about those activities. Conversely, a quality improvement project may involve research even if there is no intent to publish the results.

The following are examples of activities that are NOT generalizable:

- When the activity is limited to oral history, ethnographic, or journalism, when published materials will be limited to documenting or reporting on events, situations, policies, institutions, or systems without the intent to form hypotheses, draw conclusions, or generalize findings.
- When the outcomes of the activity will remain specific to the SUNY Downstate programs or services, although other organizations may use the results for their own programs.
- When the activity is limited to an internal training or educational activity that is not designed to develop or contribute to generalizable knowledge (e.g., project with sole intent to meet course requirements, classroom activity that develops a survey tool without the intent to use the tool for research purposes).

HEALTH CARE OPERATIONS

Health care operations mean any of the following activities to the extent the activities relate to the functions of the institution:

- Quality assessment and improvement activities, including outcomes evaluation and development of clinical guidelines providing that the obtaining of generalizable knowledge is not the primary purpose of such activity,
- Patient safety activities,
- Population based activities related to improving health or reducing health care costs,
- Clinical protocol development,
- Case management,
- Care coordination,
- Contacting of health care providers and patients with information about treatment alternatives,
- Related functions that do not include treatment,
- Reviewing the competence or qualifications of health care professionals,
- Conducting training programs in which students, trainees, or practitioners in the areas of health care learn under supervision to practice or improve their skills as health care providers,
- Training of non-health care professionals,
- Accreditation, certification, licensing, or credentialing activities,
- Conducting or arranging for medical review, legal services, and auditing functions,
- Business planning and development,
- Business management and general administrative activities,
- Compliance activities,
- Customer service activities, including data analysis, provided PHI is not disclosed to a policy holder, plan sponsor, or customer,
- Resolution of internal grievances,
- Sale, transfer, merger, or consolidation of the parts of the institution, including due diligence related to such,
- Creating de-identified health information or a limited data set, or
- Fundraising for the benefit of the institution.

PROTECTED HEALTH INFORMATION

For this policy, ***Protected Health Information (PHI)*** includes individually identifiable health information transmitted or maintained in any form or medium pertaining to the past, present or future physical or mental health or condition of an individual. PHI encompasses data containing HIPAA identifiers that connects health details to an individual (CFR §160.103)

Examples of PHI:
• Name, address, date, or medical record number when linked to health information
• Medical records, test results, billing records
• Health insurance numbers, appointment schedules
• Health information linked to any of the 18 HIPAA identifiers (see Downstate HIPAA-6 policy)

Note: PHI does not apply to an individual who has been deceased for more than 50 years.

ALCOHOL OR SUBSTANCE ABUSE INFORMATION

For this policy, ***alcohol or substance abuse information*** includes information regarding an individual's diagnosis, treatment, or referral of treatment for alcohol abuse, substance abuse, or

chemical dependency.

GENETIC INFORMATION

For this policy, ***genetic information*** includes the following:

- An individual's genetic test.
- Genetic test of family members (including an embryo or fetus).
- The manifestation of a disease or disorder of an individual or a family member.
- Any request for, or receipt of, genetic services, or genetic test; or
- Participation in clinical research including genetic services, by the individual or any family member of the individual.

IDENTIFIABLE INFORMATION

For this policy, data (including data about specimens) is ***identifiable information*** under any of the following circumstances:

- Investigators can readily ascertain the identity of the research participant.
- There is actual knowledge that it would be possible to identify the research participant.
- The identity of the research participants can be associated with the information.
- Any data containing any HIPAA identifiers listed in Downstate HIPAA-6 policy is identifiable, unless it is for PHI of an individual who has been deceased for more than 50 years.

DE-IDENTIFIED DATA AND DE-IDENTIFIED SPECIMENS

For **non-FDA regulated research**, for the purposes of this policy, ***de-identified*** describes data sets (including data about specimens) that meet the following criteria:

- All HIPAA identifiers listed in Downstate HIPAA-6 policy are removed from the data set OR a qualified statistician has 1) determined that the risk is very small that research participants can be identified and 2) documented the methods and results of the analysis, AND
- The identity of the research participants cannot be readily ascertained by the investigator or be associated with the information, AND
- There is no actual knowledge that it would be possible to identify the participant.

CODED MATERIALS

For **non-FDA regulated research**, for the purposes of this policy, ***coded*** refers to:

1) Identifying information (such as name or social security number) that would enable the investigator to readily ascertain the identity of the individual to whom the private information or specimens pertain has been replaced with a number, letter, symbol, or combination thereof (i.e., the code); and
2) A key to decipher the code exists, enabling linkage of the identifying information to the private information or specimens.

Coded data or specimens **are identifiable** unless the research follows the rules below to convert it to a *de-Identified* format.

RULES TO CONVERT "CODED" PRIVATE INFORMATION OR SPECIMENS TO "DE-IDENTIFIED":

For **non-FDA regulated research**, the following rules apply for changing the status of private information or specimens from "coded" to "de-identified"; however, the IRB strongly recommends requesting an IRB determination to document whether such activities require IRB approval:

- Do NOT collect data or specimens specifically for the currently proposed research project through an interaction or intervention with the individual(s) about whom the data pertains.
- Establish an agreement, statement for the record, or a written document that prohibits the release of the key code to the investigators under any circumstances.
- The re-identification code:
  - May not be derived from or related to information about the individual or otherwise be capable of being translated to identify the individual (e.g., patient initials, DOB, SSN, partial SSN, scrambled SSN, Medical Record #, etc.),
  - Cannot be used or disclosed for any other purpose, and
  - The mechanism for re-identification cannot be disclosed.
- The individual creating the coded or de-identified data or specimens, such as an Honest Broker, must be a member of the workforce with a right to access the identifiable materials for a non-research purpose (e.g., clinical purpose, health care operations activity) and **CANNOT be an investigator** for the project. The Honest Broker may be recognized and acknowledge for their efforts in a publication but **CANNOT be an author**.

  Important notes, regarding investigators:

  - ✓ *The IRB considers the term investigator to include anyone involved in conducting the research.*
  - ✓ *The IRB does not consider the act of solely providing coded private information or specimens (for example, by a tissue repository) to constitute involvement in the conduct of the research. However, if an individual who provides coded information or specimens collaborates on other activities related to the conduct of this research with the investigators who receive such information or specimens, then the IRB would consider such additional activities to constitute involvement in the conduct of the research. Examples of such additional activities include but are not limited to: (1) the study, interpretation, or analysis of the data resulting from the coded information or specimens; and (2) authorship of presentations or manuscripts related to the research.*
- The individual providing the data set removes all HIPAA identifiers listed in Downstate HIPAA-6 policy:
  - Names.
  - All geographic subdivisions smaller than a State, including street address, city, county, precinct, zip code (except for the initial three digits if according to publicly available data from the Bureau of the Census the geographic unit formed by combining all zip codes with the same three initials digits contains more than 20,000 people).
  - All elements of dates (except year) for dates directly related to the patient, including date of birth, admission and discharge dates, date of death and all elements of dates indicative of ages over 89, except that such ages and elements may be aggregated into a single category of age 90 or older.
  - Telephone numbers.
  - Fax numbers.

- E-mail addresses.
- Social security numbers.
- Medical record numbers.
- Health plan beneficiary numbers.
- Account numbers.
- Certificate/ license numbers.
- Vehicle identifiers and serial numbers (including license plates).
- Device identifiers and serial numbers.
- Web Universal Resource Locators (URL's).
- Internet Protocol (IP) address numbers.
- Biometric identifiers, including finger and voice prints.
- Full face photographic images and any comparable images; and
- Any other unique identifying number, characteristic or code.

LIMITED DATA SET

A ***limited data set*** allows for retention of specific elements of identifying private information.

A ***limited data set*** is PHI that *excludes* the following direct identifiers of the individual, or of relatives, employees, or household members of the individuals:

1) Names.
2) Postal address information, other than town or city, State, and zip code.
3) Telephone numbers.
4) Fax numbers
5) Electronic mail addresses
6) Social security numbers
7) Medical record numbers.
8) Health plan beneficiary numbers
9) Account numbers
10) Certificate/license numbers
11) Vehicle identifiers and serial numbers, including license plate numbers.
12) Device identifiers and serial numbers.
13) Web Universal Resource Locators (URLs).
14) Internet Protocol (IO) address numbers.
15) Biometric identifiers, including finger and voice prints; and
16) Full face photographic images and any comparable images.

Note: The IRB considers a Limited data set as identifiable data under the HIPAA regulations. However, the IRB considers it a de-identified data set under the Common Rule if an Investigator cannot readily identify the individuals about whom the data pertains and does not have access to the key to any codes to identify the individuals.

Investigators at Downstate may use or disclose a limited data set when Downstate establishes a Data Use Agreement (DUA).

SUMMARY OF ACTIVITIES REQUIRING IRB APPROVAL

IRB approval is required for all FDA regulated investigations and FDA regulated activities. The Downstate IRB uses the definitions in the Common Rule and the HIPAA regulations to determine if any non-FDA regulated activity requires IRB approval. The IRB retains final

judgment as to whether a particular activity must obtain IRB approval under this policy consistent with the ethical principles of the Belmont Report.

Even when research is exempt from the federal regulations or when the activity does not meet the definition of human research, the HIPAA regulations still apply, if PHI is involved in a research activity. If PHI is involved, a HIPAA Wavier, HIPAA Authorization, BAA, DUA, Certification for PHI of Decedents, Subject Recruitment Authorizations, or another HIPAA instrument is usually required.

The activities that require prospective IRB review and approval are:

- Human research (including pilot studies, exempt research, clinical trials, or other clinical investigations, planned emergency research).
- The use of human specimens to evaluate the safety and effectiveness of an investigational agent.
- Use of a Humanitarian Use Device (HUD) for a clinical or research purpose (except IRB approval is not needed for certain exceptions for emergency use, but notification to the IRB is required within 5 days of use).
- Expanded access (compassionate use, preapproval access) to an investigational drug/biologic for treatment (except IRB approval is not needed for certain exceptions for emergency use, but notification to the IRB is required within 5 days of use).
- Research activities that involve an interaction or intervention with a living individual.
- Research activities that involve obtaining, accessing, using, reviewing, sharing, analyzing, or disclosing PHI, individually identifiable private data, identifiable sensitive information, or personal data, regardless of whether it is recorded or eventually de-identified.
- Research activities involving the use, analysis, or generation of identifiable biospecimens.
- Research requiring IRB approval as required by NYS Article 24A, the Common Rule, FDA regulations, foreign regulations, or tribal law passed by an official governing body of the American Indian or Alaskan Native tribe; and,
- Any activity which meets the definition of research under the Common Rule, regardless of whether it is supported or conducted by a federal department or agency or regulated by the FDA or NY State.

Activities that require IRB review and approval beyond the initial review include:

- Acknowledgements (e.g., notices from an external IRB, external reportable events, new training documents, etc.).
- Amendments (all changes, including staff changes) to previously approved non-exempt research.
- Amendments (some changes) to previously approved exempt research, when required by this policy (see below).
- Continuing review/progress reports, when required.
- Check-In reports, when required by the IRB.
- Reportable events.
- Closure (final) reports; or
- Other considerations, as described in this policy or regulations.

ACTIVITIES THAT DO NOT REQUIRE IRB REVIEW AND APPROVAL

For the purposes of this policy, the following Downstate activities **DO NOT** require IRB review and approval; however, it is best to submit an IRB Decision Aid (Application for a determination letter to state IRB approval is not required) for any activity described below, except for a preparatory to research activity.

Some activities might not require IRB submission, based on this policy; however, a Department or College may still mandate IRB review. The Downstate workforce must confirm with their business unit which activities need to be submitted, as these requirements can go beyond IRB policy and guidelines. When the IRB is aware of IRB reviews mandated by the Department, College, or Downstate Leadership, such requirements are outlined on the IRB website.

PREPARATORY TO RESEARCH ACTIVITIES

If an activity is limited to a "preparatory to research activity" (e.g., review of protected health information in preparation for research to determine if there are enough patients to recruit or records to review), IRB approval is not required, when the patients' clinicians are conducting this activity. If someone other than the patients' clinicians are accessing the patient's records, the investigator must complete the Researcher Certification for Reviews Preparatory to Research form and save it in the research record.

> *Example: An investigator needs to determine whether she will have enough patients to enroll into a new clinical trial with an inclusion criterion of sickle cell trait. She reviews the medical records to determine the number of active sickle cell trait patients at the University Hospital Brooklyn; however, she cannot contact the patients or record any patient identifiers. If she is not the clinician for the patients for whom the data pertains, she completes the Researcher Certification for Reviews Preparatory to Research form and saves it in her research records. Upon subsequently submitting an IRB application, she includes a copy of the completed form with the submission.*

Under the Common Rule and this policy, a "preparatory to research activity" is automatically "exempt" because identifiers are not recorded and therefore does not require IRB approval.

TIP: When carrying out a "preparatory to research activity" HIPAA identifiers CANNOT be recorded! For more information on how to keep the data de-identified, refer to the list of identifiers in the De-Identification of Information (HIPAA-6 policy).

CASE REPORTS OR CASE SERIES INVOLVING UP TO THREE INDIVIDUALS

IRB approval is not required for activities limited to patient case reports or case series involving up to three individuals, including relatives. Presentations or publications must ensure that no identifiable information is included.

Individual journals may require informed consent or HIPAA authorization; therefore, the project lead should consult the relevant journal regarding its specific requirements. If informed consent is necessary for publication, Downstate recommends utilizing the hospital's standard HIPAA Authorization Form. Alternatively, the project team may develop a simple consent form, which would not necessitate IRB review; however, the journal may require the use of its own form. *NOTE: If video or photographs are to be used for any marketing purposes, please contact the Office of Communications & Marketing for further guidance.*

ACTIVITIES THAT DO NOT MAKE DOWNSTATE ENGAGED IN HUMAN RESEARCH

Downstate IRB approval is not required when the workforce conducts activities which DO NOT makes Downstate engaged in human research (see OHRP guidance: Engagement of Institutions in Human Subjects Research (2008)). However, the IRB recommends the project lead obtain a copy of the external IRB approval for the activity if it includes human research and approval from the Department Chair or Dean when an activity involves interactions or interventions by the outside investigators.

SCHOLARLY AND JOURNALISTIC ACTIVITIES

Scholarly and journalistic activities (e.g., oral history, journalism, biography, literary criticism, legal research, and historical scholarship), including the collection and use of information, that focus directly on the specific individuals about whom the information is collected, do not need IRB approval.

PUBLIC HEALTH SURVEILLANCE ACTIVITIES

Public health surveillance activities may include the collection and testing of information or biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health authority. When such activities are limited to those necessary to allow a public health authority to identify, monitor, assess, or investigate potential public health signals, onsets of disease outbreaks, or conditions of public health importance (including trends, signals, risk factors, patterns in diseases, or increases in injuries from using consumer products), the activities do not require IRB approval. Such activities, including those associated with providing timely situational awareness and priority setting during an event or crisis that threatens public health (including natural or man-made disasters), do not need IRB approval.

COLLECTION AND ANALYSIS OF INFORMATION, BIOSPECIMENS, OR RECORDS BY OR FOR A CRIMINAL JUSTICE AGENCY

Collection and analysis of information, biospecimens, or records by or for a criminal justice agency for activities authorized by law or court order solely for criminal justice or criminal investigative purposes, do not need IRB approval.

AUTHORIZED OPERATIONAL ACTIVITIES

Authorized operational activities (as determined by each agency) in support of intelligence, homeland security, defense, or other national security missions, do not need IRB approval.

CLINICAL CARE

Nothing in this policy is intended to limit the authority of a clinician to provide medical care, including to the extent the clinician is permitted to do so under applicable federal, state, local law (including tribal law passed by the official governing body of an American Indian or Alaskan Native tribe) or Downstate policy.

OFF-LABEL USE OF AN FDA APPROVED DRUG OR BIOLOGIC

If a clinician wishes to use an FDA approved drug/biologic off-label for non-research purposes, the decision to do so is a clinical decision that does not require IRB approval; however, the clinician must comply with any necessary hospital policies including, when applicable, obtaining approval from the Pharmacy.

Off-label use for non-research purposes does not constitute research; therefore, the patient who receives the off-label drug or device cannot be a research participant. However, interventions or use of data from an off-label use for research must have IRB approval and may require an IND.

CHANGES NECESSARY TO ELIMINATE APPARENT IMMEDIATE HAZARDS OR TO PROTECT THE LIFE OR PHYSICAL WELL-BEING OF THE RESEARCH PARTICIPANT ENROLLED IN PREVIOUSLY APPROVED RESEARCH

Changes in a previously IRB approved research activity may be initiated without IRB review and approval of an amendment when the change is necessary to eliminate apparent immediate hazards or to protect the life or physical well-being of the research participant. The Principal Investigator is required to report any changes not approved by the IRB that are made to eliminate a hazard or protect the life or physical well-being of a research participant. This reporting must be done in accordance with the section on Reportable Events and within the specified time frame.

EMERGENCY USE OF AN INVESTIGATIONAL OR UNLICENSED DRUG, BIOLOGIC, OR DEVICE

Emergency use is the use of a test article (investigational or unlicensed drug, biologic, or device) for a patient in a life-threatening situation in which no standard acceptable treatment is available and in which there is not sufficient time to obtain IRB approval.

Life-threatening, as defined by FDA, includes the scope of both life-threatening and severely debilitating, as defined below.

- ***Life-threatening*** means diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted and diseases or conditions with potentially fatal outcomes, where the end point of clinical trial analysis is survival. The criteria for life-threatening do not require the condition to be immediately life-threatening or to immediately result in death. Rather, the subjects must be in a life-threatening situation requiring intervention before review at a convened meeting of the IRB is feasible.

- ***Severely debilitating*** means diseases or conditions that cause major irreversible morbidity. Examples of severely debilitating conditions include blindness, loss of arm, leg, hand or foot, loss of hearing, paralysis, or stroke.

TIP: The IRB can only authorize a single emergency use of an investigational agent per institution.
The clinician should contact the IRB to determine if the IRB has previously approved the one-time use mechanism.
In general, the IRB will acknowledge the use of a test article more than once if it is in the best interest of a patient. However, subsequent use without IRB approval may represent serious or continued non-compliance. If considered by the IRB to be serious or continuing non-compliance, the IRB must report the serious or continued non-compliance to the FDA.

FDA acknowledges, however, that it would be inappropriate to deny emergency treatment to a second individual if the only obstacle is that the IRB has not had sufficient time to convene a meeting to review the issue.

If a clinician intends to administer an unapproved test article (e.g., investigational drug, biologic, or device) in an **emergency**, the following steps must be followed to ensure compliance with institutional policy and **FDA regulations**:

1. OBTAIN INSTITUTIONAL APPROVALS PRIOR TO USE

- Secure approval from the Downstate's **Chief Medical Officer (or designee)** and the **Department Chair (or designee)** before proceeding with emergency use.
- The IRB recommends obtaining **written confirmation** of this approval (e.g., email or signed memo).

2. NOTIFY THE IRB

- Notify the **IRB Chair** of the intent to use the test article in an emergency as soon as possible prior to administration. Save a copy of this email for later submission to the IRB.

3. COORDINATE WITH THE MANUFACTURER

- Contact the **manufacturer or supplier** to ensure timely delivery of the test article.
- Confirm the manufacturer is willing to release the unapproved article in compliance with FDA regulations.
  - The manufacturer may request institutional assurance that the emergency use complies with all applicable **FDA and institutional policies**.
  - Upon request, the IRB can issue a letter stating that **there is insufficient time to obtain full IRB approval** before the emergency use.

4. CONTACT THE FDA, IF REQUIRED

- If the manufacturer has not obtained an **IND (Investigational New Drug)** or **IDE (Investigational Device Exemption)** for the test article, the clinician must contact the **FDA directly** to obtain:
  - An **Emergency IND** (per 21 CFR 312.310), or
  - An **Emergency IDE** (per 21 CFR 812.35(a)).

5. OBTAIN INFORMED CONSENT WHEN FEASIBLE

- Whenever possible, obtain **prospective informed consent** from the **adult** patient, or the **parent of a child along with child assent**, as applicable.
- If informed consent is **not feasible**, the test article may be used without consent only if both the treating physician and an independent physician (not involved in the patient's care or study) **certify in writing**, in the patient's medical record, all the following:
  - The patient is in a **life-threatening condition** requiring immediate use of the test article.
  - The patient is unable to provide informed consent due to their medical condition, such as the inability to communicate.

- There is **insufficient time** to obtain consent from a legally authorized representative (LAR).
- No alternative approved therapy offers an equal or better chance of saving the patient's life.

6. SUBMIT POST-USE REPORT TO THE IRB

- Within **5 calendar days** of administration, submit a written report to the **IRB** through the IRB electronic system using the **Application for Reportable Event**.
  - The report must include:
    - Patient coded ID. Do not include PHI in IRBNet.
    - Date of administration
    - Clinical justification for emergency use
  - Include a copy of the communication from the Chief Medical Officer (see item 1, above)
  - Include a copy of the communication to the IRB Chair (see item 2, above)
- The IRB will issue an **acknowledgment** of the emergency use.

7. COMPLY WITH FDA POST-USE REPORTING REQUIREMENTS

- Follow applicable **FDA regulations** for emergency use reporting:
  - **Drugs/Biologics**: 21 CFR Part 312
  - **Medical Devices**: 21 CFR Part 812
  - **HUD/HDE Devices**: 21 CFR Part 814

8. FUTURE USE

- If future emergency use of the same test article is anticipated, submit a **prospective IRB application** to formally request approval for additional uses.

OTHER ACTIVITIES THAT DO NOT REQUIRE DOWNSTATE IRB APPROVAL

In general, the following activities do not require Downstate IRB approval; however, it is best to submit an IRB Decision Aid (Application for a determination letter to state IRB approval is not required) for any activity described below:

- A Healthcare Operations Activity (HOA) (e.g., Performance Improvement, Resident Training) NOT designed to develop NOR contribute to generalizable knowledge. For more information, refer to the definition of "generalizable" and the examples provided with the definition.
- Activities that do not involve systematic investigations.
- Activities limited to using data from deceased individuals, provided the data does not contain any PHI or involve accessing or using PHI.
- Activities limited to using data from individuals who have been deceased for more than 50 years.
- Activities that includes using or accessing PHI from individuals who have been deceased for less than 50 years, when a Researcher Certification for PHI of Decedents Form is submitted and approved by the Privacy Officer (or Downstate IRB).

- Activities limited to de-identified specimens obtained from a producer or supplier (e.g., commercial cell line).
- Activities are limited to a pilot activity, feasibility activity, or evidence-based practice activity not involving human research as defined by this policy.
- Activities that DO NOT involve interactions or interventions, but include the following types of data sets, including when such data is about any specimens:
    - Limited data set when a Data Use Agreement (DUA) is in place, assuming the investigator cannot readily identify the individuals about whom the data pertains and does not have access to the key to any codes to identify the individuals (as noted below),
    - De-identified data, or
    - Coded private information when the code cannot be released to the investigators, for example through one of the following:
        - An agreement is in place to prohibit the release of the code to the investigators,
        - A written document or policy is in place to prohibit the release of the code to the investigators, or
        - An Independent Honest Brokers Assurance Agreement is in place to prohibit the release of the code to the investigators.

IRB APPLICATION SUBMISSION PROCESS

IRB AND PRIVACY BOARD MEETING SCHEDULE

The IRB posts the meeting schedule and deadlines for submitting a full board IRB application on the Downstate IRB website.

Note: Exempt and expedited studies are not reviewed by the full board unless an IRB Member refers the review to the full board process, or as otherwise required by this policy or guidance posted on the IRB website.

IRB CONSULTATIONS

An investigator may consult with the IRB to answer specific questions about the IRB policies and procedures at any time. The IRB encourages individual appointments with the IRB administrative staff for first-time submissions.

ELECTRONIC SUBMISSIONS AND MANAGEMENT OF DOWNSTATE IRB ACTIVITIES

BASIC PROCEDURES FOR IRB SUBMISSIONS

1. Check the Downstate IRB Electronic Submission Process website.
2. Follow website instructions and include all required materials. Use the website's tips for a smooth review.
3. Contact the IRB with questions or for help.
4. Complete all listed requirements before submitting to the IRB.
5. Quickly answer any IRB requests for information to keep the review moving.

TYPES OF DOWNSTATE IRB APPLICATIONS

Multiple types of IRB applications are accessible at Step 11 of the IRB Electronic Submission Process website. As of this policy update, the following application forms are available for Human Research submissions; however, please consult the website for the most up-to-date versions.

- Form 11-A1: Application for Exempt Review
- Form 11-A1B: Application for Exempt Review - DOJ/DIJ Funded Research Only
- Form 11-A2: Application for Expedited or Full Review
- Form 11-A3: Application for External IRB Oversight (see additional information in next section)
- Form A7: Application for Independent Honest Broker Assurance Agreement
- Form 11-8: Exclusion of Pregnant People and/or Plans to Study Outcomes of Unexpected Pregnancies
- Form 11-9: Research involving Pregnant People and/or Fetuses

The following applications are available for Expanded Access (treatment) and Clinical use of a Humanitarian Use Device:

- Form 11-A5: Application for Expanded Access to Investigational Drug/Biologic for Treatment Use
- Form 11-A6: Application for HUD for Clinical Purposes

The following applications are available for acknowledgement or IRB determinations of Not Research, Not Human Research, or Institution Not Engaged:

- Form 11-4C: Checklist for Acknowledgment of a SELF-DETERMINATION of "Not Research" or "Not Human Research" and Attestation of Institutional Compliance
- FORM 11-A4Q: Application for an IRB Determination of "NOT Research" or "NOT Human Research" for a Quality Improvement, Quality Assurance, Performance Improvement, or Evidence Based Practice Activity.
- Form 11-A4: Application for Determination Letter (IRB Decision Aid) for "Not Research, Not Human Research, or Institution Not Engaged"
- Form 11-10: Application For Downstate Workforce Activation of Exempt Research or IRB Determinations (Not Research, Not Human Research, or Downstate Not Engaged) Approved by an (External) Reviewing IRB

Post-IRB approval applications may be downloaded from the IRB website and include the following:

- Form 20-B1: Application for Acknowledgment
- Form 20-B2A: Application for Amendment
- Form 20-B2B: Application for Amendment - STAFF CHANGES ONLY
- Form 20-B3: Application Form for Reportable Event
- Form 20-B4: Application for Continuing Review/Check-In/Study Closure/Re-Activation

The following applications are available when participating in the Quality Assessment Program:

- Form 21-1: Quality Assessment Form
- Form 21-2: Corrective & Preventative Action Plan (CAPA) Form

For information on selecting the appropriate application, completing fillable PDF forms, and required submission materials, consult the instructions and guidance provided on the IRB website or contact the IRB Office.

ADDITIONAL PROCEDURES FOR EXTERNAL REVIEWING IRB

Refer to the Downstate IRB Electronic Submission website for guidance on using an external reviewing IRB (i.e., commercial IRB, multisite IRB, sIRB) for multi-site research, including the process for establishing IRB Reliance Agreements.

Downstate must use of a single IRB (sIRB) for multi-site research for all human research covered by federal funding and it is anticipated that the FDA will soon require the use of an sIRB for multi-site FDA regulated Clinical Investigations.

For certain research, more than single IRB review may be required by law (e.g., tribal law passed by the official governing body of a Native American or Alaska Native tribe, research for which any federal department or agency supporting or conducting the research determines and documents that the use of a single IRB is not appropriate).

ADDITIONAL PROCEDURES FOR EXPANDED ACCESS (COMPASSIONATE USE OR PREAPPROVAL ACCESS) TO AN INVESTIGATIONAL DRUG/BIOLOGIC FOR TREATMENT USE

Full IRB review and approval is required for Expanded Access (Compassionate Use) to investigational drug/biologic for treatment use, except for Emergency Use situations or when Form FDA 3926 is approved by the FDA for **individual patient expanded access use** of an investigational drug.[20] The Clinician submits the Form 11-A5, Application for Expanded Access To Investigational Drug/Biologic For Treatment Use.

TIP: The FDA has created a mechanism for IRB Chair approval of individual patient expanded access treatment use of investigational drugs. To request this, the physician (or sponsor) must complete Form FDA 3926. For more information, see FDA Guidance: Expanded Access to Investigational Drugs for Treatment Use – Q&A.

When requesting the IRB approval for expanded access for treatment use, COI disclosures are not required, unless a clinician on the IRB application has or declares a conflict of interest. Human research protections training is not required but recommended.

ADDDITIONAL PROCEDURES FOR HUD APPLICATIONS

HUDs are medical devices intended to benefit patients in the treatment or diagnosis of diseases or conditions that affect or are manifested in not more than 8,000 individuals in the United States per year. In seeking marketing authorization under an HDE application, the first step is the preparation and submission of a HUD designation request to FDA's Office of Orphan Products

20 Waiver of IRB Requirements for Drug and Biological Product Studies

Development (OOPD). The IRB should be cognizant that FDA has made a determination that the probable benefits to health outweigh the probable risks for use of the HUD only within its approved indication(s).[21]

When the FDA has issued an HDE, that means that the device is approved by the FDA for marketing and the use of the HUD does not constitute research. Therefore, the FDA and its HDE regulations do not require informed consent as defined by the FDA's research regulations (21 CFR 50). However, the Downstate IRB requires documented consent from patients prior to the clinical use of a HUD, whenever possible. Research use of a HUD requires that subjects provide a standard research consent.

The Downstate IRB's approval for the "use" of a HUD to treat or diagnose patients while providing clinical care does not mean that there has been IRB approval of a clinical investigation involving the HUD. The IRB is not required to review and approve each individual use of a HUD, nor is it required to audit medical records of patients who receive a HUD.

NOTE: There is a distinction between "use" (in the practice of medicine) of a HUD and "investigational use/clinical investigation" of a HUD. If a HUD will be used for a clinical investigation (e.g., effectiveness data is collected for an FDA Premarket Approval), a full board IRB application must be completed and reviewed under an IDE if it is SR device study. An informed consent document is always required for a "clinical investigation" of a HUD.

1) IRB Submission:
   a) There are 3 pathways for an IRB submission for an HUD:
      i) A Clinician may submit a request for IRB approval to "use" a Humanitarian Use Device (HUD) for the practice of medicine , using "Form 11-A6: Application for HUD for Clinical Purposes."
      ii) A Clinician may "use" a Humanitarian Use Device (HUD) for the practice of medicine in certain emergencies where prior IRB approval is not required or when there is no time for IRB approval. For emergency situations, refer to the Emergency Use section of this policy.
      iii) A Clinical Investigator may request approval of an HUD is involved in a clinical investigation, using Form 11-A2 or 11-A3, as applicable. The IRB submission requirements are outlined in the IRB Application for HUDs.
   b) The appropriate materials, as applicable, must be submitted to the IRB to request to use a HUD:
   1. Attach a CV or NIH Biosketch with relevant publications, or a statement of qualifications detailing education, training, credentials, and experience that demonstrate clinician/investigator qualifications.
      i) A copy of the HDE approval order,
      ii) HDE #,
      iii) A description of the device;
      iv) The product labeling;
      v) The patient information packet that may accompany the HUD;
      vi) A sample consent form for the use of the HUD in clinical care, if applicable or when required by the IRB,

21 FDA Guidance Document: Humanitarian Device Exemption (HDE) Program

vii) A summary of how the physician proposes to use the device, including a description of any screening procedures, the HUD procedure, and any patient follow-up visits, tests or procedures.
viii) Plans for billing the patient
ix) If applicable, provide written information that describes how the physician/investigator wants to use a HUD outside its FDA approved indication(s).

c) Conflict of Interest Disclosures
   i) Follow the same practice for COI disclosures if this submission is a Clinical Investigation (research) with an HUD.
   ii) When requesting the use of a HUD for the practice of medicine, Downstate COI disclosures to the Downstate financial COI committee are required, when a clinician on the IRB application has or declares a conflict of interest.

d) Human research protections training
   i) Follow the same requirements if this submission is a Clinical Investigation (research) with an HUD. The optional CITI training module on HUDs is recommended.
   ii) When requesting the use of a HUD for the practice of medicine, the standard IRB training is recommended but not required. The optional CITI training module on HUDs is recommended.

APPLICABLE CLINICAL TRIALS AND REGISTRATION ON CLINICALTRIALS.GOV

ClinicalTrials.gov is a public registry for publicly and privately supported research studies conducted in the United States and around the world. The FDA's Final Rule regarding "Applicable Clinical Trials (ACT)" requires the responsible party to register the following ACTs at www.ClinicalTrials.gov:

- All NIH funded Clinical Trials
- Any ACT initiated after September 9, 2007, which meets the requirements of FDAA 801.
- An ACT initiated after January 18, 2017, defined by the Clinical Trials ACT Checklist.
- A clinical trial which meets the criteria of the VA, CMS, WHO, PCORI, or ICMJE journals.

For ACTs, the exact following language is included in 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.

Use the following criteria to determine the Responsible Party at Downstate:

1. The sponsor (funding agency) - either the holder of the IND or the IDE.
2. Downstate PI that initiates the Clinical Trial when awarded a grant (i.e., the NIH grantee). ***NOTE:*** *In the case of Cooperative Agreements, the PI and study team must agree ahead of time who will be the responsible party. It will not be the NIH.*
3. The funder of a procurement agreement (i.e., funding by a contract). However, determine in advance if NCI is the responsible party, which may be the case in certain instances.
4. The provider of the study drug (typically the industry or pharmaceutical company providing the funding). The contract should clearly outline the responsible party. ***NOTE:*** *In the case of an investigator-initiated clinical trial, the Downstate PI is the responsible party, regardless of whether an IND is involved*

If a Downstate PI is the "responsible party," (s)he must contact the Downstate Protocol Registration and Results System (PRS) Administrator to establish a user name and password to

register the ACT in the PRS. The responsible party must register the ACT: 1) before enrolling the first research participant, when there are plans to publish results in an ICMJE journal, or 2) within 21 days after enrolling the first research participant. In addition, the responsible party must submit administrative and scientific information including adverse events and results of the research within the required reporting timelines.

CAUTION:

Failure to meet FDA requirements for an Applicable Clinical Trial (ACT) may result in serious consequences, including but not limited to:

- **Immediate suspension of all federal funding** to Downstate by government agencies.
- **Civil monetary penalties** of up to **$250,000** against the responsible party, or **$10,000 per day** assessed against the Downstate department or college associated with the non-compliant investigator.
- **Prohibition from publishing** results in journals that follow the standards of the **International Committee of Medical Journal Editors (ICMJE)**.
- **IRB enforcement actions**, including:
  - Suspension or termination of the study.
  - Placement of an enrollment hold.
  - A formal IRB determination of **serious or continuing non-compliance**.

Such IRB actions must be **reported to federal oversight agencies and funding sponsors**, which may further impact institutional research privileges and reputational standing.

INVESTIGATORS AND RESEARCH TEAM

PRINCIPAL INVESTIGATOR

The principal investigator (PI) oversees scientific, technical, and day-to-day management of the research. The PI must have appropriate qualifications and experience. The PI holds the lead responsibility for the research protocol, including oversight of its implementation and the activities of other investigators and research staff, and management of any funding associated with the protocol, and all compliance.

PIs should include one or more additional qualified co-investigator(s) if they need incorporate additional skills beyond those held by the PI. In general, PIs should be on-site where the research takes place at least 50% of their time or include additional qualified co-investigator(s) or multiple PIs to address any safety and leadership concerns.

PI STATUS

For the purposes of this policy, the Principal Investigator (PI) listed on an IRB application must meet at least one of the following eligibility criteria:

- Be a member of the Downstate faculty.
- Hold emeritus status as a Downstate faculty member.
- Be a clinician holding clinical privileges at NYC Health + Hospitals, Kings County.

- Be a faculty member under recruitment to Downstate who has received written approval to serve as PI from a Dean or Department Chair, via memo or email.
- Qualify to be a PI at an external site, which includes an activity which makes Downstate engaged in human research (see OHRP guidance: Engagement of Institutions in Human Subjects Research (2008)). This includes scenarios where federal funding or support is provided to Downstate or when the research involves any of the following co-investigators or key personnel:
    - An employee of SUNY Downstate,
    - An employee of the Research Foundation for SUNY Downstate,
    - A resident or fellow participating in a GME program affiliated with Downstate,
    - A student enrolled in a Downstate academic program.

The PI must provide a CV, NIH Biosketch, or other statement of qualifications showing education, training, credentials, and experience that qualifies the investigator to be an expert in the research. For clinical investigations the PI/CI must be an expert in the research of the applicable drug, biologic, or device under investigation.

A PI who is an external employee to Downstate and listed on a Downstate IRB application agrees to abide by Downstate policies for the study, through an Independent Investigator Agreement or the institution where an external PI is employed, must execute an IRB Reliance Agreement, as applicable to the submission.

Multiple Co-PIs are not permitted on a study which is funded or supported extramurally. The PI must be the same PI as the PI listed on a grant, award, or other type of funding or support agreement.

CLINICAL INVESTIGATOR (FDA REGULATED STUDY)

The table below includes the regulatory definitions for Clinical Investigator/Investigator as described in FDA regulations.

Regulation	Regulatory Definition (Exact Text)
21 CFR 56 (IRB)	21 CFR 56.102(h)[22] ***Investigator*** means an individual who actually conducts a clinical investigation (i.e., under whose immediate direction the test article is administered or dispensed to, or used involving, a subject) or, in the event of an investigation conducted by a team of individuals, is the responsible leader of that team.
21 CFR 312 (IND - Drugs/Biologics)	21 CFR 312.3(b)[23]: "***Investigator*** means an individual who actually conducts a clinical investigation (I.E., under whose immediate direction the drug is administered or dispensed to a subject). In the event an investigation is conducted by a team of individuals, the investigator is the responsible leader of the team. "Subinvestigator" includes any other individual member of that team."

22 21 CFR 56.102 Definitions
23 21 CFR 312.3 (b) Definitions and interpretations

21 CFR 812 (IDE - Investigational Devices)	21 CFR 812.3(i)[24]: "***Investigator*** means an individual who actually conducts a clinical investigation, i.e., under whose immediate direction the test article is administered or dispensed to, or used involving, a subject, or, in the event of an investigation conducted by a team of individuals, is the responsible leader of that team."

CLINICAL INVESTIGATOR (CI) STATUS

For this policy, for **FDA regulated research**, a Clinical Investigator (CI) on an IRB application must meet the following criteria and must submit supporting documentation to the IRB for verification:

- Must have PI status.
- Must be a licensed practitioner with appropriate credentials, when applicable, as approved by the Department Chair or Dean, which may be verified upon request by the IRB. The IRB may contact the Downstate Medical Board for confirmation of credentials. The IRB may request a copy of the practitioner's license or medical board appointment from the CI or Institution.
- Be part of the Downstate Workforce or authorized at a Reliance Agreement site; external CIs must be eligible to be a CI at their home institution.
- Sponsor approval required.
- IND studies: complete FDA Form 1572.
- IDE studies: sign investigator agreement with sponsor.
- Possess appropriate training, education, and experience for FDA-regulated research, including when applicable (i.e., for higher risks, vulnerable populations, novel technologies) prior clinical experience with the test article or study procedures.[25]
- Hold necessary licensure if clinical procedures or oversight are involved, confirmed by Department Chair via IRB e-signature.
- Meet all institutional credentialing and privileging requirements, confirmed by Department Chair via IRB e-signature.

Note: The requirements and responsibilities of a PI noted in this policy, IRB Applications, and on the IRB website also apply to CIs.

SPONSOR-INVESTIGATOR

Sponsor-Investigator[26] means an individual who both initiates and actually conducts, alone or with others, a clinical investigation, i.e., under whose immediate direction the test article is administered or dispensed to, or used involving, a subject. The term does not include any person other than an individual, e.g., it does not include a corporation or agency. The obligations of a sponsor-investigator under FDA regulations are both those of a sponsor and those of an investigator.

MULTIPLE PRINCIPAL INVESTIGATORS

24 21 CFR 812.3(i) Definitions
25 IRB Responsibilities for Reviewing Qualifications of Investigators, Adequacy of Research Sites, and the Determination of Whether an IND/IDE is Needed
26 21 CFR 56.102 Definitions

Typically, only one individual may serve as Principal Investigator (PI) per IRB application. However, pursuant to this policy, Downstate permits the designation of multiple PIs on an IRB application when multidisciplinary projects necessitate shared responsibility for the scientific and technical direction of the research.

Applicants opting for a multiple PI model must clearly articulate their rationale within the IRB submission, providing detailed descriptions of each PI's roles, responsibilities, and collaborative relationship. All designated PIs are required to possess appropriate qualifications for their respective positions and must contribute meaningfully toward achieving the research objectives. Unless specified otherwise, the first PI listed in the IRB application who holds an affiliation with the submitting institution will function as the contact PI.
Unless specified in a grant or award, multiple PIs cannot be listed for funded or sponsored research.

Multiple Co-CIs are not permitted on an FDA Regulated study.

PRINCIPAL INVESTIGATOR (PI) RESPONSIBILITIES

The Principal Investigator (PI) is required to adhere to professional and ethical standards when conducting research. Investigator responsibilities are outlined in this policy, the IRB application, and the research protocol; additional responsibilities may be specified by regulations, sponsors or agreements as applicable. As applicable or relevant to the research, PI responsibilities include, but are not limited to, the following:

ETHICAL CONDUCT & PARTICIPANT PROTECTIONS

- Conduct research ethically, prioritizing the rights and welfare of participants.
- Design scientifically sound studies that minimize risk.
- Use procedures already performed for diagnostic or treatment purposes when appropriate.
- Protect participant privacy and ensure data confidentiality.
- Implement safeguards for vulnerable populations.
- Maintain a process for addressing participants or information requests.
- Ensure the availability of medical or psychological care resulting from participation.
- Ensure the availability of adequate resources for conducting the study and safeguarding research participants. This includes access to an appropriate population for recruitment, sufficient time allocation, qualified personnel, and suitable facilities.

IRB OVERSIGHT & COMPLIANCE

- Obtain prior written IRB review and approval for any research involving human participants or their data.
- Comply with all IRB determinations, conditions, and requirements.
- Submit accurate IRB materials and conduct research as approved.
- Request IRB approval of amendments, including those affecting funding status or risk, before implementing any changes to approved research.

- Promptly secure IRB review and approval of proposed modifications prior to implementation, except in circumstances where immediate action is required to mitigate immediate hazards or to protect the life or physical well-being of the research participant.
- Review IRB-approved documents and request corrections if needed.
- Report all reportable events, such as unanticipated problems, adverse events, or non-compliance to the IRB within specified deadlines, including applicable corrective action plans.
- Submit progress reports, requests for continuing review, check-in reports, study closures, or reactivations on a timely basis.
- Notify the IRB of relocation of research activities or PI extended leave.
- Secure IRB approval for multi-site studies and maintain consistency across sites.
- Fully participate in Quality Assessment Program (QAP) reviews and provide timely responses to the IRB, including any required Corrective and Preventative Action Plan (CAPA).

RECRUITMENT & ENROLLMENT

- Use only IRB approved recruitment methods and advertisements.
- Recruit research participants in a fair and equitable manner and according to IRB approved methods.

INFORMED CONSENT PROCESS

- Ensure only IRB-approved investigators obtain informed consent.
- Obtain and document informed consent, permissions, and HIPAA authorizations using IRB-approved forms.
- Provide copies of signed consent forms to participants.
- Store original signed consent forms securely.
- Do not enroll participants prior to consent unless waived by the IRB.

RESEARCH TEAM OVERSIGHT

- Maintain a qualified and trained research team.
- Clearly assign responsibilities and ensure staff understand the protocol.
- Verify credentials and licensure of those performing procedures that require them.
- Ensure all key personnel receive training in ethical and regulatory research practices.
- Maintain current documentation of staff CVs/resumes, credentials, and training certifications.

REGULATORY & INSTITUTIONAL COMPLIANCE

- Comply with all relevant Federal, State, institutional, and sponsor requirements.
- Follow FDA regulations for clinical trials and device studies.
- Submit appropriate FDA forms (e.g., 1571, 1572) as required.
- Complete required ancillary reviews and obtain institutional approvals (e.g., STAR approval at NYC H+H, Kings County).
- Adhere to institutional information security and data retention policies, including secure backups.

- Use proper billing practices aligned with CMS and institutional policies.
- Cooperate with audits, monitoring visits, and investigations.
- Disclose conflicts of interest and any new significant conflicts of interests in a timely manner.

CLINICAL TRIAL & DRUG/DEVICE OVERSIGHT

- Ensure authorized prescription and administration of investigational drugs, biologics, and devices.
- Supervise the use and handling of these products per regulatory and protocol requirements.
- Register Applicable Clinical Trials at ClinicalTrials.gov, keeps current, and complete FDA Form 3674.
- Include required language in consent documents for Applicable Clinical Trials.
- Obtain Certificates of Confidentiality if necessary.

STUDY CONDUCT & DOCUMENTATION

- Ensure adequate participant recruitment, time, staff, and facilities to conduct research.
- Maintain secure and complete research records in accordance with institutional and regulatory standards.
- Provide participant enrollment lists upon request, as permitted by policy.
- Secure approvals for budgets, contracts, or required agreements, such as Material Transfer Agreement (MTAs), Clinical Trial Agreement (CTA), Data Use Agreement (DUA), Data Agreement (DA), Business Associate Agreement (BAA), Facility Use Agreement (FUA), Confidentiality Agreement (CA).
- Ensure plans to monitor the data collected for the safety of the participants
- Ensure proper use, review, and documentation of laboratory reports.

ADMINISTRATIVE AND SYSTEM RESPONSIBILITIES

- Electronically sign and submit the IRB application using the designated system.
- Obtain required electronic or alternative signatures from Department Chairs and other reviewers.
- Complete all required ancillary reviews prior to initiating research.

CO-INVESTIGATORS AND KEY PERSONNEL

Co-investigators and key personnel assist the PI in fulfilling his/her responsibilities as outlined in the PI Responsibilities section of this document. For the purposes of this policy, the Downstate IRB follows the OHRP Investigator Responsibilities FAQs (Who are “investigators”?) to determine who are investigators (or key personnel), whose involvement would include:

- Obtaining information about living individuals by intervening or interacting with them for research purposes.
- Obtaining identifiable private information and identifiable biospecimens about living individuals for research purposes.
- Obtaining the voluntary informed consent of individuals to be research participants in research; or

- Studying, interpreting, or analyzing identifiable private information or data for research purposes.

Co-investigators and key personnel are responsible for research protocols with research participants, and must have suitable qualifications, including: (1) familiarity with research methods and procedures; (2) familiarity with research regulations and other applicable regulatory requirements; and (3) certificates for required training courses.
The PI may wish to distinguish between co-investigators and key personnel on the IRB application, as it may be a preference of a sponsor or a publication; however, for the purpose of this policy, they are treated the same, even if they are distinguished separately on the IRB application or related materials.

The IRB application must list Hospital staff, research coordinators and research assistants as co-investigator or key personnel if they conduct human research including any of the activities described above; however, the FDA provides an exception for delegating clinical trial tasks to hospital staff and residents, as described in the section below.
Co-investigators and key personnel can include physicians, scientists, nurses, administrative staff, teachers, and students, among others.

DELEGATION OF CLINICAL TRIAL TASKS TO HOSPITAL STAFF AND RESIDENTS

For FDA regulated clinical trials (IND, IDE, NSR device studies), the PI may delegate certain tasks; however, the PI is responsible for all research activities and must provide adequate supervision of those who tasks are delegated. For more information on investigator responsibilities, see FDA Guidance for Investigator Responsibilities and the FDA FAQs for Form 1572.

The PI must ensure that any individual performing a delegated task is appropriately qualified, by education, training, experience, licensure, certification, or credentialing, to perform the delegated task. The IRB strongly encourages the PI to maintain a delegation log in the research record to describe the delegated tasks, qualifications, and training, to avoid any appearance of non-compliance. In all cases, a qualified clinician is responsible for all trial-related medical decisions and care.

Hospital staff (e.g., nurses, residents, fellows, or office staff) who have only an occasional role in the conduct of the research by providing ancillary or intermittent care and do not make a direct and significant contribution to the clinical data do not need to be listed on the IRB application for FDA regulated clinical trials. This includes for example, an on-call physician who temporarily dealt with a possible adverse effect or a temporary substitute for any research staff. When it is difficult to identify rotational staff (e.g., residents, nurses) who might perform specified protocol procedures or collect clinical data, rather than listing the specific names of the rotational staff on an IRB application, please document the names of such individuals along with the procedures they may perform in the research records.

The decision about whether to list other hospital staff (e.g., pharmacist, nurse, medical technologist, x-ray technician, sonographer, research coordinator, statistician, etc.) as co-investigator or key personnel on the IRB application is a matter of judgment, dependent upon the contribution that the individual makes to the study. For example, a pharmacist may prepare test articles and maintain drug accountability for many clinical studies that are ongoing concurrently at an institution. Because the pharmacist would not be making a direct and significant

contribution to the data for a particular study, it would not be necessary to list the pharmacist as a co-investigator in the IRB application; however, the IRB recommends including the pharmacist's name(s) in the investigator's study records or listing them as non-research staff on the IRB application.

Generally, a research coordinator has a greater role in performing critical study functions and making direct and significant contributions to the data. For example, if a research coordinator is recruiting research participants, collecting, or evaluating study data, and maintaining study records, (s)he may be listed as co-investigator or key personnel. Some PIs prefer to list research coordinators as research staff when they have more of an intellectual role or can defend the results of the study.

Delegated staff members are encouraged to take CITI training but are not required to do so.

NON-RESEARCH STAFF

In general, individuals that carry out activities to support a research study who are doing something that would **not** make them an investigator as described above, are not investigators on an IRB application, and therefore would not need to complete the requirements (e.g., training and COI disclosures) of an investigator. The PI may list these individuals as non-research staff, if desired.

Non-research staff may perform routine clinical or administrative services to support research (e.g., perform a clinical lab test, take an x-ray, perform healthcare operations activities, etc.) provided these are part of their routine responsibilities without being listed as an investigator; however, they cannot collaborate as an investigator or conduct any research activities.
Some examples of non-research activities, may include, but are not limited to the following:

- Performing a commercial or other service (e.g., qualified laboratory services, transcription services, obtaining blood or urine, radiology services, nursing services) for investigators, provided all the following conditions are met:
    - the services performed do not merit professional recognition or publication privileges.
    - the services performed are typically performed by those institutions for non-research purposes; and
    - the individual does not administer any study intervention being tested or evaluated under the protocol, or
- Releasing identifiable information, materials, or specimens to investigators,
- Releasing de-identified information, materials, or specimens to investigators (e.g., an employee who serves as an honest broker),
- Reviewing identifiable information for the purposes of auditing or other healthcare operations activities,
- Receiving de-identified specimens for the purposes of analytical testing, or
- Reviewing de-identified data for the purpose of authoring, describing, or presenting a research study.

Individuals performing operations activities relevant to the research (e.g., research audit, audit preparation, IRB review, protocol development, scientific review, methodological review, consulting, or advising) are not considered research staff, if they do not perform or conduct any activities described under the above section regarding "Co-Investigators and Key Personnel."

Non-Research staff members are encouraged to take CITI training but are not required to do so.

KEY CONTACT OR IRB LIAISON

The PI may list a Key Contact or an IRB liaison on the IRB application and registration form to have access to the IRB application materials, or a member of the study team can share access in the electronic IRB submission and reporting system. They may review these materials as a Healthcare Operations Activity. Examples of key contacts include administrative personnel that have a need to follow or assist in the research but not conduct investigator activities.

External sites with an IRB Authorization Agreement may have a liaison who receives copies of communications from the IRB. The individuals may have access to the study files, regardless of whether the PI includes them on the IRB application.

ADEQUACY OF RESEARCH SITE

When the IRB is not familiar with the research site, the IRB may require additional assessment of the site's adequacy. The IRB may need to assess the adequacy of the facility's staff and medical equipment, including the adequacy of emergency or specialized care, if the need arises. If needed, the IRB may require a statement from the research site indicating the site is adequate or require a description from the PI that includes a description of the facility where the research will take place, including staffing and resources relevant to the research under review.

GENERAL CRITERIA FOR IRB APPROVAL

Before granting approval, the IRB must determine all the criteria for IRB approval are satisfied, as specified in federal and state regulations. When the research does not meet the criteria for approval, the IRB requests revisions.

EXEMPT RESEARCH

Some human research activities are exempt from HHS or FDA federal regulations; however, the Downstate still has oversight of these activities. In general, the IRB prospectively determines when the research is exempt. However, an independent determination by an investigator is acceptable solely for the purpose of making and documenting representations for reviews preparatory to research, as described elsewhere in this policy.

To approve exempt human research, except for Reviews Preparatory to Research, the IRB must determine that the research as described in the IRB application and associated materials meets the specific criteria for exempt research.

The HIPAA regulations apply to exempt research that involves PHI and, therefore, the IRB will confirm the appropriate and relevant HIPAA protections are in place (e.g., HIPAA authorization, HIPAA waiver, DUA, BAA, Certification for PHI of Decedents, Subject Recruitment Authorizations, etc.) for such research.

The IRB will confirm the research meets all requirements and verify it meets the criteria for exempt research; however, it may require additional protections, particularly when vulnerable populations are involved.

When an exempt study requires "limited IRB review" as defined by the Common Rule for certain Exempt studies, an IRB member must determine that there are adequate provisions to protect the privacy of research participants and to maintain the confidentiality of the data. Limited IRB review does not preclude an IRB member from requiring other reasonable protections outside of the context of privacy or confidentiality, as applicable to the research.

NON-EXEMPT HUMAN RESEARCH

To approve non-exempt human research or FDA regulated clinical investigations the IRB must determine all the following requirements (as described in the Common Rule at 45 CFR 46.111 or FDA regulations at 21 CFR 56.111) are satisfied, based on review of IRB application materials.

- Risks to research participants are minimized:
  - by using procedures which are consistent with sound research design, and which do not unnecessarily expose research participants to risk, and
  - whenever appropriate, by using procedures already being performed for diagnostic or treatment purposes.

  Note: To evaluate the above for a clinical investigation involving an IND, the IRB may wish to obtain and review the following information, as applicable for the review:
  - *Published literature about the chemistry, manufacturing, and control of the drug substance and product.*
  - *A summary of previous human experience with the drug product.*
  - *Sufficient information regarding the source, purity, quality, and method of preparation and delivery of the drug used in the research; and*
  - *Information regarding the pharmacology and toxicity of the drug product in animals.*
- Risks to research participants are reasonable in relation to anticipated benefits, if any, to research participants, and the importance of the knowledge that may reasonably be expected to result. In evaluating risks and benefits, the IRB considers only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies research participants would receive even if not participating in the research). The IRB does not consider possible long-range effects of applying knowledge gained in the research (e.g., the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.
- Selection of research participants is equitable. In making this assessment the IRB considers the purposes of the research, the adequacy of inclusion and exclusion criteria, and the setting in which the research will be conducted. The IRB is particularly cognizant of the special problems of research that involves a category of research participants who are vulnerable to coercion or undue influence, such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons. For FDA regulated clinical trials, vulnerable populations also include pregnant people, mentally disabled persons, and handicapped individuals.
- Informed consent (and HIPAA research authorization, when applicable) will be sought from each prospective research participant or his/her LAR/surrogate, in accordance with, and to the extent required by the federal regulations and will be appropriately documented, unless waived.

    - The IRB members review the informed consent document to ensure all required elements and appropriate additional elements are provided to the research participant at the time of initial review.
    - At the time of continuing review, the IRB must also review the informed consent document to determine if any additional changes are required.
- Informed consent (and HIPAA research authorization, when applicable) will be appropriately documented or waived in accordance with this policy.
- When appropriate, the research plan must make adequate provision for monitoring the data collected to ensure the safety of research participants.
- When appropriate, there are adequate provisions to protect the privacy of research participants and to maintain the confidentiality of data.
- When some or all the research participants are likely to be vulnerable to coercion or undue influence, such as children, prisoners, adults with impaired decision-making capacity, or economically or educationally disadvantaged persons, the IRB must evaluate whether additional safeguards have been included in the study to protect the rights and welfare of these research participants based on the IRB application materials. The IRB may require additional safeguards, if needed. For FDA regulated clinical trials, vulnerable populations also include pregnant people, mentally disabled persons, and handicapped individuals.
- To approve research involving some or all research participants that include vulnerable populations, the IRB must also ensure the research complies with regulations to the extent required by 45 CFR 46, subpart B, C, and D. See next sections for more details.
- To approve FDA regulated clinical investigations involving some or all research participants that include children, the IRB must also ensure the research complies to the extent required by 21 CFR 50, subpart D. See next sections for more details.
- FDA requires the sponsor or the sponsor-investigator to determine whether an IND or IDE is required for a particular study. The IRB may request the basis for the determination or request supporting documentation from the FDA. If the IRB is unable to resolve a controverted issue regarding the IND or IDE, it cannot approve the study until the matter is resolved.
    - The IRB should assess whether the investigator and/or sponsor determined that an investigational new drug application (IND) or investigational device exemption (IDE) is required a proposed study, if applicable, and the basis for this determination.
- The IRB must determine that a device study is significant risk (SR) or non-significant risk (NSR) at a **convened (full board) meeting and document the determination along with the reason for the determination in the IRB minutes**.[27] A SR device study must have an IDE from the FDA before the IRB can approve the investigation.

RESEARCH REGULATED UNDER NYS ARTICLE 24A

Certain research, as outlined in NYS Article 24A, requires additional IRB approval, including authorization from the NYS Commissioner of Health, unless the research complies with federal regulations. At a minimum, Downstate applies the Common Rule, Subpart A, to all research activities not governed by FDA or HIPAA regulations; as a result, NYS Article 24A does not apply to research conducted at Downstate.

27 FDA Guidance: Minutes of IRB Meetings (September 2017)

RISK

Risk means a potential harm (injury) associated with the research that a reasonable person in the position of research participants would be likely to consider significant in deciding whether to participate in the research. The concept of risk includes discomfort, burden, or inconvenience a research participant may experience because of the research procedures. Underlying the consideration of risk is the implicit moral guideline that all investigators have a duty not to harm their research participants and must minimize potential risk to the greatest extent possible.

The five major types of risk are:

- **physical risk** (e.g., pain, bruising and infection associated with venipuncture, adverse reactions to drugs, muscle soreness and pain because of exercise testing, heart attack induced by maximal exercise test).
- **psychological risk** (e.g., depression and confusion because of administration of drugs, feelings of guilt precipitated by a sensitive survey, feelings of coercion or undue influence during enrollment).
- **social risk** (e.g., invasion of privacy, loss of community standing, breach of confidentiality).
- **legal risk** (e.g., criminal prosecution or revocation of parole); and
- **economic risk** (e.g., loss of employment, loss of potential monetary gain).

MINIMAL RISK

IRB members must determine the level of risk for each non-exempt study. For more information, refer to the definitions below. One may also wish to refer to the Secretary's Advisory Committee on Human research Protections (SACHRP) document on Understanding Minimal Risk.

GENERAL DEFINITION

Generally, ***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.[28]

The IRB calibrates the interpretation of *minimal risk* to the life of normal, healthy individuals and to daily life of activities to which most individuals are exposed. However, the IRB may consider whether minimal risk procedures for normal healthy individuals constitute greater than minimal risk for populations that are vulnerable by virtue of their condition or circumstances.

PRISONER RESEARCH

In non-FDA regulated prison research, minimal risk is 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.[29]

28 45 CFR 46.102(j)
29 45 CFR 46.303(d)

RESEARCH INVOLVING VULNERABLE POPULATIONS

The following requirements apply to research which is funded, conducted, or supported by a federal agency or department or to FDA regulated research with Children. In general, the IRB may apply the federal requirements to all research regardless of funding or support or where it is conducted.

CHILDREN

45 CFR Subpart D and 21 CFR 50 Subpart D (for FDA regulated clinical investigations) applies to all research involving children (including neonates).

The IRB must make the determinations necessary to approve the research found in this section of the regulations. The IRB Members may document their determinations in the electronic IRB submission and reporting system.

In general, assent of children over the age of seven (7) is expected and parental or legal guardian permission is sought, unless the IRB waives the requirement for such.

For the purposes of this policy, a *legal guardian* is an individual authorized under applicable law or by court order to provide consent on behalf of a child.

When conducting or reviewing FDA regulated clinical investigations involving children, IRB members should consider if the protocol clearly justifies why children must be enrolled, minimizes risk through appropriate design and monitoring, and fits within the applicable pediatric risk category (including whether there is a prospect of direct benefit). IRB reviewers should consider the FDA draft guidance, *Ethical Considerations for Clinical Investigations of Medical Products Involving Children* (September 2022).[30]

The IRB determines the placement of the approval in one of the following allowable categories, provided the research with children meets the criteria listed below:

- **Category 404/50.51:** Human research or a clinical investigation not involving greater than minimal risk (45 CFR 46.404 and 21 CFR 50.51)
  - Requires assent of the child (unless waived); and
  - The IRB may find that permission of one parent (or legal guardian) is sufficient.

- **Category 405/50.52:** Human research or a clinical investigation involving greater than minimal risk but presenting the prospect of direct benefit to the individual research participants (45 CFR 46.405 and 21 CFR 50.52)
  - Requires assent of the child, unless waived.
  - The IRB may find that permission of one parent (or legal guardian) is sufficient (unless waived).
  - The IRB must find that the intervention or procedure holds out the prospect of direct benefit for the individual participant, or by a monitoring procedure that is likely to contribute to the participants' well-being.
  - The risk is justified by the anticipated benefit to the participants; and

30 FDA draft guidance, Ethical Considerations for Clinical Investigations of Medical Products Involving Children (September 2022)

- The relation of the anticipated benefit to the risk is at least as favorable to the participants as that presented by available alternative approaches.

- **Category 406/50.53:** Human research or a clinical investigation involving greater than minimal risk (minor increase over minimal risk) but no prospect of direct benefit to the individual research participants but likely to yield generalizable knowledge about the research participants' disorder or condition. (45 CFR 46.406 and 21 CFR 50.53)
  - Requires assent of the child, unless waived.
  - The permission, unless waived, must be obtained by both parents (or legal guardians), unless one is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.
  - The risk represents a minor increase over minimal risk.
  - The intervention or procedure presents experiences to participants that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations.
  - The intervention or procedure is likely to yield generalizable knowledge about the participants' disorder or condition which is of vital importance for the understanding or amelioration of the participants' disorder or condition; and
  - If children who are wards of the state or any other agency, institution, or entity are included, the IRB requires additional requirements of 45 CFR 46.409 (or 21 CFR 50.56 for clinical investigations).

- **Category 407/50.54:** Human research or a clinical investigation that is not otherwise in category 404, 405, or 406, which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children. (45 CFR 46.406 and 21 CFR 50.54)
  - Requires assent of the child (unless waived)
  - The permission (unless waived) must be obtained by both parents (or legal guardians), unless one is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.
  - The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children.
  - If children who are wards of the state or any other agency, institution, or entity are included, additional requirements outlined in 45 CFR 46.409 (or 21 CFR 50.56 for clinical investigations) must be met; and
  - The OHRP (or by the FDA, if FDA regulated) must also approve the research.

CHILDREN WHO ARE WARDS

For this policy, a *child* who is placed in the legal custody of the state or other agency, institution, or entity, consistent with applicable federal, state or local law.
Investigators must describe research involving a child with a ward status in the IRB application at the time of initial review or through an amendment proposal. As applicable, additional protections must be provided for the Wards as described in 45 CFR 46.409 or 21 CFR 50.56.

PREGNANT PEOPLE, FETUSES, NEONATES, OR IN-VITRO FERTILIZATION

When reviewing research that involves pregnant people, fetuses, neonates, or In-Vitro fertilization, the IRB must ensure it satisfies all of the conditions covered by Subpart B - Additional Protections for Pregnant People, Human Fetuses and Neonates.

When reviewing FDA regulated clinical investigations involving pregnant people, IRB members should be mindful of the need to balance protections for both the pregnant participant and the fetus while ensuring the protocol includes appropriate safeguards. FDA draft guidance is available as a practical resource to inform IRB review and discussion of these issues: *Pregnant Women: Scientific and Ethical Considerations for Inclusion in Clinical Trials*.[31]

PREGNANT PEOPLE OR FETUSES

Pregnant people or fetuses may be involved in research under the following conditions:

- Where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies, including studies on non-pregnant people, have been conducted and provide data for assessing potential risks to pregnant people and fetuses.
- 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;
- Any risk is the least possible for achieving the objectives of the research.
- 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;
- If the research holds out the prospect of direct benefit solely to the fetus, then the consent of the pregnant woman and the father is obtained in accord with the informed consent provisions, 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.
- Everyone providing consent is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate.
- For children who are pregnant, assent and parental/legal guardian permission are obtained in accord with the provisions of the IRB.
- No inducements, monetary or otherwise, will be offered to terminate a pregnancy.
- 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
- Individuals engaged in the research will have no part in determining the viability of a neonate.

NEONATES OF UNCERTAIN VIABILITY AND NONVIABLE NEONATES

31 Pregnant Women: Scientific and Ethical Considerations for Inclusion in Clinical Trials (FDA Draft Guidance, April 2018, Revision 1)

Neonates of uncertain viability and nonviable neonates may be involved in research under the following conditions:

- Where scientifically appropriate, preclinical, and clinical studies have been conducted and provide data for assessing potential risks to neonates.
- Individuals providing consent are fully informed regarding the reasonably foreseeable impact of the research on the neonate.
- Individuals engaged in the research will have no part in determining the viability of a neonate.

NEONATES OF UNCERTAIN VIABILITY.

Until it has been ascertained whether a neonate is viable, a neonate may not be involved in ANY research covered by this policy unless the following additional conditions have been met:

- The IRB determines that:
  - 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
  - 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
- 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 LAR/surrogate is obtained in accord with regulatory requirements, except that the consent of the father or his LAR/surrogate need not be obtained if the pregnancy resulted from rape or incest.

NONVIABLE NEONATES

After delivery, a nonviable neonate may not be involved in research covered by this policy unless all the following additional conditions are met:

- Vital functions of the neonate will not be artificially maintained.
- The research will not terminate the heartbeat or respiration of the neonate.
- There will be no added risk to the neonate resulting from the research.
- The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means; and
- The legally effective informed consent of both parents of the neonate is obtained. Waivers and alteration provisions 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, except that the consent of the father need not be obtained if the pregnancy resulted from rape or incest.

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 for Children.

RESEARCH INVOLVING PLACENTA, DEAD FETUS, OR FETAL MATERIAL

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 regulation and any state, or local laws and regulations regarding such activities.

NOTE: The Downstate Office of General Counsel determined there are no additional regulatory requirements for the state of NY.

If information associated with material described in 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 participants and all IRB requirements applicable.

RESEARCH NOT OTHERWISE APPROVABLE WHICH PRESENTS AN OPPORTUNITY TO UNDERSTAND, PREVENT, OR ALLEVIATE A SERIOUS PROBLEM AFFECTING THE HEALTH OR WELFARE OF PREGNANT PEOPLE, FETUSES, OR NEONATES.

Downstate may conduct research involving pregnant people fetuses, or neonates that the IRB does not believe meets the requirements of the above policy, only if:

- The IRB finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant people, fetuses, or neonates; and
- OHRP, after consultation with a panel of experts in pertinent disciplines (for example: science, medicine, ethics, law) and following opportunity for public review and comment, including a public meeting announced in the Federal Register, has determined either:
    - That the research in fact satisfies the conditions for research with pregnant people or fetuses, as applicable; or
    - The following:
        - ✓ The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant people, fetuses, or neonates.
        - ✓ The research will be conducted in accordance with sound ethical principles; and
        - ✓ Informed consent will be obtained in accordance with the informed consent provisions.

IN-VITRO FERTILIZATION

Federal agencies prohibit funding for in-vitro fertilization (IVF) research. However, investigators involved in IVF research or the IRB may wish to consult the references below for historical perspectives, regulations, and ethical considerations.

- American College of Obstetrics and Gynecologists (ACOG)
- American Society for Reproductive Medicine (ASRM)

PRISONERS

When reviewing **non-FDA regulated** research involving prisoners the IRB must ensure it satisfies all of the conditions covered by Subpart C - Additional Protections Pertaining to Biomedical and Behavioral research Involving Prisoners as Research Participants.
The IRB Member who is the prisoner representative must review the research. OHRP must also approve the federally supported or conducted research. To approve research that involves prisoners, the IRB must find that the proposed research falls into one of the permissible categories of research, and make the following seven findings:

1. The research under review represents one of the permissible categories of research:
    - **Category #1:** Study 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 research participants.
    - **Category #2:** Study 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 research participants.
    - **Category #3:** 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 OHRP has consulted with appropriate experts including experts in penology, medicine, and ethics, and published notice, in the Federal Register, of his/her intent to approve such research; or
    - **Category #4:** Research on practices, both innovative and accepted, which have the intent and reasonable probability of improving the health or well-being of the research participants. 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 OHRP 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.

2. 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 receiving such advantages in the limited-choice prison environment is impaired;
3. The risks involved in the research are commensurate with risks that would be accepted by non-prisoner volunteers.
4. Procedures for the selection of research participants within the prison are fair to all prisoners and immune from arbitrary intervention by prison authorities or prisoners. Unless the PI provides the IRB with written justification for following some other procedures, control research participants must be selected randomly from the group of available prisoners that meet the characteristics needed for that research proposal.
5. The information is presented in language that is understandable to the research participant population.
6. Adequate assurance exists that parole boards will not consider 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

7. Where the IRB finds there may be a need for follow-up examination or care of participants after the end of their participation, the IRB ensures adequate provisions are in place for such examination or care, considering the varying lengths of individual prisoners' sentences, and for informing participants of this fact.

To make these findings, the IRB must be familiar with the specific conditions in the local prison(s) or jail site(s) that are pertinent to protections, before approving the proposal for the local site.

EPIDEMIOLOGIC RESEARCH INVOLVING PRISONERS

Note: See Section "Activities That Do Not Require IRB Review and Approval; Public Health Surveillance Activities" to determine whether IRB approval is required for such activities.
Health and Human Services has waived the applicability of 45 CFR 46.305(a) (l) and 46.306(a) (2) for certain research conducted or supported by HHS that involves epidemiological studies that meet the following criteria:

1. In which the sole purposes are:
   a. To describe the prevalence or incidence of a disease by identifying all cases, or
   b. To study potential risk factor associations for a disease, and
2. Where the IRB has approved the research and has fulfilled its duties under 45 CFR 46.305(a)(2)–(7) and determined and documented that the following conditions are met:
   a. The research presents no more than minimal risk and no more than inconvenience to the research participants, and
   b. Prisoners are not a particular focus of the research.
3. The specific type of epidemiological research subject to the waiver involves no more than minimal risk and no more than inconvenience to the research participants. The waiver would allow the conduct of minimal risk research that does not now fall within the categories set out in 45 CFR 46.306(a) (2).
4. The range of studies to which the waiver would apply includes epidemiological research related to chronic diseases, injuries, and environmental health. This type of research uses epidemiologic methods (such as interviews and collection of biologic specimens) that generally entail no more than minimal risk to the research participants.
5. For the IRB to approve a study under this waiver, the IRB would need to ensure that, among other things, there are adequate provisions to protect the privacy of research participants and to maintain the confidentiality of the data.

OTHER POTENTIALLY VULNERABLE POPULATIONS

Please refer to the IRB Guidance for Students, Residents, Fellows, or Volunteers, as Research Participants, when seeking information on this this topic.

When some or all the research participants are patients of the investigators, consult the IRB guidance within the IRB applications or on the IRB website.

CERTIFICATES OF CONFIDENTIALITY: REQUIREMENTS AND CONSENT LANGUAGE

Certificates of Confidentiality (CoC), issued by the National Institutes of Health (NIH) or other HHS agencies, protect sensitive identifiable research information from forced disclosure (e.g., in court or legal proceedings). A CoC is required when:

- Research is funded in whole or in part by NIH and collects identifiable, sensitive information.
- The study involves genomics, biospecimens, behavioral or mental health data, or criminal behavior.
- The study poses a risk of stigmatization or legal consequences.

HOW TO OBTAIN A COC

- For NIH-funded research, CoC coverage is automatically provided and noted in the Notice of Award (NOA).
- For non-NIH-funded studies, investigators may apply via the NIH CoC online portal. Consult the NIH Certificate of Confidentiality Kiosk for assistance.

INFORMED CONSENT REQUIREMENTS

Consent forms for studies with CoC protections must include a specific statement outlining:

- The protections offered by the CoC
- The limitations (e.g., mandatory reporting of child abuse or communicable diseases)
- Any planned disclosures

SAMPLE LANGUAGE FOR CONSENT FORMS

Please consult the IRB website for template language to be used in the consent document.

MEDICAL RECORD COPY OF SIGNED INFORMED CONSENT

IMPORTANT: A copy of the signed informed consent document which includes the CoC disclosure language must be filed in the medical record to prevent unintentional disclosure by HIM pursuant to a request that does not require patient authorization (e.g., court subpoena).

DEVICE STUDIES

The PI must provide information in the IRB application to assess whether the investigator or sponsor determined that an IDE is required for a device study, if applicable. Additional supportive documentation is required in the application submission (e.g., letters from the FDA or sponsor).

The IDE regulations (21 CFR 812) apply to all clinical investigations to determine the safety OR effectiveness of a medical device; unless the investigation meets the criteria for an IDE exemption (see IDE exempted investigations).

A medical device is an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part or accessory that is:

- Listed in the Devices@FDA database,
- Intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or
- Intended to affect the structure or any function of the body of man or other animals, and which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of its primary intended purposes [21 U.S.C. 321(h)].

A device that is substantially equivalent to an FDA approved device may have a 510(k) approval to demonstrate the device is safe and effective. Search the FDA 510(k) Premarket Notification Database to determine the status of a device in the system.

Studies that involve devices, but do not evaluate the safety and effectiveness of the device, do not fall under the IDE regulations. However, the IRB still needs to ensure the risks are minimized by using procedures which are consistent with sound research methods or practice, and which do not unnecessarily expose participants to risk, and whenever appropriate, by using procedures already being performed on the research participants for diagnostic or treatment purposes. If a device or scientific equipment is not FDA approved for the indicated use in the research, the IRB needs to assess whether it is safe to use in the study.

IDE EXEMPTED INVESTIGATIONS

The IDE regulations (21 CFR 812) do not apply to investigations of the following categories of devices:

- 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,
      Note: The FDA does not consider a venipuncture as invasive.
    - Does not require an invasive sampling procedure that presents significant risk,
    - Does not by design or intention introduce energy into the research participant, and
    - 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 commercial distribution, if the testing is not for the purpose of determining safety or effectiveness and does not put the research participants at risk.
- A device intended solely for veterinary use.
- A device shipped solely for research on or with laboratory animals and labeled in accordance with 812.5(c).

- A custom device as defined in §812.3(b), unless the device is being used to determine safety or effectiveness for commercial distribution.

An exempted device study does not require an IDE from the FDA but does require IRB review.

DEVICE SOFTWARE FUNCTIONS

Software functions and mobile medical applications may be considered to be medical devices by the FDA. For complete details, see the FDA's policy for Device Software Functions and Mobile Medical Applications[32] for a description, examples, and criteria for determining whether software functions are medical devices and software functions which FDA intends to exercise enforcement discretion.

DETERMINING WHICH DEVICE POSE A SIGNIFICANT RISK OR NON-SIGNIFICANT RISK

The sponsor may initially propose whether the device is a significant risk (SR) or non-significant risk (NSR); however, the IRB must make the NSR/SR determination at the full board meeting before approving a study. A medical device study requires an IDE when:

- The investigation is designed to evaluate the safety and effectiveness of a medical device,
- An IDE has not been issued by the FDA, and
- The study is not IDE exempted.

If the FDA has already made the SR or NSR determination for the study, the FDA's determination is final. If the FDA does not designate the device as NSR, NSR determination must be made at a **full board meeting.**[33]

FDA requires an IDE for a SR device; however, an IRB can review a study that qualifies as a NSR device study (under abbreviated IDE requirements), provided the following:

- The device is not a banned device.
- The FDA has NOT notified the sponsor that an IDE is required.
- PI maintains the required records and reporting responsibilities to the FDA, 21 CFR 812, Subpart G and complies with the prohibitions against promotion and other practices described in 21 CFR 812.7.

Under 21 CFR 812.3(m), an SR device means an investigational device that:

- Is intended as an implant and presents a potential for serious risk to the health, safety, or
- welfare of a subject;
- Is purported or represented to be for use supporting or sustaining human life and presents a
- potential for serious risk to the health, safety, or welfare of a subject;
- Is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease,

32 FDA Guidance: Policy for Device Software Functions and Mobile Medical Applications (September 28, 2022)
33 FDA Guidance: Minutes of IRB Meetings (September 2017)

- or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety, or welfare of a subject; or
- Otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.

Examples of SR devices are dental lasers for hard tissue applications, vascular hemostasis devices, biliary stents, and collagen and bone replacements.

NSR devices are devices that do not pose a significant risk to human subjects. FDA does not have a specific definition for a NSR device.

NOTE: Do not confuse a NSR with minimal risk; a term used to identify certain studies that IRBs may approve through an expedited review procedure.

For more information, see FDA guidance on SR and NSR Medical Device Studies.[34]

RESPONSIBILITIES FOR DEVICE STUDIES

Consult the FDA website on IDE Responsibilities to understand the requirements of Sponsors, Investigators, and Monitors.

DRUGS AND BIOLOGICALS

The following applies to all research involving drugs and biologics:

- Conduct the research according to all regulatory guidelines and Downstate's policies and procedures.
- Obtain approval from the IRB before initiating any research activities.
- Comply with Downstate's Investigational Drug/Dispensing and Utilization policy (PHA-11).

INVESTIGATIONAL NEW DRUG (IND) REQUIREMENTS

When the principle intent of the investigational use of a test article is to develop information about the product's safety or efficacy, an Investigational New Drug (IND) may be required. An IND goes into effect 30 days after the FDA receives the IND request, unless the sponsor receives earlier notice from the FDA.

The PI must provide information in the IRB application to assess whether the investigator or sponsor determined that an IND is required for a proposed study, if applicable. Additional supportive documentation is required in the application submission (e.g., letters from the FDA or sponsor).

Investigators must indicate on the IRB application whether the research involves drugs. If so, they must indicate whether an IND is required for the research. If so, they must provide evidence of the IND, which could be an:

- Industry sponsored protocol with IND.

34 FDA Guidance: Significant Risk and Nonsignificant Risk Medical Device Studies

- Letter from FDA.
- Letter from industry sponsor.
- Other document and/or communication verifying the IND.

The IRB reviewer verifies the IND number is consistent across documents. The IRB is not required to monitor the PI's performance of required FDA paperwork.

If the research involves drugs and there is no IND, the PI must provide a rationale why it is not required, upon request from the IRB. The IRB may include a determination as to whether the research requires an IND, and the IRB should document this determination in the IRB Minutes. The IRB may ask the PI to request a consultation from the FDA as to whether there is a need for an IND.

If the IRB requires an IND, it cannot grant approval until the PI provides one of the following:

- Documentation to confirm an IND number, or
- Documentation from the FDA indicating that the FDA does not require an IND.

IND EXEMPTION

The clinical investigation of a drug product lawfully marketed in the United States is exempt from the IND requirements if all the following apply:

- 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.
- 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.
- 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.
- The investigation is conducted in compliance with the requirements for institutional review and with the requirements for informed consent set forth 21 CFR parts 56 and 50, respectively; and
- The PI conducts the investigation in compliance with the requirements concerning the promotion and sale of drugs (21 CFR 312.7).

NOTE: *The FDA does not require an IND for a placebo drug or for in vitro testing of a drug.*

RESPONSIBILITIES ASSOCIATED WITH AN IND

- The PI must comply with the FDA Investigator's Responsibilities for INDs
- For investigator-initiated IND studies, the PI must comply with FDA Investigator Responsibilities for Investigator-Initiated IND Applications,
- If the sponsor terminates an investigation with an IND, inform the IRB and the Research Pharmacist.

- The PI will report to the sponsor any adverse effect that may reasonably be regarded as caused by, or probably caused by, the drug (21 CFR 312 (b)) according to the procedures in the protocol.

BIOAVAILABILITY AND BIOEQUIVALENCE RESEARCH

Clinical investigations for measuring bioavailability or demonstrating bioequivalence shall be subject to principles and requirements of 21 CFR 320.

RESEARCH INVOLVING ENDOGENOUS COMPOUNDS, LIVE ORGANISMS, COSMETICS, FOODS, OR RESEARCH WITH NONCOMMERCIAL INTENT

Consult the FDA Guidance: INDs – Determining Whether Human research Studies Can Be Conducted Without an IND for guidance on determining if an IND is required for research involving endogenous compounds, live organisms, cosmetics, foods, or for research with noncommercial intent.

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 must meet the regulatory requirements of both FDA and the NIH Novel and Exceptional Technology and Research Advisory Committee (NExTRAC). Include the following in the submission to the IRB:

- IND for human gene transfer from the FDA,
- Approval of the U.S. Department of Health and Human Services (DHHS), NIH NExTRAC, and
- Approval by the Downstate Institutional Biosafety Committee (IBC).

RESEARCH INVOLVING MARIJUANA (CANNABIS)

In addition to obtaining IRB approval, conducting clinical research using marijuana (cannabis) involves interactions with three federal agencies, and the NYS DOH, including:

- Obtaining the marijuana for research from the National Institute on Drug Abuse (NIDA) within the National Institutes of Health.
- Review of an investigational new drug (IND) application and the research protocol by the Food and Drug Administration (FDA),
- An investigator registration and site licensure by the Drug Enforcement Administration (DEA),
- Obtaining a Class 7 Researcher (Individual) License from the NYSDOH Bureau of Narcotics Enforcement (BNE).
- Obtaining a Certificate of Confidentiality from the NIH, if the research is not NIH funded.

For more information, see the FDA Guidance on Marijuana research with Research Participants.

RESEARCH INVOLVING ARTIFICIAL INTELLIGENCE (AI) AND DIGITAL HEALTH TECHNOLOGIES

Research that uses artificial intelligence (AI), machine learning (ML), natural language processing (NLP), digital health apps, wearable devices, or algorithm-based decision tools **may** present unique risks related to:

- Algorithmic bias and fairness
- Algorithm stability
- Adaptive learning systems
- Data provenance and identifiability
- Human oversight in automated decision-making

Investigators proposing research involving such technologies must provide a clear description of the following information **as applicable** to the study:

- The role and scope of the algorithm/AI tool
- The training and validation datasets (including whether they include PHI or identifiable data)
- Any intended adaptive learning processes or performance drift monitoring
- Plans to minimize bias and ensure equity in outcomes
- Plans to maintain information security and confidentiality

The Downstate IRB encourages investigators to consult the MRCT-WCG AI Research Review Framework as the IRB will use this as a framework for review. Investigators may be asked to submit additional documentation to evaluate the ethical and regulatory implications of algorithm-driven research.

PLANNED EMERGENCY HUMAN RESEARCH OR CLINICAL TRIALS

Emergency research refers to the study of acute, life-threatening clinical situations that necessitate urgent intervention. Often, informed consent from the participants is not feasible because the participant lacks the capacity to provide their own consent (e.g., unconscious) and/or there is insufficient time because treatment must be promptly administered. The conduct of planned emergency human research or clinical trials in life-threatening emergent situations requires special consideration by the IRB, including consideration of whether to grant an exception form informed consent requirements for emergency research.

EXCEPTION FORM INFORMED CONSENT REQUIREMENTS FOR EMERGENCY RESEARCH

For FDA regulated research, the IRB may review and approve a clinical investigation without requiring informed consent of all research participants, if the 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) finds and documents each of the following:

(1) 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 interventions.

(2) Obtaining informed consent is not feasible because:

(i) The research participants will not be able to give their informed consent because of their medical condition.

(ii) The intervention under investigation must be administered before consent from the research participants' 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.

(3) Participation in the research holds out the prospect of direct benefit to the research participants because:

(i) Research participants 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 research participants; and

(iii) Risks associated with the investigation are reasonable in relation to what is known about the medical condition of the potential class of research 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.

(4) The clinical investigation could not practicably be carried out without the waiver.

(5) 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 research participant 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 the IRB at the time of continuing review.

(6) The 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 research participants or their legally authorized representatives in situations where use of such procedures and documents 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 research participant's participation in the clinical investigation consistent with paragraph (7)(v) below.

(7) Additional protections of the rights and welfare of the research participants 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 research participants will be drawn.

(ii) Public disclosure to the communities in which the clinical investigation will be conducted and from which the research participants 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) 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 research participant's family member who is not a legally authorized representative and asking whether he or she objects to the research participant'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.

The IRB is responsible for ensuring that procedures are in place to inform, at the earliest feasible opportunity, each 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, of the participant's inclusion in the clinical investigation, the details of the investigation and other information contained in the informed consent document. The IRB shall also ensure that 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 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 clinical investigation and the participant's condition improves, the participant is also to be informed as soon as feasible. 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.

The IRB determinations required by paragraph (a) of this section and the documentation required by paragraph (e) of this section are to be retained by the IRB for at least 3 years after completion of the clinical investigation, and the records shall be accessible for inspection and copying by FDA in accordance with 56.115(b).

Protocols involving an exception to the informed consent requirement under this section must be performed under a separate investigational new drug application (IND) or investigational device exemption (IDE) that clearly identifies such protocols as protocols that may include participants who are unable to consent. The submission of those protocols in a separate IND/IDE is required even if an IND for the same drug product or an IDE for the same device already exists. Applications for investigations under this section may not be submitted as amendments under 312.30 or 812.35.

If an IRB determines that it cannot approve a clinical investigation because the investigation does not meet the criteria in the exception provided under paragraph (a) of this section or because of other relevant ethical concerns, the IRB must document its findings and provide these findings

promptly in writing to the clinical investigator and to the sponsor of the clinical investigation. The sponsor of the clinical investigation must promptly disclose this information to FDA and to the sponsor's clinical investigators who are participating or are asked to participate in this or a substantially equivalent clinical investigation of the sponsor, and to other IRB's that have been, or are, asked to review this or a substantially equivalent investigation by that sponsor.

For additional guidance, see:

- FDA 21 CFR 50.24: Exception from Informed Consent (EFIC) Requirements for Emergency research
- FDA Guidance on Exception from Informed Consent Requirements for Emergency research
- OHRP Guidance: Informed Consent Requirements in Emergency research, for research not subject to FDA regulations

ENROLLMENT LIST

Upon request, provide an enrollment list to the IRB, Downstate Leadership, auditors, or government inspectors, unless the IRB waived documentation of informed consent under the condition that the only record linking the participant to the research is the informed consent form and the primary risk would be potential harm resulting from a breach of confidentiality.
At a minimum, this list should include the names of participants and their medical record number, if the research participants are also patients. The enrollment list should not be provided to anyone that is not otherwise listed above or in an IRB approved HIPAA instrument. The IRB, Privacy Officer, or Data Security Officer may use the enrolment list to notify research participants of possible breaches or concerns that might occur in the research.

TIP: If the IRB waives documentation of informed consent, the investigator signature and a witness signature may be included on an enrollment list, when there is IRB approval to enroll cognitively impaired adults or those with limited English proficiency.

MEDICAL RECORD RESEARCH NOTE FOR CLINICAL TRIALS

The research team must place a research note in the Electronic Medical Record (EMR) when enrolling a research participant into a **clinical trial involving an IND or IDE** at Downstate who is also a **patient.** This helps ensure clinicians and the pharmacy aware of contraindications.
When a standard research note is not part of the programing within the EMR, the research team must enter the following information manually:

- IRB study number.
- Study name.
- Sponsor.
- Principal Investigator.
- Main contact information for the study.
- Date the patient was enrolled.
- Known contraindications.
- Anticipated length of study period (years).

For areas that do not use an EMR, the research team must place the above information in the beginning of the paper medical records.
External institutions may have their own requirements about research notes (e.g., Kings County).

LEGALLY EFFECTIVE INFORMED CONSENT AND HIPAA RESEARCH AUTHORIZATION

REQUIREMENTS

Investigators conducting non-exempt human research under the auspices of Downstate may involve participants after (s)he or his/her LAR/surrogate , or parent/guardian provides prospective legally effective informed consent/permission (and HIPAA Authorization, when PHI is involved), unless the waiver of such requirements has been approved by IRB.

Assent and (or documentation of assent, when required) of a child or a cognitively impaired adult must also be obtained, unless waived by the IRB.

The IRB will evaluate both the consent process and the procedures for documenting informed consent to ensure that both are adequate.

The following procedures describe the requirements for obtaining consent from participants in research conducted at Downstate.

LEGALLY AUTHORIZED REPRESENTATIVE (LAR) OR SURROGATE

For the purposes of this policy, a *legally authorized representative (LAR, personal representative or legally empowered representative or surrogate)* is an individual, judicial, or other body authorized under applicable law to provide consent on behalf of an adult prospective research participant for the research participation of an adult who is cognitively impaired and unable to provide consent. A *LAR* is an individual authorized to provide permission on behalf of a prospective research participant to be involved in the research.

Base the designation of a *LAR* in individual cases on the presence or absence of a power of attorney, living will, or health care proxy (as above).

The informed consent process must comply with institutional policy. For research at Downstate, this includes Policy CONS-01. Only one person from the list below, from the class of highest in priority may authorize the research when persons in prior classes are not reasonably available. The surrogate must be willing and competent to act. The person who is designated may designate another person on the list to be surrogate, as long as no one in the class higher in priority objects. However, if one surrogate does not provide consent, the investigator must honor that decision and not seek consent from another surrogate on the list.

- Healthcare Agent (legal guardian) with authority to provide consent to healthcare decisions (highest priority)
- Guardian authorized to decide about health care, pursuant to Article 81 of the NYS Mental Hygiene law
- Spouse or domestic partner (provided there is no legal separation)
- Adult child (son or daughter)
- Parent
- Adult sibling (brother or sister)
- Close adult friend (must be 18 years or older and present a signed statement of relationship to a patient/participant) (lowest priority)

REQUIREMENTS FOR INFORMED CONSENT AND HIPAA RESEARCH AUTHORIZATION

Pease review the IRB Guidance for obtaining legally effective informed consent and HIPAA authorization. This is available on the IRB website.

POSTING CONSENT FORMS FOR A FEDERALLY CONDUCTED OR FUNDED CLINICAL TRIAL TO A FEDERAL WEBSITE

The Common Rule defines a *Clinical Trial* as a research study in which one or more research participants are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of the interventions on biomedical or behavioral health-related outcomes.

For each clinical trial, as defined (see paragraph above) by the Common Rule, conducted or supported by a Federal department or agency, the awardee or the Federal department or agency component conducting the trial must post one IRB-approved informed consent form used to enroll research participants on a publicly available Federal Web site established as a repository for such informed consent forms. This posting must take place **after the clinical trial is closed to recruitment and no later than 60 days after the last study visit** by any research participant, as required by the protocol.

A Federal department or agency supporting or conducting the clinical trial may determine that certain information should not be made publicly available on a Federal Web site (e.g., confidential commercial information) and may permit or require redactions to the information posted.

The following websites are available for posting the consent form:

- www.ClinicalTrials.gov, or
- Docket folder on www.Regulations.gov (Docket ID: HHS-OPHS-2018-0021).

BROAD CONSENT FOR STORAGE, MAINTENANCE, AND SECONDARY RESEARCH OF IDENTIFIABLE PRIVATE INFORMATION OR IDENTIFIABLE BIOSPECIMENS

The Downstate IRB will not approve research under exemption categories 7 or 8, as this time.

Please follow the current requirements for obtaining consent or waivers to store, maintain or use such identifiable private information or identifiable specimens for research purposes. Contact the IRB for additional information, when needed.

INFORMED CONSENT PROCESS

The IRB evaluates and ensures the informed consent process is adequate and determines whether informed consent is documented and sought in accordance with regulations and policies based on information provided in the IRB application materials, including the IRB application and protocol.

WAIVING THE REQUIREMENTS OF INFORMED CONSENT OR HIPAA AUTHORIZATION

Most prospective human research requires a legally effective informed consent process, including the documentation of a signed (including in an electronic format) consent from the participants (or LAR/surrogate); however, when certain criteria are met, the IRB may grant a waiver of the informed consent or pediatric assent requirements. The PI must provide written justification for how the criteria can be met or the IRB can make this determination based on the information available in the protocol or IRB application materials. Requests for waivers of informed consent/assent requirements are not required if the research is considered exempt; however, a HIPAA waiver or HIPAA Authorization may still be required, for research involving PHI.

There are several types of waiver requests, as outlined below.

WAIVER OF THE PROCESS FOR INFORMED CONSENT OR ELEMENTS OF INFORMED CONSENT

For **non-FDA regulated** research, the criteria[35] for waiving informed consent or elements of informed consent are as follows:

1. The research does not involve non-viable neonates[36]
2. The research involves no more than minimal risk to the research participants.
3. The research could not practicably be carried out without the requested waiver or alteration.
4. If the research involves using identifiable private information or identifiable biospecimens, the research could not practicably be carried out without using such information or biospecimens in an identifiable format.
5. The waiver or alteration will not adversely affect the rights and welfare of the participants.
6. Whenever appropriate, the research participants or LARs/surrogates will be provided with additional pertinent information after participation (e.g., debriefing research participants involved in deception research).
7. Alteration of the consent process can only omit or alter the basic and/or additional elements of informed consent; however, this is not applicable, if waiving the entire process of informed consent.

The Downstate IRB cannot waive the requirement to obtain informed consent for research under which broad consent is required to be obtained.

For **non-FDA regulated** research, which is federally supported or conducted research or demonstration projects to be conducted by or subject to the approval of state or local government officials (e.g., research approved by the HHS Secretary, NYS DOH, etc.), the criteria for waiving informed consent or elements of informed consent are as follows:

1. The research does not involve non-viable neonates.[37]
2. The research or demonstration project is to be conducted by or subject to approval of state or local government officials and is designed to study, evaluate, or otherwise examine one or more of the following:

35 45 CFR 46.116(f)(3)
36 45 CFR 46.205(c)(5)
37 45 CFR 46.205(c)(5)

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; and

3. The research could not practicably be carried out without the waiver or alteration.
4. Alteration of the consent process can only omit or alter the basic and/or additional elements of informed consent; however, this is not applicable, if waiving the entire process of informed consent.

EXCEPTION FROM INFORMED CONSENT REQUIREMENTS FOR FDA REGULATED MINIMAL RISK CLINICAL INVESTIGATIONS

When the Downstate IRB is responsible for the review, approval, and continuing review of an **FDA regulated** clinical investigation the IRB may approve an informed consent procedure that does not include or that alters some or all the elements of informed consent or may waive[38] the requirement to obtain informed consent, provided the IRB finds and documents the following:

1. The clinical investigation involves no more than minimal risk to the subjects;
2. The clinical investigation could not practicably be carried out without the requested waiver or alteration;
3. If the clinical investigation involves using identifiable private information or identifiable biospecimens, the clinical investigation could not practicably be carried out without using such information or biospecimens in an identifiable format;
4. The waiver or alteration will not adversely affect the rights and welfare of the subjects; and
5. Whenever appropriate, the subjects or legally authorized representatives will be provided with additional pertinent information after participation.

FDA ENFORCEMENT DISCRETION FOR REQUIREMENT FOR INFORMED CONSENT FOR IN VITRO DIAGNOSTIC DEVICE STUDIES USING LEFTOVER HUMAN SPECIMENS THAT ARE NOT INDIVIDUALLY IDENTIFIABLE

For FDA regulated in vitro diagnostic device studies using de-identified specimens, the FDA may exercise enforcement discretion to not require informed consent as described in the FDA Guidance for "In Vitro Diagnostic Device Studies Using Leftover Human Specimens that are Not Individually Identifiable". Therefore, the Downstate IRB generally does not require informed consent for the use of discarded de-identified remnants of specimens collected for routine clinical care or analysis for in vitro diagnostic device studies.

WAIVER OF PARENTAL PERMISSION

For **non-FDA regulated research**, if the IRB determines that a research protocol is designed for conditions or for a population for which parental or guardian permission is not a reasonable requirement to protect the research participants (for example, neglected or abused children), it may waive the consent requirements, provided an appropriate mechanism for protecting the

38 21 CFR 50.22

children participating in the research is substituted, and provided further that the waiver is not inconsistent with federal, state, or local law. The choice of an appropriate mechanism would depend upon the nature and purpose of the activities described in the protocol, the risk and anticipated benefit to the research participants, and their age, maturity, status, and condition.

WAIVERS OF CHILD ASSENT FOR NON-FDA REGULATED RESEARCH

For **non-FDA regulated research**, 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 circumstances in which consent may be waived in accord with the general requirements of informed consent.[39]

WAIVERS OF CHILD ASSENT FOR FDA REGULATED RESEARCH

For **FDA regulated** research, the assent of the children is not a necessary condition for proceeding with the clinical investigation if the IRB determines:

- That the capability of some or all the children is so limited that they cannot reasonably be consulted, or
- That the intervention or procedure involved in the clinical investigation 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 clinical investigation.

Even if the IRB determines the children can assent, the IRB can approve a wavier when the PI provide justifications to meet the following criteria:

- The clinical investigation involves **no more than minimal risk** to the research participants.
- The waiver or alteration will not adversely affect the rights and welfare of the participants.
- The clinical investigation could not practicably be carried out without the waiver or alteration; and
- Whenever appropriate, the research participants will be provided with additional pertinent information after participation.
- The permission of the parent(s)/guardian(s) will be documented in accordance with informed consent requirements.

WAIVER OF DOCUMENTATION OF INFORMED CONSENT FOR NON-FDA REGULATED RESEARCH

Request a waiver of documentation of informed consent to obtain (verbal) informed consent without documentation (e.g., signed informed consent). When requesting this type of wavier, the IRB generally requires the investigator to provide an information sheet to the research participant. This form may be downloaded at Step 8 from the IRB Submission Website.

39 45 CFR 46.408 & 45 CFR 46.116

The IRB may approve a request to waive documentation of informed consent for **non-FDA regulated research**, when it meets the one of the following criteria:

- The research is no greater than minimal risk and involves no procedures for which written consent is normally required outside of the research context, OR
- The only record linking the participant to the research is the informed consent form and the primary risk would be potential harm resulting from a breach of confidentiality. Under this condition, each participant (or LAR/surrogate) must be asked whether (s)he wants to sign documentation linking her/him to the research and her/his wishes will govern, OR
- For research, which is **not regulated by DOJ**, the IRB may waive documentation of informed consent, if the research participant (or LAR/surrogate) are members of a distinct cultural group or community in which signing forms is not the norm, that the research presents no more than minimal risk of harm to participants and provided there is an appropriate alternative mechanism for documenting that informed consent was obtained.

WAIVER OF DOCUMENTATION OF INFORMED CONSENT FOR FDA REGULATED RESEARCH

For **FDA regulated research**, the IRB may, for some or all research participants, waive the requirement that the research participant, or their legally authorized representative, sign a written consent form if it finds 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.

In cases where the documentation requirement is waived, the IRB may require the investigator to provide subjects with a written statement regarding the research.

WAIVERS OF SIGNATURES INVOLVING PROTECTED HEALTH INFORMATION

If the study involves PHI, a HIPAA Authorization with a signature must be included, unless the IRB approves a HIPAA alteration (see below). It is permissible to combine a HIPAA Authorization with the Information Sheet.

HIPAA WAIVERS

The IRB may approve the uses and disclosures of PHI for research purposes when the investigator submits a HIPAA Waiver (of the HIPAA research authorization requirement). If the IRB approves a partial HIPAA waiver (e.g., for recruitment purposes), the IRB conditions the use or disclosure upon compliance with any HIPAA research authorization requirements not waived (e.g., obtaining a HIPAA authorization once consent is obtained). This form may be downloaded at Step 8 from the IRB Submission Website.

The requested waiver must satisfy all the following criteria:

- The use or disclosure involves no more than a minimal risk to the privacy of the research participants because:
    - There is an adequate plan to protect the "identifiers" from improper use or disclosure. Refer to Downstate Policy on De-Identification of Information (HIPAA-6) for the types of information considered to be identifiers.

    - There is an adequate plan to destroy the identifiers at the earliest opportunity, unless there is a health or research justification for retaining the identifiers or their retention is required by law; and
    - There are adequate written assurances that the protected health information (PHI) will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research study or for other research for which the use or disclosure of PHI is otherwise permitted.
- The research could not practicably be conducted without the waiver- research involving treatment will almost never be eligible since most clinical trials could practicably be conducted without a waiver; and
- The research could not practicably be conducted without access to and use of the PHI- If de-identified information or a limited data set can practicably be used, a waiver of authorization should not be granted.

The PI should submit the request for waiver using the *HIPAA Waiver of Authorization Form.* The IRB will review and approve the waiver, if appropriate, under either normal or expedited review procedures. Refer to Downstate Policy Uses and Disclosures for Research Purposes (HIPAA-28) for more information.

The section below described the three types of HIPAA Waivers (full, partial, and alteration).

FULL HIPAA WAIVER

A *Full HIPAA Waiver* removes the requirement to obtain a HIPAA research authorization from research participants for the use and disclosure of their PHI to conduct a study. Examples where this is appropriate include:

- Retrospective chart reviews, or
- Exempt research involving PHI, when it is impracticable to obtain a HIPAA research authorization.

When applicable, the IRB may use the information in the HIPAA waiver to grant a waiver of informed consent.

PARTIAL HIPAA WAIVER

Request a *Partial HIPAA Waiver* to review PHI for recruitment purposes; however, include the HIPAA research authorization language within an informed consent document that uses subsequent PHI.

HIPAA ALTERATION

A *HIPAA Alteration* is a type of HIPAA waiver that when approved permits the use of a research authorization that does not contain all the required elements or statements (e.g., signature or another element), or that otherwise deviates from the format or process prescribed by the HIPAA regulations. This may be useful, for example, when a PI is also seeking waiver of documentation of informed consent, when the only link of a participant to a study is their signature on a consent form and HIPAA research authorization, if it can be considered impracticable to the study's completion to obtain a signed research authorization form as such a requirement might prevent study completion.

There also may be other circumstances where a simplified consent and authorization document are appropriate given the nature of the population enrolling in the research and in these cases a request to waive certain but not all elements or required statements of the authorization would be made.

SCREENING, RECRUITING, OR DETERMINING ELIGIBILITY

The Downstate IRB may approve a research protocol in which an investigator will obtain information or biospecimens for screening, recruiting, or determining the eligibility of prospective research participants or the LAR/surrogate, when one of the following conditions are met; however, a HIPAA waiver or HIPAA Authorization may still be required:

- The investigator will obtain information through oral or written communication with the prospective research participant or the LAR/surrogate, OR
- The investigator will obtain identifiable private information or identifiable biospecimens by accessing records or stored identifiable biospecimens.
- The research is not regulated by FDA or DOJ.

DISTRIBUTION OF COPIES OF SIGNED INFORMED CONSENT MATERIALS

Below is a summary of informed consent material distribution:

- Signed original: Kept securely and easily accessible in the research file.
- Copies provided to:
  - The person giving authorization (participant, legal representative, or parent/guardian).
  - Downstate Medical Record, if a Downstate patient joins a clinical trial with an IND or IDE.
  - Other facilities' medical records, as required by those organizations.

ANCILLARY REVIEWS

Ancillary reviews may be required by various departments or committees. To determine if an ancillary review is required prior to IRB approval consult the IRB website or contact the IRB.

When an ancillary review is NOT required prior to IRB approval, the investigator must document approval of any pending required ancillary review within the research record prior to starting the research or enrolling any research participants, as applicable.

INSTITUTIONAL REVIEW BOARD (IRB)

The Downstate Institutional Review Board (IRB) is a committee established to review and approve human research. The purpose of the IRB is to ensure the ethical conduct of all human research in accordance with all applicable regulations and policy.
The IRB must ensure compliance of clinical trials involving investigational or unlicensed test articles (drugs, biologics, and devices), including when necessary, ensuring appropriate exemptions.

Duties and responsibilities of Downstate IRB include, but are not limited to the following:

- Conducting prospective review of human research activities carried out by a Downstate faculty member that result in Downstate being engaged in human research, regardless of whether the activity is considered a clinical trial, human research, or exempt human research;
- When necessary, require modifications to informed consent documents, HIPAA Authorizations, or information sheets, for study approval or activation.
- Confirming the competency of the PI.
- Reviewing protocols, Investigator Brochures (IB) [typically required for studies conducted under an IND, and sometimes for medical device studies][40], consent forms, advertisements and all other study-related materials submitted to the Downstate IRB.
- Reviewing reportable events, as submitted.
- Acting as Privacy Board under 45 CFR Part 164 for research reviewed by Downstate IRB and consulting with the Downstate Privacy Officer or Downstate Data Security Officer, as needed to address relevant matters.
- Maintaining and retaining all records of IRB proceedings required by applicable laws and regulations, for at least three (3) years, and up to ten (10) years, when practicable, including the following:
    - Research proposals reviewed,
    - Scientific evaluations, if any,
    - Approved sample consent forms,
    - Progress reports submitted by investigators,
    - Reports of injuries of research participants,
    - Minutes,
    - Records of continuing review activities, including the rationale for conducting continuing review of research that does not require continuing review as described in this policy,
    - Copies of all correspondence between the IRB and investigators.
    - IRB rosters,
    - Written policies and procedures,
    - Statements of significant findings provided to research participants,
    - The rationale for an expedited reviewer's determination that research appearing on the expedited review list is more than minimal risk, and
    - Documentation specifying the responsibilities that the Downstate Medical Center undertakes to ensure compliance of this policy (e.g., this policy, OCAS policies, IRB guidance, etc.).
- Conducting continuing review of approved studies.
- Reviewing data safety monitoring board reports and taking appropriate actions when needed.
- Reviewing any alleged or suspected incident of noncompliance and making determinations regarding these events.
- Auditing human research, as necessary.
- Providing written standard operating procedures to investigators regarding the process and requirements for IRB application and necessary reporting.
- Making IRB determinations as to whether a Downstate activity must be approved by the Downstate IRB.
- Providing copies of all IRB minutes to the IO and the Executive Director, Human Research Protections and Quality Improvement; and,

40 FDA Information Sheet: IRBs FAQs February 2025. FAQ #23

- Providing relevant approved IRB Minutes (may be redacted) to an external institution, upon request.

The IRB approves each research protocol or plan according to criteria based on policy, applicable laws, regulations, codes, guidance, and best practices.

IRB CHAIR

The IRB Chair is responsible for seeing that the IRB discharges its functions in an appropriate and regulatory-compliant manner. (S)he holds ultimate responsibility for convening the Board and facilitating meetings, providing to the Institutional Official (IO) recommendations for IRB Membership (including recommendations for pairing primary members with alternates on the IRB roster), and ensuring the IRB operations comply with applicable regulations. (S)he may designate some responsibilities to the Vice-Chairs, experienced IRB Members, or IRB Administrators.

The IRB Chair or designate will make determinations regarding events reported to the IRB, or consult with the IRB, IO, Privacy Officer, Information Security Officer, or General Counsel as needed.

IRB VICE-CHAIRS

The Vice-Chairs assist the IRB Chair in carrying out the responsibilities noted in the IRB Chair section and are primarily responsible for the oversight of their designated Full Board meeting. When a Vice-Chair plans to be absent from a full board meeting, the Vice-Chair or IRB Chair may designate an experienced IRB member to run the meeting, or the IRB Chair will fulfill this duty.

IRB MEMBERS

Downstate establishes an IRB & Privacy Board Roster in accordance with requirements of the regulations, policies, guidance, and practice.

Experienced IRB Members may determine whether an activity requires review and approval by the IRB and whether reviews may take place via exempt, expedited, or a full board review process.

IRB MEETING GUIDELINES AND DUTIES, RESPONSIBILITIES, AND GOALS OF IRB MEMBERS, ADVISORS, GUESTS, AND IRB ADMINISTRATORS

For comprehensive information regarding the duties, responsibilities, and objectives of the IRB, please refer to the IRB Guidance document titled “Meeting Guidelines and Duties, Responsibilities, and Goals of IRB Members, Advisors, Guests, and IRB Administrators,” available on the IRB website.

IRB REVIEW PROCEDURES

The following provides a comprehensive summary of the IRB review process for all types of submissions, such as initial reviews, continuing reviews, amendments, and reportable events. Specific procedural distinctions by submission category are detailed below.

REVIEW AND REVIEWER ASSIGNMENT

The IRB administrative staff performs a preliminary review of all protocol materials for determination of completeness, accuracy, and required ancillary reviews and accepts complete submissions. The IRB administrative staff informs the PI through an email or via the electronic application and reporting system of any missing materials or requirements and applicable response deadlines.

Experienced IRB administrative staff determine whether an activity requires review and approval by the IRB and whether reviews may take place via exempt, expedited, or a full board review process. The IRB administrative staff will assign protocols for review, based on the scientific content of the protocol and the potential reviewer's area of expertise. If there are any questions, the IRB staff will consult with the Executive Director, Vice-Chair, or IRB Chair for guidance for a determination.

An experienced IRB member or experienced IRB Administrator may make IRB Determinations, including IRB Exemptions, but an IRB member must make all determinations that qualify for limited IRB review or include HIPAA waivers or HIPAA authorizations.

The IRB may use a primary and secondary reviewer process (e.g., two reviewers) to assign full board reviews based on special knowledge and expertise of the members (e.g., clinical expertise, informed consent reviewer, research design, statistics, regulatory and policy, ethics) or a combination thereof. The IRB will seek out the review of a consultant when the IRB receives a protocol that may be outside of the knowledge base of any of the IRB. When a consultant reviews the research, the consultant must be given at a minimum the protocol (or a summary) and the informed consent document, if applicable for the research, for review. The IRB must defer the review of research to either another meeting or an external IRB when appropriate expertise is not available among the IRB members or consultants to determine the research meets all the criteria to approve the research.

The IRB administrative staff assign at least one IRB Member to review a study that qualifies for expedited review. They assign at least two reviewers to each full board protocol. They may assign several protocols or other research items for review. Reviewers are assigned to all protocols requiring initial review, continuing review, and modifications. In general, the reviewers are responsible for the following:

- Having a thorough knowledge of all the details of the proposed research.
- Performing an in-depth review of the proposed research and all uploaded documents.
- Leading the discussion of the proposed research at the convened meeting, presenting both positive and negative aspects of the research, and leading the IRB through the regulatory criteria for approval.
- Making suggestions for changes to the proposed research, where applicable.
- Completing all applicable IRB reviewer forms or placing comments in the electronic IRB submission and reporting system.

IRB members should complete their written reviews in advance of the IRB meetings within the electronic IRB submission and reporting system, including IRB determinations; however, the

reviews are not the final work product of full board studies. The IRB minutes and IRB approval/notification letters capture the final work product of the review including information discussed at the meeting and any required determinations.

SUBMISSION INTAKE AND TRIAGE PROCEDURES

1) Completeness check (Pre-review)
   a) Refer to the procedures and guidance for COI requirements and training on the IRB website.
   b) The IRB Coordinator confirms all required training and COI disclosures are complete and documents the findings in IRBNet.
   c) If there are any pending or outstanding issues, the Associate IRB Administrator notifies the Principal Investigator (PI), (or Clinical Investigator [CI], Project Lead [PL], or Clinician, as applicable to the submission type) that the submission is incomplete.
   d) If there are any pending or outstanding issues, the Associate IRB Administrators notify the PI/CI the submission is incomplete.
   e) The IRB Coordinator checks for prior review lapses and ensure they are addressed by reminding the PI to submit closure reports to the IRB and updating a note in IRBNet to let the Associate IRB Administrator know of the lapse.
   f) The Associate IRB Administrators screens each new submission to ensure:
      i) Required documents are included with the submission (protocol, consent(s), recruitment, instruments, PI CV or NIH Biosketch [including relevant publications], ancillary approvals, etc.), based on applicable materials required for the submission as outlined on the IRB website.
   g) The Associate IRB Administrators determines review type (new, exempt, expedited, full board) or consult with the IRB Director or Chair for guidance or determinations, if needed.
2) If the submission is incomplete, Associate IRB Administrators:
   a. Return the submission to the PI/CI in IRBNet, by unlocking the package in IRBNet with a note describing missing elements. If additional instructions are email correspondences to the PI/CI, the email is attached in the Reviewer comment section in IRBNet.
   b. Do not assign to a meeting or reviewer until deficiencies are resolved.
3) Regulatory determination and review pathway
   a) IRB staff determine whether the activity is:
      i) Not Human Subjects Research / Not a Clinical Investigation,
      ii) Exempt research, or
      iii) Non-exempt research.
         (1) IRB staff propose a review pathway (expedited vs convened).
         (2) The IRB Member Reviewer confirms the determination by continuing the review process or modifies the determination as needed. Any IRB Member may refer the review to a higher level of review, when applicable.
4) IRB and reviewer assignment
   a) Associate IRB Administrators do the following:
      i) Review and make Exempt determinations and determine the categories of exemption(s).
      ii) Assign each submission to IRB members for an Expedited review and determine the categories for expedited review and level of risk.
      iii) Assign the submission to a convened IRB committee based on population, risk, and expertise.
      iv) Prepare the agenda and schedule the IRB meeting.

v) shares the FDA Guidance Document: Humanitarian Device Exemption (HDE) Program Guidance[41] with IRB Members to help them conduct the review.

b) For convened reviews, primary reviewers are assigned based on appropriate expertise. Secondary reviewers are generally assigned to review consent forms and related materials such as recruitment scripts and advertisements.

c) If the IRB Office is not sure if the IRB member has the necessary expertise to review a study, the submission should be referred to the IRB Chair to determine and assign the review to a consultant to provide feedback to the IRB or determine whether the review should be sent to an external IRB.

d) All IRB members have access to all studies in IRBNet, including the materials that are placed on the agenda for convened review.

5) See additional details for review types below.

IRB MEMBER REVIEW RESPONSIBILITIES

1) Consult with the IRB Office, Director, or Chair as needed.
2) If at any time, an IRB member does not feel they have the expertise to review a study, they must contact the IRB to request that it be assigned to another member.
3) Review all materials in detail, including protocol, consent documents, and instruments.
4) Apply the regulatory approval (111) criteria,[42] including requirements of informed consent.
5) Conduct meaningful and substantive reviews. The informed consent document must contain all required (basic) elements of informed consent. When applicable, it should also incorporate any additional elements as mandated[43]. These requirements may vary based on whether the research falls under FDA regulations or the Common Rule or both. Furthermore, supplementary consent provisions may be stipulated by the funding agency or sponsor.
6) Follow the IRB Guidance for review of Full Board and Expedited studies at the time of initial and continuing review to make required regulatory determinations at the time of initial review and to confirm or make regulatory determinations at the time of continuing review and for amendments, when applicable.[44]
7) Evaluate risks, benefits, subject selection, consent process and documentation, privacy and confidentiality protections, and additional safeguards for vulnerable populations.
8) Make determinations based on the risk/benefit, selection of subjects, privacy/confidentiality, consent, monitoring, vulnerable populations, etc.
9) Make any required determinations outlined in FDA, Common Rule, HIPAA, and any other applicable regulations that pertain to the submission under review.
10) Follow any reviewer guide, IRB Policy, IRB Guidance, and enter their comments in IRBNet, noting any request for modifications or determinations.
11) Ensure additional safeguards for Children, Prisoners, Pregnant women, fetuses, neonates, and other vulnerable groups (e.g., cognitively impaired, economically disadvantaged).
12) Determine required subpart findings and category determinations.
13) Verify IND/IDE requirements
14) Make SR vs NSR determinations in the convened meeting.
15) Make the determinations required for HUD uses, expanded access, and treatment use, when applicable.
16) Review and approve waivers and alterations.

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41 FDA Guidance Document: Humanitarian Device Exemption (HDE) Program
42 IRB Guidance: “111 Criteria” for IRB Approval (Full Board and Expedited Review)
43 FDA Guidance: Informed Consent
44 Guidance for IRB Members: Initial Review of a Full Board or Expedited Study.

17) Set shorter approval periods, when applicable, based on risk-based frequency.
18) Vote on IRB actions at the convened meeting.
19) See additional details for review types below.

RECUSALS

FULL BOARD MEETINGS

Members with conflicts of interest are **recused**, do not vote, and are excluded from quorum counts for the relevant agenda item, though they may provide information before leaving for deliberations and voting.

Most meetings will be held virtually; therefore, if an IRB member is conflicted at a convened meeting, they must verbally notify the IRB in the meeting.

OTHER REVIEW ACTIVITIES

An IRB Member or IRB Staff member with a potential or real conflict of interest will be considered recused and cannot approve any IRB submission, including those not requiring full board review (e.g., expedited review, exempt review, IRB determination, administrative review, consulting review, etc.).

Conflicted individuals must notify the IRB Staff or IRB Chair/Vice-Chair so that the review assignment can go to another individual.

IRB REVIEW PROCESS

All human research requires, based on the criteria set forth below, either full review, expedited review, or exempt review. An investigator may propose the type of review; however, the IRB makes the final determination.

If a project does not need IRB review and approval, the IRB will issue a determination letter to this effect. An experienced IRB Member or an experience IRB Administrator who is not an IRB Member may review IRB Determinations or IRB Decision Aid requests. When it is necessary for the reviewers to consult with General Counsel, OCAS, or the Privacy Officer, the reviewer should document such communications in the IRB records.

CEDED REVIEWS

When an external (reviewing) IRB approves a study, through ceded review, the Downstate IRB Office will confirm local Downstate requirements are met and will acknowledge the expiration date determined by the external IRB (ceded review). The Downstate IRB will use this expiration date of IRB approval for the expiration date of Downstate IRB activation.

The Downstate IRB may be required to conduct a pre-review of the research, prior to the review of the external (reviewing) IRB to ensure local Downstate requirements are met.

EXEMPT RESEARCH REVIEW PROCESS

The exemption categories listed on the IRB application describe the type of research which is eligible for exempt review.

The IRB reviews exemption requests upon submission. There are no scheduled deadlines for submission, as the review process will start immediately.

The IRB office staff will conduct an administrative review of the research to determine whether the submission is complete and verify the study meets the criteria for an exempt review. If the IRB office staff member is also an experienced IRB Member and has the expertise necessary to conduct the review, (s)he may review and approve the research; otherwise, it will be assigned to another IRB Member.

The IRB Member may require additional changes or make recommendations before approving the study. The IRB Member can refer the study to the IRB Chair or another IRB Member, if the topic is out of his/her area of expertise. An IRB Member cannot disapprove exempt research but may refer it to the full board review.

An experienced IRB Administrator who is not an IRB Member may review exempt research or IRB Decision Aid requests; however, only an IRB Member may approve exempt research requiring limited IRB review (see below). Novel studies may be assigned to other IRB members.

LIMITED IRB REVIEW PROCESS

If an exempt review requires limited IRB review, the IRB member reviewers ensure there are adequate provisions to protect the privacy of research participants and to maintain the confidentiality of data.

An experienced IRB Administrator, who is also an IRB member typically reviews and approves exempt reviews, including submissions which meet the Common Rule category for limited IRB review. Novel studies may be assigned to other IRB members.

EXPEDITED REVIEW PROCESS

A new study may qualify for *expedited review* if it presents no more than minimal risk to the research participants and it meets the criteria for expedited review as fully described within the Federal Register: November 9, 1998 (Volume 63, Number 216).

The Downstate IRB may use the expedited review procedure to review any of the following:

- For **FDA** regulated research, a new study qualifies for **expedited review process for initial review,** if it presents no more than minimal risk to the research participants and it meets the criteria for expedited review as fully described within the Federal Register: November 9, 1998 (Volume 63, Number 216). FDA requires the IRB "reviewer(s)" to find that the research on the list involves no more than minimal risk for the IRB to use the

expedited review procedure. This rule for determining risk applies to FDA regulated research that is also subject to the Common Rule.

- For **non-FDA regulated research**, a new study qualifies for **expedited review process for initial review,** when it fully described within the Federal Register: November 9, 1998 (Volume 63, Number 216), **unless** the reviewer determines the study involves more than minimal risk. Should an expedited reviewer determine that non-FDA regulated research initially qualifying for expedited review presents more than minimal risk, this assessment and its rationale must be documented. The IRB will record such determinations in IRBNet or include them within the investigator's approval or determination letter.
- If an expedited reviewer determines that the non-FDA regulated research appearing on the expedited review list is more than minimal risk, and therefore no longer qualifies for expedited review, the reviewer must document the rationale for making this determination. The IRB should document this in the IRBNet or within the approval or determination letter to the investigator.
    - *For **non-FDA regulated research**, as permitted by OHRP, category #5 includes research involving materials that were previously collected for either non-research or research purposes, provided that any materials collected for research were not collected for the currently proposed research. Research may involve materials that will be collected solely for non-research purposes.*
    - (Note: Some research in category 5 may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(4). This listing refers only to research that is not exempt.)
- **Continuing review** research, which qualifies for expedited review, when it meets the criteria described at when it fully described within the Federal Register: November 9, 1998 (Volume 63, Number 216).
- **Continuing review** for all ongoing **HUD approvals**, including those intended for clinical (non-research) use (see additional details under continuing review).
- For **non-FDA regulated research** for which **limited IRB review** is a condition of exemption (see above).
- For previously approved research, the review of amendments for **minor changes**, **reportable events**, and o**ther considerations** shall be done via expedited review whenever permissible under the regulations during the authorized approval period.

Do not use expedited review procedures to circumvent the convened meeting requirements. Examples of such misuse may be any of the following actions:

- Interim expedited approval pending review of the proposed study at a later convened meeting.
- Approval granted for the one-patient nonemergency use when the protocol does not meet the requirements of expedited review.
- Expedited approval based on IRB approval of the protocol at another institution for which no cooperative agreement exists.
- Expedited review of a claimed emergency use when the circumstances do not meet the requirements for emergency use.

All Reportable Events are reviewed by the Vice-Chair, or Chair when the Vice-Chair is not available, or may be referred to the full board.

Expedited review of new or continuing studies previously approved by the IRB is conducted by the IRB Chair and/or designated IRB Member(s), rather than through a convened (full) IRB review. This process may reduce the time required for approval; however, all projects must

continue to satisfy established requirements. Submissions are accepted on a rolling basis with no scheduled deadlines, as the review commences promptly upon receipt.

The expedited reviewer follows IRB guidance when conducting their review and completes any required checklist related to the review. They may also wish to refer to the full board review process below, to ensure all determinations are met.

The IRB reserves the right to request revisions or provide recommendations prior to granting approval. If the subject matter falls outside an IRB Member's area of expertise, the review may be referred to the IRB Chair, Vice-Chair, or another qualified IRB Member. While an IRB Member cannot disapprove research under expedited review, they may refer the submission for full board consideration for further evaluation or acknowledgement.

Experienced IRB Members are authorized to review and approve research packages eligible for expedited review. They may also require modifications or make recommendations before final approval. Should the study's complexity or novelty warrant additional scrutiny, it may be assigned to members holding advanced degrees such as a PhD or MD.

An experienced IRB Administrator who holds IRB membership may also conduct and approve expedited reviews. The IRB Chair maintains final authority in cases where concerns arise. Although the IRB Chair cannot disapprove a project through the expedited review process, deferral to the convened IRB for a conclusive decision remains permissible.

CHECK-IN ADMIDISTRATIVE REVIEW

The Downstate IRB conducts administrative review of research that has 3-year check-in period. This is not considered to be an expedited review under the regulatory framework.

FULL (CONVENED) IRB REVIEW PROCESS

It is the responsibility of the PI to submit all required materials and signatures according to the posted schedule on the IRB website prior to a scheduled IRB meeting, unless special extenuating circumstances are approved by the Executive Director, Vice-Chair, or IRB Chair.

The full board reviews human research that does not meet the criteria for exempt (including limited IRB review) or expedited review. Other than the initial or continuing review submissions that require full board review (described elsewhere in this policy), the IRB must also review the following submission events by the full IRB:

- Amendments changing the level of risk of the study to greater than minimal risk.
- When an IRB member determines and requires full board and documents the reason for such referral.
- When determining or confirming serious or continuing noncompliance.
- When determining or confirming an unanticipated problem.
- When determining or confirming a suspension of IRB approval.

1) Meeting and agenda preparation

1. Once an item is confirmed for the agenda, Associate IRB Administrators promptly forward the submission to the Convened Board meeting space in IRBNet and assign primary and

secondary IRB members to review it in IRBNet, notifying them according to their areas of expertise.

a) The Lead Associate IRB Administrator for the meeting finalizes the meeting agenda and make it available to the IRB Members as soon as possible.

b) Whenever possible, all IRB Members receive access to agenda and all submission materials, approximately ten (10) business days before the scheduled meeting to allow sufficient time for the review process. However, late submissions may be approved by the IRB Chair, Vice Chair, or Executive Director, if this is not possible due to extenuating circumstances (i.e., potential lapse of continuing review, urgent review request from PI). When the agenda item is delayed, the IRB Office will reach out to the IRB Member(s) to check their availability for a more rapid review and update the PI if the review is not possible.

c) All IRB members and IRB Office staff have access to all materials in IRBNet. All IRB Members should review all studies requiring full IRB review and be prepared for the discussion.

d) To improve efficiencies and communication regarding any new study undergoing initial review by the full committee, the Associate IRB Administrator invites the PI to attend to present the study and answer any questions of the IRB. It is in the best interest of the PI to attend or call into the meeting. Study team members may also attend with or on behalf of the PI; however, if they cannot answer IRB questions, the IRB may need to disapprove the study or require additional modifications or clarifications to grant final approval. *Note: They are placed in a waiting room and brought into the meeting when the IRB is ready to discuss their submission. They are absent from the room during any deliberation and vote.*

e) Prior meeting IRB Minutes, applicable business items and audits, and appropriate continuing education materials will be made available approximately five (5) business days before the scheduled meeting.

f) The IRB Coordinator notifies the board by email once the agenda is finalized and sends a calendar invite.

2) The IRB Chair and IRB Members follow the guidance and reviewer checklists posted on the IRB website.

3) IRB Members should record their comments in IRBNet, complete any required checklist before the meeting, and upload checklists and edited documents to the reviewer space.

4) The Lead Associate IRB Administrator confirms quorum requirements are met, including the presence of a non-scientist and MD for FDA regulated studies, before the meeting may begin.

5) The Lead Associate IRB Administrator reminds the IRB of any COI Management Plans that are relevant to the review of an agenda item.

6) The Chair (or Vice-Chair, in the absence of the Chair) confirms any conflicts of interest among members, including any conflicts of investigator sand manages recusals of conflicted IRB members. The Chair leads the meeting using the guidance posted on the IRB website.

7) During the initial review of the submission of an HUD, the Chair (or Vice-Chair, in the absence of the Chair) confirms any conflicts of interest including financial ties to the HDE holder or investigator and manages recusals. Chair introduces the HUD item as either:
   iii) Clinical HUD use application, or
   iv) Research study involving a HUD (on-label or off-label).

8) Typically, the primary reviewer presents their findings first, followed by the secondary reviewer. The other IRB members should refrain from interrupting their presentations and hold their questions until after the primary and secondary reviewers complete their presentations to the committee.

9) Primary Reviewer(s) presents a concise summary including:

i) High level summary of the study
ii) Proposed risks and any applicable determinations.
iii) If they are reviewing an HUD application, the following should be discussed:
(1) HUD/HDE status, indication, and labeling.
(2) How and in whom the device will be used locally.
(3) Whether the use is clinical vs research, and on-label vs off-label.
(4) Key risk–benefit considerations and any special risk mitigation strategies.
(5) Adequacy of consent/patient information plan and safety reporting plan.
(6) Discuss whether the clinician has include a request to use a HUD outside its approved indication(s).
(7) Professionals' qualifications through training and expertise to use the device.

b) Secondary Reviewer(s) presents a concise summary of the informed consent and recruitment materials, including:
i) Any area of concerns not presented by the primary reviewer.
ii) Any areas of disagreement with the primary reviewer.
iii) Any concerns on the patient facing material such as the Informed Consent document (if applicable), patient brochure, and any information provided to the patient.

10) At the meeting, the IRB has discussion sand makes determinations, such as, but not limited to the following:
a) Reviewing the qualifications of the PI/CI and study staff. See additional details in the section below
b) Reviewing the adequacy of the research site(s), including any institutional requirements for sponsor-investigator studies.
c) Risk level of the research. At the time of initial and continuing review, the IRB will determine the risks associated with the research protocols and whether risks can be minimized through appropriate measures. Risks associated with the research will be classified as either "minimal" (no greater than minimal risk) or "greater than minimal" based on the regulatory definitions of minimal risk. The level of risk is entered in the electronic IRB submission and reporting system.
d) The IRB assesses the potential benefits of the research to the research participants and society, based on the IRB application materials and experience of the IRB. The IRB considers whether the benefits that may be reasonably expected to result provide a reasonable basis for assuming the risks of the research. Compensation and reimbursement are NOT considered a benefit.
e) The IRB must make all determinations required to approve research involving children. For research involving children to meet the criteria for approval under category 406 (45 CFR 46.406 or 21 CFR 50.53), the IRB must determine that the research risk represents only a minor increase over minimal risk.
f) Whether the study involves research participants that are likely to be vulnerable to coercion or undue influence, and, if so, whether additional safeguards have been included to project their rights and welfare.
g) Assessing whether the CI or sponsor determined that an IND or and IDE is required and the basis for this determination.
h) Making and documenting SR/NSR determinations for FDA regulated medical devices and indicating the reason for the determination.[45]
i) Determining the applicability of additional protections for pregnant individuals, fetuses, neonates, children and prisoners and ensuring such research complies with applicable regulations.

45 FDA Guidance: Minutes of IRB Meetings (September 2017)

j) Determining the approval period and whether the research requires review more often than annually.
k) Determining if the research needs verification from sources other than the investigator (i.e., sponsor, third party, QAP) that no material changes have occurred since previous IRB review.
l) If an HUD is reviewed, the following is discussed:
    i) Determine how to approve use of a HUD
    ii) Determine any appropriate follow-up precautions and evaluations, or other criteria the IRB determines to be appropriate.
    iii) Whether local use is consistent with the HDE indication and FDA's risk–benefit framework.[46]
    iv) Adequacy of patient selection criteria and clinical oversight.
    v) Whether the proposed consent or information process is ethically and legally sufficient.
    vi) Whether monitoring, Reportable Events reporting and device accountability plans are adequate.
    vii) For research use, whether an IDE is required (e.g., off-label research use) vs IDE-exempt (on-label research under HDE).
    viii) The IRB may impose conditions or limitations on HUD use, including:
        (1) Restricting use based on disease progression or prior treatment outcomes.
        (2) Limiting use to certain providers, services, or settings.
        (3) Setting specific reporting requirements to the IRB or others.
        (4) Requiring evidence of failure or ineligibility for standard treatments before HUD use.
        (5) Mandating additional or periodic case reports.
        (6) Requiring completion of manufacturer or institutional training before use.

11) All IRB members participate in the discussions and ask questions as needed.
12) The invited PI is released from the holding room to be asked to join the meeting when the IRB is ready to ask questions. They may be placed back in the holding room if needed and called back when needed or they may be excused after all questions are asked.
13) The IRB continues discussions after the PI is excused.
14) The IRB determines the frequency of review at the time of initial review and at continuing review. The IRB re-reviews protocols at intervals appropriate to the degree of risk but no less than once per year unless continuing review is not required by this policy. In some circumstances, a shorter review interval (e.g., biannually, quarterly, or after accrual of a specific number of participants) may be required. The IRB office enters the expiration date of the approval period in the electronic IRB submission and reporting system, and the approval letter will reflect the expiration date. In specifying an approval period of less than one year, the IRB may define the period with either a time interval or a maximum number of research participants either studied or enrolled. When the IRB determines the approval-period based on the enrollment of a maximum number of research participants, this approval period in no case can exceed one year. Most research requiring continuing review, the IRB grants a one-year review period unless otherwise specified by the IRB. The IRB considers the following factors when determining which studies require review more frequently than on an annual basis:
    - Significant risk to research participants (e.g., death, permanent or long-lasting disability or morbidity, severe toxicity) with the possibility of direct benefit to the research participants.

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- The inclusion of significantly vulnerable populations where, even in the presence of possible direct benefit, there is also a possibility of significant risk associated with the research procedures.
- The probability and magnitude of anticipated risks to research participants.
- The likely medical condition of the proposed research participants.
- The overall qualifications of the PI and other members of the research team.
- The specific experience of the PI and other members of the research team in conducting similar research.
- The novelty of the research making unanticipated adverse events more likely.
- The nature of any risks posed by the research project.
- The degree of uncertainty regarding the risks involved.
- The vulnerability of the research participants' population.
- The experience of the investigators in conducting research.
- The IRB's previous experience with the investigators (e.g., compliance history, previous problems with the investigator obtaining informed consent, or prior complaints from research participants about the investigator).
- The projected rate of enrollment.
- Whether the research project involves novel interventions.

15) The IRB may decide to require consent monitoring, or require verification from sources other than the investigators that no material changes occurred during the IRB-designated approval period, such a QAP review. For more details, see below.
16) Any other factors that the IRB deems relevant. The Chair calls for a motion and vote. Typically, the primary member makes the motion; however, the Chair can call on anyone present to make the motion.
17) Eligible IRB members vote on each submission or study action, based on voting procedures. Voting procedures are described below and in separate IRB guidance.
18) After the meeting ends, the Associate IRB Administrators and IRB Coordinator draft the minutes and the letters regarding the discussion that was held at the meeting. They may review the recording or transcript of the meeting to assist with this process.
    a) If a HUD was reviewed at the meeting, the IRB approval letter (or minutes) for a HUD application explicitly states:
        i) Whether approval is for clinical HUD use or for a research study involving a HUD.
        ii) The specific indication(s) and patient population approved.
        iii) Any limitations (e.g., services, clinicians, setting, requirement for prior treatment failure).
        iv) Requirements for continuing review (at least annually) and what information must be provided (e.g., number of patients treated; summary of safety outcomes).
        v) Requirements for adverse event, device malfunction, and unanticipated problem reporting to IRB and HDE holder/FDA.

INVESTIGATOR QUALIFICATIONS

The IRB needs information about the qualifications of the investigator(s) to conduct and supervise the proposed research. Depending upon the nature and risks of the proposed research and the relationship between the IRB and the investigator or the location of the research, this may be relatively simple and straightforward, or it may entail a more involved assessment to evaluate the investigator's qualifications.

Such steps ***may*** include, as appropriate (such as the case for external study team members, when the IRB is not familiar with the PI, or for clinical trials that follow GCP requirements):

- Reviewing the PI's/CI'sCV, NIH Biosketch, or other statement of qualifications showing education, training, credentials, and experience that qualifies the investigator to be an expert in the research.
- Reviewing other investigator's expertise.
- Verifying professional associations, references, or medical licensure, when applicable,
- Reviewing relevant and recent publications and the investigator's training in good clinical practice, as appropriate, and/or
- Assessing the investigator's training and experience specifically related to the proposed study, particularly if the proposed research involves extremely high risks, vulnerable research participants, or novel technologies.

For clinical trials overseen by a PI from an external site, other than NYC H+H, Kings County, the PI should provide a statement from an administrator of the external institution to confirm the PI qualifications. This should come from a Credentialing Office, IO, Department Chair, or Dean and include information about the clinical investigator's qualifications, their credentials and licensure, and whether there have been any institutional disciplinary actions brought against the PI.

If a PI does not have the appropriate privileges or credentials to carry out a research intervention in a research study, the applicable activities may be conducted by another appropriately qualified PI (multiple PIs may be permitted for some non-FDA regulated and unfunded research), or Co-investigator, approved by the IRB.

The IRB may check lists posted on FDA's website, Clinical Investigator Status (Biologics), Inspection Classification Database Search, Clinical Investigators - Disqualification Proceedings, Inspections, Compliance, Enforcement, and Criminal Investigations to determine whether an investigator has been the subject of an inspection by the agency and the results of such inspections (e.g., Warning). The FDA also posts on its website a listing of all investigators who have been notified of the initiation of a disqualification proceeding or have been disqualified. The IRB may check FDA's Inspections, Compliance, Enforcement, and Criminal Investigations website for information related to clinical investigator inspections, warning letters, disqualification proceedings, and debarments.

VERIFICATION THAT NO MATERIAL CHANGES HAVE OCCURRED

The IRB recognizes that protecting the rights and welfare of research participants sometimes requires that the IRB obtain independent verification, utilizing sources other than the investigators that no material changes occurred during the IRB-designated approval period.

Independent verification from sources other than the investigator (e.g., auditor, IRB, sponsor, or other third party) may be necessary at times, for example, in cooperative studies, or another multi-center research.

The IRB may consider the following factors when determining which studies require independent verification:

- Protocols where concern about possible material changes occurring without IRB approval have been raised based on information provided in continuing review reports or from other sources.
- Protocols conducted by a PI who has previously failed to comply with federal regulations and/or the requirements or determinations of the IRB.

- Protocols selected for internal audit.
- Whenever else the IRB deems verification from outside sources is relevant.
- The probability and magnitude of anticipated risks to research participants.
- The likely medical condition of the proposed research participants.
- The probable nature and frequency of changes that may ordinarily be expected in the type of research proposed.

In making determinations about independent verification, the IRB may prospectively require that such verification take place at predetermined intervals during the approval period or may retrospectively require such verification at the time of continuing review, review of amendments and/or adverse events.

The IRB may require the monitor to submit a report of the findings to the IRB, for which the IRB can review and may require additional actions.

For more information, please see the related section on the Quality Assessment Program (QAP) in this document.

CONSENT MONITORING

Occasionally, the IRB may determine that special monitoring of the consent process by an impartial observer (consent monitor) is required to reduce the possibility of coercion and undue influence, ensure that investigators follow the approved consent process, or ensure that the investigators are truly obtaining legally effective informed consent. The IRB may particularly warrant monitoring for any the following:

- Studies involving extremely high or significant risks.
- Studies that involve particularly complicated procedures or interventions, when research participants are likely to have difficulty understanding the information to be provided.
- Studies involving highly vulnerable populations (e.g., ICU patients, children).
- Studies involving study staff with minimal experience in administering consent to potential study participants.
- Studies requiring additional monitoring to minimize concerns of undue influence or coercion.
- When the IRB determines monitoring is an appropriate as a corrective action where the IRB has identified problems associated with a particular investigator or a research project.
- Other situations when the IRB has concerns over that the consent process.

When the IRB requires consent monitoring, the IRB notifies the PI of the determination and the reasons for the determination and should include the following, as applicable to the research:

- who monitors the process,
- the arrangements to be made by the PI,
- the number of research participants requiring monitoring, and,
- whether the monitor must sign the informed consent document to attest to the validity of the consent process.

When observing the consent process, the monitor will determine:

- Whether the informed consent process was appropriately completed and documented,

- Whether the research participants had sufficient time to consider study participation,
- Whether the consent process involved coercion or undue influence,
- Whether the information was accurate and conveyed in understandable language, and
- Whether the research participants appeared to understand the information and gave their voluntary consent.

The monitor submits a report of the findings to the IRB, for which the IRB can review and may require additional actions.

IRB ATTENDANCE, QUORUM, AND VOTING

By regulation, final actions on protocols that require full IRB review only occur at a convened meeting. The IRB posts the meeting schedule on the IRB website. The IRB Chair or Vice-Chair may call for additional meetings for administrative, educational purposes, for an emergency or otherwise critical review.

A necessary quorum for the IRB to consider a proposal is a majority of the total number of primary members for the Committee, including a member whose primary concern is in a nonscientific area, before taking regulatory actions at these meetings. See section on IRB Minutes for additional information. If research involving an FDA-regulated article is involved, a licensed physician must be included in the quorum. A quorum must be present before a vote can take place. Members must be present in person or via teleconference or video conference. When there is an even number of Primary Members on the IRB Roster, calculate the majority using the “half-plus-one” technique. For example, if the total number of Primary Members is 14, then majority is 8 (half of 14 is 7, 7+1 =8). However, when the IRB has an odd number of Primary Members on the Roster, the majority is calculated by taking half of the number of Primary Members on the Roster, then rounding up to the next whole number. For example, if the total number of Primary Members is 15, then the majority is 8 (half of 15 is 7.5 and rounding up to the next whole number is 8).

All members receive all pertinent material prior to the meeting, and the IRB considers them present when they actively and equally participate in all discussions through teleconferencing or videoconferencing.

The IRB does not permit advanced (proxy) votes for voting on regulatory actions that are required during a convened IRB meeting; however, an IRB Member may record their recommendations in the electronic IRB submission and reporting system in advance of the meeting. Voting for non-regulatory required actions (e.g., approval of IRB Minutes or other business-related decisions), may take place via e-mail or phone.

No IRB may have a member participate in the board's initial or continuing review of any project in which the member has a conflicting interest, except to provide information requested by the IRB.

An IRB member who is listed as PI, Co-investigator, or key personnel is conflicted and therefore is automatically recused from participation and voting; except (s)he can provide any information that is requested by the IRB.

A discussion takes place for each submission at the convened meeting, prior to making a motion and taking the vote. The primary member for the month will vote at the meeting. However, if the primary member is absent or recused, the vote will go to the alternate member, if present.

Designated reviewers vote on the item they reviewed if they are the eligible voting member for their voting pair (primary, or alternate substituting for an absent/recused primary). If a designated reviewer is not the eligible voter for that pair, they may still present and discuss, but do not vote.

The IRB approves a submission when it receives the approval of the majority of the eligible voting members at the meeting. If there is an even number of eligible voting members present, calculate the majority using the "half-plus-one" technique. For example, if the total number of eligible voting members is 10, then majority is 6 (half of 10 is 5, 5+1 =6). However, there is an odd number of eligible voting members present, the majority is calculated by taking half of the number of eligible voting members present, then rounding up to the next whole number. For example, if the number of eligible voting members is 11, then the majority is 6 (half of 11 is 5.5 and rounding up to the next whole number is 6). If an IRB Chair or Vice-Chair entertains a motion under which the IRB votes on groups of studies (sometimes called "block voting"), IRB Members can voice their vote "for" on some studies, "against" on others, and "abstain" on others.

If all the reviewers are absent from the meeting, the IRB Vice Chair will determine if the study in question must be tabled for a review at a future meeting. If the present members have sufficient information and expertise, the IRB Vice Chair may determine the review may proceed.
Most meetings are virtual, so IRB members should keep cameras on to monitor attendance and quorum during voting. Voting may be done by show of hands, emojis, chat, or built-in voting features in Zoom or Teams if votes can be attributed. For details, see the IRB Guidance: "IRB Meeting Guidelines and Duties, Responsibilities, and Goals of IRB Members, Advisors, Guests, and IRB Administrators".

PROCEDURES FOR CONTINUING REVIEWS

Regardless of whether a continuing review application for a non-exempt study is reviewed by expedited or by the convened board, the review must be meaningful and substantive.

When conducting continuing review, the IRB should start with the assumption that the research, as previously approved, satisfied all the criteria for approval and should focus on any new information provided by the investigator or sponsor, or otherwise available to the IRB, that may alter the IRB's prior determinations, particularly with respect to the IRB's prior evaluation of the potential benefits or risks to the research participants. The IRB also should assess whether there is any new information that would necessitate revision of the protocol and/or the informed consent document. If the IRB determines that a research activity no longer meets the criteria for approval, the IRB is not permitted to reapprove it but may either disapprove it or require modifications in order to secure re-approval or grant conditional approval with directed changes.

When conducting continuing review and evaluating whether research continues to satisfy the criteria for IRB approval of research, the IRB should pay particular attention to the following areas: 1) risk assessment and monitoring, 2) adequacy of informed consent, 3) local issues, and 4) research progress.

The amount of time the IRB spends on the continuing review of a particular study will vary depending on the nature and complexity of the research, the amount and type of new information presented to the IRB and whether the investigator is seeking approval of substantive changes to the research protocol or informed consent document. For many studies, continuing review can be straightforward, and the IRB should be able to complete its deliberations and review

promptly.

IRB members are encouraged to review OHRP and FDA guidance on continue review for additional information.[47,48]

PROCEDURES FOR CONTINUING REVIEW OF HUD USE (CLINICAL AND RESEARCH)

The IRB is required to conduct continuing review at least once annually for all ongoing HUD approvals, including those intended for clinical (non-research) use. The IRB utilizes an expedited review procedure for the continuing review of HUDs used in medical practice, unless an IRB Member, Chair, or Vice-Chair determines that full board review is necessary.

At continuing review, the IRB requires:

1. Number of patients treated with the HUD since the last review.
2. Summary of adverse events, device malfunctions, unanticipated problems, and reports to manufacturer or FDA.[49]
3. Any changes in labeling, HDE status, or FDA communication about the HUD.
4. Significant institutional or service-level issues (e.g., training gaps, logistical problems).
5. For research, continuing review follows standard IRB device procedures, including IDE status where relevant.

FULL BOARD IRB ACTIONS

The convened IRB can make a motion to vote on the following actions at the convened board meeting:

- Approve
- Conditional Approval With Specific Directed Changes
- Modifications Required
- Disapprove

The IRB, Chair, or Vice-Chair can also decide to Table a study without action.

IRB ACTIONS TABLE (WITH DEFINITIONS AND REGULATORY CITATIONS)

This table outlines IRB actions, along with their definitions, relevant regulatory citations, and guidance regarding their authority. It also explains the follow-up process and includes additional notes and examples when necessary.

Separate IRB Actions or Motions may be necessary to make and determine required findings, such as NSR/SR determinations, Risk determinations, determinations required for vulnerable

47 OHRP Continuing Review Guidance (2010)
48 IRB Continuing Review After Clinical Investigation Approval | FDA

49 FDA Regulations: 21 CFR 814 Subpart H, HUDs

populations, resolution of controverted issues, etc. All actions or motions must be documented in the IRB minutes along with the separate votes for each.

IRB Action (Motion)	Definition/Follow-up process	Regulatory Citations/Guidance for the authority
Approve	The IRB determines all regulatory criteria for approval are fully satisfied. Research may begin once all institutional requirements are met.	• 45 CFR 46.111 - Criteria for approval • 21 CFR 56.111 - FDA criteria for approval • 45 CFR 46.109(a) - Authority to approve • 21 CFR 56.109(a) – FDA Authority to approve
Conditional Approval with Specific Directed Changes	The IRB finds that approval criteria can be met if the investigator makes specific, verifiable changes. **Follow up process:** The directed changes must be verified by administrative review (see details in notes below).	• 45 CFR 46.109(a) / 21 CFR 56.109(a) - Authority to require modifications to secure approval • 45 CFR 46.111 / 21 CFR 56.111 - Approval criterion • OHRP Guidance (2010): IRB Approval of Research with Conditions[50] • FDA Guidance: IRB Continuing Review after Clinical Investigational Approval (2012).[51]
Directed changes require the PI (a) make specified changes to the research, such as the protocol or informed consent document(s), (b) confirm specific assumptions or understandings on the part of the IRB regarding how the research will be conducted, or (c) submit additional documents such that, based on the assumption that the conditions are satisfied, the IRB can make all the determinations required for approval under the regulations, **and** the directed changes must be verified by a Downstate IRB member or multiple IRB members (or other individual[s] designated by the IRB) via an **administrative review** procedure to determine on behalf of the IRB whether the directed changes, submitted by the PI are satisfactory. This administrative review **does not** qualify as an expedited review process and, accordingly, should not be documented as such in the final approval letter. *CAUTION:* • *With this framework, the IRB generally CANNOT request clarifications, explanations, or descriptions of items as it demonstrates the criteria for approval cannot be satisfied and as such would be a MODIFICATIONS REQUIRED (see below).* • *Additional amendments may NOT be submitted by the PI/CI in response to the conditional approval. An amendment may only be submitted to the IRB once the study is approved.* • *The IRB can document its understanding from the Full Board meeting, and request the PI confirm these understandings. If the PI cannot confirm the understanding, then the response must return for review by a Full Board meeting.* • *Minutes should clearly include a summary or discussion of items that demonstrate the IRB's understanding that lead to the directives in the letter to the PI.*		

50 Approval of research with Conditions: OHRP Guidance (2010)
51 FDA Guidance: IRB Continuing Review after Clinical Investigational Approval (2012), page 16-17.

Examples:

- Inserting boilerplate consent language.
- Correcting administrative errors.
- Confirmation of IRB assumptions, such as verifying excluded populations (e.g., children excluded).
- Submission of additional required documents, such as training certificates or ancillary approvals.
- Submission of additional required signatures, such as Department Chair, Dean.
- Specific, directive wording changes to the protocol or consent form.
- Substantive changes permitted when parameters are clearly defined, allowing the PI to revise within IRB-specified boundaries.
- Directive to revise the protocol based on information clarified by the study team at the IRB meeting, provided the required changes are clearly defined and do not alter risk–benefit determinations.

For more information, refer to the OHRP guidance on Approval of research with Conditions or FDA Guidance on IRB Continuing Review after Clinical Investigation Approval.

Modifications Required	The IRB cannot approve the submission at this time because the IRB must request clarifications, explanations, or descriptions of items to demonstrate the criteria for approval can be satisfied **Follow up process:** Re-review occurs at a subsequent convened meeting.	• 45 CFR 46.109(a) / 21 CFR 56.109(a) — Authority to require modifications • 45 CFR 46.111 / 21 CFR 56.111 — Approval criteria • 21 CFR 56.110(b) — IRB Members may only approve or require modifications

Examples of requests that require Modifications Prior to Approval:

- Request for SRC or CMRC review.
- Revising risk statements.
- Updating dose escalation schema
- Adding Data Safety Monitoring (DSM) plan
- Altering dosing schedules
- Changing inclusion/exclusion criteria that impact safety
- Modifying AE reporting rules
- Revising stopping rules or DSMB oversight plans
- Adding genetic testing
- Adding vulnerable populations
- Adding invasive procedures or imaging exposures
- Request additional information needed to make the 111 determinations
- Justification for placebo use when withholding available treatment for a serious condition.
- Justification for enrolling children and explanation of how Subpart D requirements are met.
- Revision of study hypothesis or study design, requiring reassessment of scientific validity.

• Description of control-group procedures needed to evaluate risks and comparability. • Clarification of key risk-related information, such as exclusion criteria tied to safety (e.g., aspirin use and bleeding risk). • Clarification of when and how informed consent will be obtained, requiring evaluation of consent process adequacy. • Plan for additional subject monitoring in response to serious adverse events or emerging safety concerns.		
Disapprove	The IRB determines that the research does not meet approval criteria and revisions are insufficient to make the study approvable. Only a convened IRB may disapprove research. **Follow up process:** The PI is notified of the reasons. Re-review of a revised submission may occur at a subsequent convened meeting.	• 45 CFR 46.109(a) / 21 CFR 56.109(a) — Authority to disapprove • 45 CFR 46.111 / 21 CFR 56.111 — Approval criteria • 21 CFR 56.110(b) — Expedited review cannot disapprove
Table Without Action	The IRB takes no regulatory action because necessary information is missing, expertise is lacking, or quorum is lost. No approval criteria are evaluated until the study returns for review. **Follow up process:** The PI is notified of the reasons. Re-review of a revised submission may occur at a subsequent convened meeting.	• 45 CFR 46.108(b) — Quorum requirements • 21 CFR 56.108(c) — IRB operations, quorum, and voting • Institutional policy — Tabling/deferral is not a regulatory determination

IRB ACTIONS OUTSIDE OF FULL BOARD REVIEW

The Downstate IRB or IRB Office can take the following actions outside of the full board review:

IRB ACTIONS EXPEDITED REVIEW

An IRB Member may request modifications to approve a study, may approve a study, or may refer it to the full board, but may not disapprove a study.

IRB ACTIONS EXEMPT REVIEW

An IRB Member, Associate IRB Administrator, Senior IRB Coordinator, Executive Director, may or request modifications to make a determination that a study is exempt, that are not considered "limited reviews" may approve a study as exempt, or may refer it to the full board, but may not disapprove an exempt study.

An IRB Member, may or request modifications to make a determination that a study is exempt which qualify as "limited reviews" under the Common Rule, and may approve a study as exempt, or may refer it to the full board, but may not disapprove an exempt study.

IRB ACTIONS ADMINISTRATIVE REVIEW

An IRB Member, Associate IRB Administrator, Senior IRB Coordinator, Executive Director, may or request modifications to make IRB determinations and conduct administrative reviews, such as reviewing local research context for ceded reviews.

IRB LETTERS AND NOTIFICATIONS

Once an IRB Member completes his/her review (expedited/exempt) or after a full board meeting, the IRB Office will generate a letter to the PI dependent on the decision of the IRB, using the electronic IRB submission and reporting system. The selected letter depends on the decision of the IRB. Once the letter is generated, the IRB Office may notify the assigned Expedited reviewer (through committee messages in the electronic IRB submission and reporting system) if the letter needs to be reviewed for any clarification or feedback (e.g., adding notes or requirements from the IRB), if needed. The IRB member conducting the review may edit and publish the letter.

The IRB Office Staff drafts and publishes IRB letters. In general, letters pertaining to full board reviews other than straight approvals must be reviewed by the Executive Director, Human Research Protections and Quality Assurance (or designate) before they go to a Vice-Chair (or designate. Events concerning privacy or data security are also reviewed by the relevant Privacy or Data Security Officer. The Vice-Chair (or designate) finalizes these letters, consulting the IRB Chair when needed. All other letters are prepared and published by an IRB Member or Office and may be referred to relevant parties for quality or regulatory review.
In general, the goal of the IRB is to publish letters within five (5) business days of the IRB's determination; however, adjusts based on workload and staffing. The research team may contact the IRB to escalate the letter publication if it has been five (5) business days past the date of IRB meeting or approval. When publishing letters in IRBNet, the PI and anyone who has access to the submission will receive an e-mail notice that the letter is available.

Upon request, the IRB may include the names of the investigators approved to be on the study for the purposes of obtaining password approvals for access to electronic medical records.

Upon IRB approval, the PI receives a letter of approval, and the research may be conducted within the policies and procedures outlined by the IRB and within the constraints of other institutional and federal requirements. IRB approval does not in itself constitute administrative approval to initiate the research project, as additional requirements may also apply, before the

research may begin (e.g., ancillary approvals, contract approval, STAR approval for NYC H + H, Kings County research, etc.).

Note: The IRB provides the details for any recusals in the IRB approval letter, if necessary or when requested by the research team or the sponsor.

IRB DETERMINATION LETTERS AND FDA REGULATORY CITATIONS

For clinical investigations involving FDA-regulated test articles (e.g., drugs, biologics, and medical devices), IRB determinations are issued under the authority of the FDA human subject protection regulations, regardless of the source of funding. Accordingly, IRB approval, approval with conditions, required modifications, or disapproval for these studies may be documented in IRB correspondence with explicit reference to the applicable FDA regulations, including but not limited to 21 CFR 50 (Informed Consent), 21 CFR 56 (Institutional Review Boards), 21 CFR 312 (Investigational New Drug Applications), and 21 CFR 812 (Investigational Device Exemptions). These citations reflect the IRB's role in fulfilling its obligations under 21 CFR 56.109 (IRB review and authority) and 21 CFR 56.111 (criteria for IRB approval of clinical investigations), independent of any requirements that may arise from federal funding or the Common Rule.[52]

PI RESPONSE TIMEFRAMES

In general, the investigators should respond within the following timeframes, or the submission is considered withdrawn. The following response times are included in the letters:

- The research team will have **2 weeks** to respond from the date of that notification letter to any IRB requests regarding missing documents, training or signatures for all initial IRB Submissions including Exempt, Expedited and Full Board studies.
- The research team will have **1 month** to respond from the date of a modification letter from the IRB requesting DIRECTED CHANGES.
- The research team will have **2 months** to respond from the date of IRB notification letter regarding MODIFICATIONS REQUESTED from a full board meeting.

When the IRB Office unlocks a submission to request modifications, the PI receives a notice from IRBNet and has **2 weeks** to respond.

The PI may request additional time by writing to IRB@downstate.edu

DETERMINING EFFECTIVE DATE OF INITIAL IRB APPROVAL AND DATE FOR CONTINUING REVIEW OR CHECK-IN

Before generating an IRB letter, the IRB must determine the approval period for the submission.

52 "Pursuant to 21 CFR 56.109(a), IRBs reviewing FDA-regulated research have the authority to issue determinations including Approve, Approve With Conditions, Require Modifications, or Disapprove, irrespective of funding source. FDA guidance further clarifies this authority (Institutional Review Boards Frequently Asked Questions, FDA) and recognizes harmonization with HHS/OHRP procedures (IRB Written Procedures: Guidance for Institutions and IRBs, OHRP/FDA)."

The IRB follows OHRP Guidance on Continuing Review[53] and the FDA Guidance on Continuing Review[54] for determining the effective date of initial IRB approval and the dates for continuing review.

CONTINUING REVIEW PERIODS

Unless the IRB determines the frequency of review is less than one year, in terms of months or conditions, the IRB must review the following approved research within a time period not to exceed **one year**:

- All FDA and DOJ regulated research
- All research determined by the IRB to be greater than minimal risk
- Use Device (HUD) clinical uses and for HUD clinical trials.

EXPIRATION DATES FOR APPROVED STUDIES WITHOUT DIRECTED CHANGES

For initial reviews and continuing reviews, the expiration date will be 1 year (minus 1 day) from the approval date for research subject to continuing review. For example, if a study is approved on **November 22, 2025**, **without any directed changes**, the expiration date of the IRB approval will be **November 21, 2026**.

EXPIRATION DATES FOR APPROVED STUDIES WITH DIRECTED CHANGES

When the IRB reviews and approves research with **directed changes** at a convened IRB meeting without requiring further review at a subsequent convened meeting, the effective date of the **initial approval is the date on which the IRB Chair or an IRB Member has administratively reviewed and accepted as satisfactory all changes** to the protocol or informed consent documents, or any other responsive materials, required by the IRB from the investigators. In such circumstances, the expiration date of the initial approval period, which is the date by which the **first** continuing review (when required) must occur, may be as late as one year (minus one day) after that effective date of initial IRB approval.

For example, a study was reviewed by the convened IRB on **November 22, 2025,** and requested directed changes and an IRB member confirmed the directed changes were made on **December 22, 2025** (effective date), the expiration date of the IRB approval will be **December 21, 2026**.

FIXED ANNIVERSARY DATE FOR THE EXPIRATION OF ANNUAL IRB APPROVALS

When (a) the IRB grants approval for one year at the time of each continuing review, and (b) the IRB performs continuing review and re-approves (with or without conditions) the research within 30 days *before* the IRB approval period expires, the IRB may retain the anniversary of the expiration date of the initial IRB approval as the expiration date of each subsequent one-year approval period. For example, if an IRB conducts initial review of a research submission on **November 22, 2025**, **without any directed changes**, the expiration date of the IRB approval will be **November 21, 2026**.

53 OHRP Guidance on Continuing Review
54 FDA Guidance on Continuing Review

The IRB may conduct its first continuing review **within 30 days of November 21, 2026,** and re-approve the research for another one-year period with an expiration on **November 21, 2027.** The same timing may be applied to each subsequent continuing review until the research activities involving human subjects are completed.

The same process for determining the continuing review dates apply when the IRB determines that research must undergo continuing review more often than annually and when the IRB reviews and approves research under an expedited review procedure.

At the time of continuing review, the IRB must consider whether the current frequency of continuing review for the study is appropriate to the degree of risk or should be adjusted. For example, if the IRB initially approved a research study for a period of a year and at the first annual continuing review determined that the risks posed to the subjects have increased significantly, the IRB might re-approve the project after determining that the criteria for approval remain satisfied but require that the next continuing review occur in 6 months.

REVIEW OF AMENDMENT

Review of an amendment during the period for which approval is authorized does not constitute continuing review of the study as a whole, and thus does not extend the date by which continuing review must occur.

Amendment reviews may take place via expedited review if the submission qualities for expedited review; otherwise, they take place during a convened (full) board meeting.

CONTINUING REVIEWS

If the **continuing review** report is reviewed and approved by the IRB **within thirty (30) days** prior to the expiration of the study, the IRB may **maintain the fixed anniversary date** for the expiration of the annual approval.

Continuing reviews may take place via expedited review if the submission qualities for expedited review.

CEDED REVIEWS

When an external (reviewing) IRB approves a study through ceded review, the Downstate IRB will recognize the expiration date set by the reviewing IRB and adopt it as the expiration date for Downstate activation.

THREE YEAR CHECK-IN REVIEW PERIODS

Unless the IRB determines and documents a shorter review period is required, for research approved after January 19, 2019, a **three-year check-in** review is required for:

- Non-FDA regulated and non-DOJ regulated research determined to be Exempt, including limited reviews.

- Research that is neither regulated by the FDA nor DOJ regulated, when the research is eligible for expedited review, unless the IRB determines a shorter review period is required.

For initial and continuing reviews of the above studies, the expiration date will be 3 years (minus 1 day) from the approval date for research subject to continuing review. For example, if a study is approved or determined to be exempt on **November 22, 2025**, the expiration date of the IRB approval/exemption period will be **November 21, 2028**.

The IRB may keep a fixed date for the 3-year anniversary, provided the check-in review takes place within 30 days of the expiration date. For example, if the IRB reviewed a check-in within 30 days of an exempt study which expires on **November 21, 2028,** the next expiration date will be **November 21, 2031.**

IRB LETTERS

The IRB generates letters for Acknowledgements, Actions, Determinations, or Actions in the IRB application and submission system. A description of these letters is provided below. Template letters are used in the system, and the IRB Office drafts the letters based on the templates. The template letters include notes on how to enter dates on the letter and whether to use terms such as “administrative review” and “expedited review”.

Template letters for Directed Changes and Modifications Requested are generally utilized during full board reviews. Nonetheless, with suitable adjustments, they may also be tailored for use in expedited review procedures, especially in cases where multiple stipulations or requirements would be challenging to convey within an 'unlock' message on IRBNet.

ACKNOWLEDGED LETTER

The IRB issues this type of letter to acknowledge the receipt of the submitted materials. No additional actions are usually required, unless specified in the IRB letter.
The IRB may use this type of letter to acknowledge an external IRB approval (under ceded review), once the Downstate IRB confirms it meets all local research context requirements.

APPROVED - EXEMPT LETTER

The IRB issues this type of letter to document approval for exempt studies under limited review or exempt review; however, any additional requirements must be met prior to conducting the research.

APPROVED LETTER

The IRB issues an approval letter when the research is approved by the IRB; however, any additional requirements must be met prior to conducting the research.

When the PI responds to a **directed changes** request, the IRB reviews the response to the directed changes by administrative review, as described above, to confirm the response meets the requirements of the directed changes, before granting **approval**.

CONDITIONAL APPROVAL WITH DIRECTED CHANGES LETTER

The IRB may direct changes, as described above. When the IRB directs changes, , the IRB notifies the PI in writing of the changes that are required.

If the IRB moves for directed changes at a convened meeting but instead requires more substantive modifications based on regulatory or policy requirements, the IRB will issue a Modifications Required letter rather than request directed changes.

MODIFICATIONS REQUIRED LETTER

When the Full Board requires modifications, clarifications, explanations, or descriptions of items that demonstrate the criteria for approval cannot be met, the IRB requests changes in writing to the PI. The PI then returns the modifications for full board review.

NOT APPROVED LETTER

When the IRB disapproves research, the IRB notifies the PI in writing of the reasons.

TABLED WITHOUT ACTION LETTER

The IRB issues a tabling letter when IRB Chair or Vice-Chair defers or tables a study to a future meeting or another committee, with or without the majority vote of the IRB, for any of the following reasons:

- The IRB is unable to review the submission for any reason.
- The Chair or Vice-Chair elect to defer the research when it is in need of substantive changes before it can be presented to the IRB.
- Loss of quorum; or
- Lack of expertise on one of the IRB Committees

If applicable, the IRB will provide a written summary of any available concerns at the time of notification.

The IRB will re-review the submission (or revised submission) at a future meeting.

CEDED REVIEW – ACTIVATION LETTER

The IRB Office issues this type of letter after the study is approved by an external (reviewing) IRB and activated by the Downstate IRB Office. This confirms all local requirements are met for activation; however, any additional requirements must be met prior to conducting the research.

CEDED REVIEW – DIRECTED CHANGES LETTER

The IRB Office issues this type of letter to direct local changes required to activate a study at Downstate when it undergoes review by an external (reviewing) IRB.

The IRB Office issues this letter to outline changes needed to be congruent with local requirements prior to activating a study at Downstate following review by an external IRB.

CEDED REVIEW - RELIANCE AGREEMENT EXECUTED LETTER

The IRB Office may issue this type of letter to document the reliance on an external (reviewing) IRB.

CLOSED LETTER

When the IRB acknowledges a closure or final report, the IRB will issue a letter to this effect. The IRB may formally issue a closure letter if a study expires, such as when the PI is no longer affiliated with Downstate or fails to respond to requests to re-open or close a lapsed study.

DETERMINATION LETTER - NOT ENGAGED IN HUMAN RESEARCH

When the Downstate IRB determines the Downstate workforce is conducting activities that do not make Downstate engaged in human research, the IRB issues a determination letter to document Downstate IRB approval is not required.

DETERMINATION LETTER - NOT HUMAN RESEARCH

When the Downstate IRB determines an activity does not meet the requirements for human research, the IRB issues a written determination letter to document Downstate IRB approval is not required.

DETERMINATION LETTER - NOT RESEARCH

When the Downstate IRB determines an activity does not meet the definition of research, the IRB issues a written determination letter to document Downstate IRB approval is not required.

WITHDRAWN BY INVESTIGATOR LETTER

When the PI withdraws a submission, a letter is issued to document this request.

WITHDRAWN BY IRB LETTER

The IRB may issue a letter to administratively withdraw a submission as needed. Typically, this is done when the response to the IRB was not submitted within the requested time frame. A new submission may be created for IRB review; however, all the pending issues must be addressed.

EXPIRED NOTICE

When the IRB approval period of a study expires, the electronic IRB submission and reporting system issues an e-mail stating such.

SUSPENSION OR TERMINATION NOTICE

The IRB will acknowledge a notice for study is suspension or termination by someone other than the IRB. If the IRB suspends or terminates IRB approval, the letter will state such actions and the reasons for such actions.

The IRB will consider any actions required to protect any research participants in the study.

QUALITY ASSESSMENT PROGRAM LETTER

The IRB sends a Quality Assessment Program letter to inform the PI when Not-For-Cause, For Cause, or IRB Records Reviews will occur and when a summary of findings is available, as well as to request follow-up actions like a CAPA plan or Reportable Event.

STAMPING REQUIREMENTS OF IRB APPROVED MATERIALS

Before using the following documents, including translated documents, the Downstate IRB must stamp the following documents, if they were reviewed by the Downstate IRB:

- Long Forms (informed consent documents, HIPAA research authorizations, information sheets, assent Documents), including addendums.
- Short Forms.
- Recruitment posters, advertisements, or flyers (if technically feasible).

The IRB# and the approval date should be on the stamp for documents approved by the Downstate IRB. An expiration date is not required.

The Downstate IRB does not stamp documents that were approved by a reviewing (external IRB); however, the Downstate IRB does stamp the RF-Payment consent, if the external IRB does not require their approval or stamp on this document. Some reviewing IRBs consider this to be an internal document that they do not review or stamp, even if they stamp their approved documents.

The study staff must check the date stamp on the informed consent materials, before enrolling research participants to make sure the most current forms are used.

The IRB publishes stamped documents in the electronic IRB submission and reporting system and the PI and anyone who has access to the submission will receive an e-mail notice that the document is available.

If it is not feasible to stamp recruitment materials with IRB stamp (i.e., newspaper and electronic advertisements), posting of the document is permitted without the stamp if there are no modifications to the IRB approved language in the material, and the IRB approval letter references the approved materials.

The IRB **does not stamp** the following documents upon approval; however, an IRB approval letter listing these materials must be on file with the investigator, before they can be used:

- Surveys.

- Recruitment letters.
- Other recruitment materials and documents that are not mentioned above.
- IRB applications.
- Protocols.
- Study brochures.
- Investigator Brochures (IB).
- Case report forms.
- Data collection tools.
- Scales and questionnaires/surveys.
- Sponsor correspondences.
- IND safety reports.
- Summaries of what will be said to a potential research participant.
- Oral consent or recruitment scripts.

MINUTES

GENERAL

1) The meeting minutes should be written based on FDA and OHRP guidance.[55,56]
2) The IRB Coordinator drafts the meeting minutes based on compiled notes from IRB Administration/staff, committee members and audio recordings taken during the meeting, and the IRB letter posted in IRBNet. The Lead Associate IRB Administrator finalizes the minutes.
3) Minutes of IRB meetings which shall be in sufficient detail to show attendance at the meetings; actions taken by the IRB; the vote on these actions including the number of members voting for, against, and abstaining; the basis for requiring changes in or disapproving research; and a written summary of the discussion of controverted issues and their resolution. **The details must be provided for all items on the agenda.**
4) Meeting minutes must include:
   a) Attendance must record full name and representative capacity of each member present.
   b) For each item reviewed, the minutes must reflect:
      i) Documentation that quorum was maintained, such as indicating the number of members required for quorum for the meeting based on the roster and documentation of the total number of members present in the meeting. To review proposed research at a convened meeting, a majority of the members of the IRB must be present, including at least one member whose primary concerns are in nonscientific areas.
      ii) Document the presence of at least one nonscientist.
      iii) Document the presence of at least one MD/DO for FDA regulated research.
      iv) Track when members exit or return from the meeting and include notes in the voting section of each item as applicable to document the accuracy of the vote, including whether an alternate member voted on motion.
      v) A summary of the discussion, including the suggested format, as applicable to the review:
         (1) General discussion
         (2) Relevant written summary of the discussion

55 FDA Guidance IRB Meetings.
56 OHRP guidance: Minutes of IRB Meetings (September 2017)

(a) Documentation should include relevant summary information when such information contributes to an understanding of the IRB's findings and determinations (e.g., a brief rationale for the IRB's pediatric risk determination).

(b) Controverted issues[57], ANY points of controversy, disagreement, debate, among IRB members during meetings, must be clearly documented, with minutes briefly noting discussions and the resolution, which can usually be summarized in a few sentences. Controverted issues may stem from objections to aspects of proposed research, particularly projects involving emergency procedures or vulnerable groups. Members may resolve such concerns through discussion, further clarification from researchers or sponsors, a vote, or another mechanism determined by the IRB. Examples of controverted issues can include but are not limited to the following:

(i) A member believes the risks are "greater than minimal," while another believes they are "minimal."

(ii) Disagreement over whether the consent language adequately discloses risks or alternatives.

(iii) Differences in views about enrolling children, prisoners, pregnant people, or cognitively impaired adults.

(iv) Debating whether a DSMB is required.

(v) Members disagree on whether PHI access is justified or whether de-identification is adequate.

(vi) Debating whether the PI is adequately trained or experienced.

(vii) Disagreement over whether weak scientific justification creates an unethical risk/benefit ratio.

(3) PI Clarifications

(4) Consultant discussion, if appliable

(5) Directed changes and/or requests for modifications

(6) Document sufficient details to show the basis for requiring changes in the research, if changes are requested.

(7) Document sufficient details to show the basis for disapproval, if the research is not approved by the IRB.

(8) Findings and determinations the IRB must make to fulfill regulatory requirements, such as a brief rationale for the IRB's determination. Such findings include the following **initial reviews** of new studies and **continuing reviews** of previously approved studies:

(a) The IRB must confirm all approval criteria for research and consent forms (or waivers or exceptions from informed consent requirements) are met, and document this in the minutes when a study is approved by the full board. Any requested changes to meet approval criteria must also be documented.

(b) Risk level, including pediatric risk determinations.

(c) The minutes must indicate that, as part of its review and approval of a study, the IRB reviewed the informed consent form(s) and determined that the form(s) meet the applicable regulatory requirements.

(d) Finding that research involving children meets the conditions for the specific categories of permissible research and determine that requirements for permission by parents or guardians and for assent by children are met.

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(e) For research supported or conducted by HHS, or for studies which follow the Common Rule requirements, document the specific findings for research involving pregnant people, human fetuses, and neonates as subjects (45 CFR part 46, subpart B).

(f) For research supported or conducted by HHS, or for studies which follow the Common Rule requirements, document the specific findings for research involving Prisoners.

(g) For Emergency Research, if the IRB reviews a proposal for research involving an exception from informed consent requirements for emergency research, the IRB must find and document that the proposed research satisfies the criteria found in OHRP's Secretarial Waiver and/or FDA's regulations at 21 CFR 50.24.

(h) NSR vs SR determinations for medical device studies, unless the FDA has already made the determination, or unless the study is exempt from IDE requirements. The minutes for convened meetings should also document FDA determinations or IDE exemption determinations, as applicable.

(i) Unless FDA has already made a risk determination for a device study (e.g., significant risk (SR), or nonsignificant risk (NSR)), or the study is exempt in accordance with 21 CFR 812.2(c), sponsors are responsible for making the initial risk determination and presenting it to the IRB. In that case, the IRB must then make its own SR/NSR determination about the study, and either agree or disagree with the sponsor's determination by reviewing relevant information provided by the sponsor at a convened meeting (21 CFR 56.108(a)(1); 21 CFR 812.66). FDA considers this determination to be part of the IRB's responsibilities for conducting its initial review of a study. Document each SR/NSR determination, along with the reason for the determination, in the minutes.[58]

(9) For reportable events, record the board's determinations (Serious non-compliance, Continuing non-compliance, Non-compliance that is neither serious nor continuing, not non-compliance, etc.), whether corrective actions are appropriate or whether any additional action is required.

(10) Approvals or determinations for waivers or alterations of the requirements of consent and/or HIPAA Authorizations.

(11) Provide any additional information or notes and attach any checklists or other documents submitted by the reviewers.

vi) Motion for the action for any vote (i.e., approve, directed changes, modifications required, disapprove). The motion is recorded as the "action" in IRBNet.

vii) Actions taken (any votes) for each protocol and the vote (numbers for/against/abstaining).

viii) Indications of whether any IRB member was absent or recused during each vote. A recused member does NOT count towards the total during a vote. The member serving as an alternate for a member who is recused counts towards the vote. The minutes must identify any member who has a conflicting interest, including the reason for the recusal when recording the votes on IRB actions.

ix) Indication that quorum was maintained during each vote and that the motion passes

x) Include any actions to suspend or terminate IRB approval that occurs at the IRB meeting.

xi) Include a note that the IRB was provided an opportunity to discuss any previous minutes and reports of expedited actions.

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xii) Include a copy of the Roster, attendance records, and final published letters as a PDF binder.

5) Minutes and supporting records are reviewed by Associate IRB Administrator who is designated as the Lead for the meeting.
6) Draft minutes are reviewed by the IRB Chair or Vice Chair for finalization and approval
7) After the Chair approves the minutes, they are shared with all IRB members for review. IRB members are given 1 week to review and respond with any corrections. If there is no response, the minutes are considered final.
8) Final IRB approved minutes are distributed and shared as a PDF binder on SharePoint.
9) All IRB Members, IRB staff, and the IO will have access to the SharePoint site for the minutes and may access them at anytime.

If the IRB determines that it cannot approve a clinical investigation because the investigation does not meet the criteria in the exception from informed consent for emergency research or because of other relevant ethical concerns, the IRB must document its findings and provide these findings promptly in writing to the clinical investigator and to the sponsor of the clinical investigation. The sponsor of the clinical investigation must promptly disclose this information to FDA and to the sponsor's clinical investigators who are participating or are asked to participate in this or a substantially equivalent clinical investigation of the sponsor, and to other IRB's that have been, or are, asked to review this or a substantially equivalent investigation by that sponsor.[59],[60]

The IRB generates meeting minutes for all IRB meetings, for which voting takes place. Minutes of IRB meetings, which shall be in sufficient detail to show attendance at the meetings; actions taken by the IRB; the vote on these actions including the number of members voting for, against, and abstaining; the basis for requiring changes in or disapproving research; and a written summary of the discussion of controverted issues and their resolution.

The minutes will note recusals. The recused member does not count towards the quorum or the total votes.

Any items approved by members or administrative staff outside of the full board meetings, will be included in the IRB Minutes to notify the board members of all such actions.

UNANTICIPATED PROBLEMS, SERIOUS OR CONTINUING NONCOMPLIANCE, SUSPENSION OR TERMINATION OF IRB APPROVAL

If at a convened meeting, the IRB reviews an issue that requires prompt reporting to the IRB, the minutes should summarize the report and must document the IRB's action, if any, resulting from that review. Any review of such information and any decisions made outside of a convened meeting (e.g., as determined by the IRB Chair or Institutional Official for subject safety reasons) should be reported to the convened IRB and the discussion summarized in the minutes. Any subsequent action taken by the convened IRB (e.g., to lift suspension or to terminate the study) must be documented in the minutes.

Reporting of Expedited Reviews, Administrative Reviews, IRB Determinations, Exempt Determinations, Limited Reviews

59 21 CFR 50.24(e)
60 FDA Information Sheet: IRBs FAQs February 2025. FAQ #30

All expedited reviews, Administrative reviews, IRB determinations, Exempt determinations, and Limited Reviews are summarized and reported to the IRB members. This report can be shared in an IRB Meeting or attached to the minutes as an addendum report. IRB members may review these submissions in IRBNet, ask questions, or raise concerns. Any such questions or concerns may be updated in a subsequent report or be taken to a convened meeting upon request by any IRB member, Director, IO, or senior leader.

DISTRIBUTION OF IRB MEETING MINUTES

The IRB office saves the copies of the approved IRB minutes on a SharePoint site. The following individuals have access to this folder:

- Institutional Official
- Executive Director, Human Research Protections
- Associate IRB Administrators
- IRB Coordinator
- IRB Members

Relevant redacted minutes are available upon request; however, the IRB Chair, Vice-Chair, or the Executive Director must review the redacted minutes before sharing with an external institution.

In lieu of providing copies of the approved IRB minutes to the Medical Executive Committee (MEC), the IRB Chair, or their alternate will attend and provide updates to the MEC, as requested.

POST IRB APPROVAL/DETERMINATION

GENERAL REQUIREMENTS

After an approval or determination letter is issued by the IRB, the PI (or Project Lead, if applicable for non-human research projects), should do the following:

- Review the IRB approval/determination letter for accuracy and appropriate determinations.
- Check the approval date and expiration date in the letter.
- Check the approval date on approved documents (consent, recruitment materials, etc.). Previously approved documents do not require a new stamp, unless they were amended.
- Contact the IRB if there are any discrepancies, errors, or questions.
- Share applicable documents with sponsor.
- File documents in study binder.
- When approval or activation is for an Applicable Clinical Trial, ensure the trial is registered by the responsible party on the www.clinicaltrials.gov website.
- Understand and ensure the requirements of sponsor.
- Follow any required responsibilities, including reporting requirements to the IRB, sponsor, and FDA.
  Only use laboratory test reports from laboratories which are properly certified and/or accredited for diagnosis, treatment, and prevention of disease.

SUBMIT POST APPROVAL APPLICATIONS

Post-IRB approval application forms may be downloaded from the IRB website and must be utilized to submit applications for acknowledgments, amendments, reportable events, continuing review, check-ins, study closure, or re-activation. Application forms are also available for participation in the Quality Assessment Program and for reporting corrective and preventive action plans.

QUALITY ASSESSMENT PROGRAM

A Quality Assessment Program (QAP) for SUNY Downstate is fully described at Step 21 of the Downstate Electronics IRB submission website. The goal of the QAP is to review inspect and verify the ethical conduct of human research, integrity of data, adherence to the IRB approved protocol, and applicable institutional, state, and federal regulations, policy, and guidance. This program is non-punitive in nature and designed to be a productive process for investigators while striving for continuous improvement in every area of the research enterprise. There are several different types of QAP reviews: IRB records only, Not-for-Cause, and For-Cause. A routine (Not-For-Cause) Quality Assessment is conducted at the discretion of the IRB, Clinical Trials Office, or OCAS, for post-IRB approval assessment. Projects are randomly selected for Routine (Not-For-Cause) Quality Assessment; however, the Assessors have the discretion to select projects based on stratification and risk level such as clinical research and clinical trials. For-Cause Quality Assessments may occur without prior notification and for any reason approved by the IRB Chair or Vice-Chair, not limited to the following: Allegation of non-compliance; Data discrepancies; Documented accounts of noncompliance or possible non-compliance; Failure to obtain continuing review or study closure; Follow-up from monitoring visit or an external inspection such as FDA, OHRP, NYSDOH; Indication of increased risks to study participants; Indication or concerns over the ethical conduct; Known or suspected issues with study conduct or data integrity.

All investigators are required to participate in the Downstate Quality Assessment Program (QAP) when their study is selected for review. The QAP is structured to promote ethical research practices, ensure data integrity, maintain protocol compliance, and uphold regulatory standards. This program operates as a constructive and non-punitive system that emphasizes continuous improvement, using identified concerns as opportunities for learning. If participation is not provided when requested, the PI's supervisors, Department Chairs, Deans, or Senior Leaders may be notified to implement corrective actions. The IRB Chair or a Senior Downstate Leader may administratively suspend or place recruitment on hold for any study if the PI does not cooperate with the QAP review. Additionally, the fully convened IRB Board may suspend IRB approval of the study.

Both investigators and assessors are responsible for recognizing and addressing recurring issues across studies, thereby contributing to readiness for external audits conducted by entities such as the FDA, OHRP, NYSDOH, or sponsors. Strategic planning and corrective action through the QAP foster ongoing quality enhancement and help safeguard research participants. Consistent preparation for both scheduled QAP reviews and unplanned audits requires adherence to best practices daily, meticulous maintenance of complete and accurate study and

IRB records and ensuring all staff members receive up-to-date training. Additional resources and information are available on the Downstate IRB website.

QAP findings are communicated to the IRB, the Clinical Trials Office (CTO), and the Office of Compliance and Audit Services (OCAS) to provide information on any actions that may be required for the research enterprise.

REPORTABLE EVENTS

Report all required reportable events to the Downstate IRB within the deadlines specified in the table below, regardless of whether a Reviewing (External) IRB has oversight. Please see definitions in IRB guidance materials for clarification of the event type or contact the IRB.

When a Reviewing (External) IRB has oversight of the research, for example with an IRB Reliance agreement or when IRB Form 11-A3, or 11-10 was used to activate Downstate research, follow the requirements of the Reviewing (External) IRB, in addition to these requirements.

An ***internal event*** is problem or event involving research participants enrolled by an institution under the purview of the Downstate IRB.

> **Internal event example:** An SAE occurs with a research participant enrolled at Hospital XYZ when the Downstate IRB has the primary oversight of the research (e.g., no external IRB).
> Note: If an internal event occurs at Downstate when the primary oversight of the research takes place by an external IRB, follow requirements of the external IRB and any additional requirements outlined in the section on the use of an external IRB within this policy.

An ***external event*** is problem or event involving research participants enrolled by other institutions in multicenter research projects that do not fall under the purview of the Downstate IRB.

> **External event example:** A research participant experiences an SAE at Hospital XYZ overseen by IRB XYZ.

When reviewing any reportable event, the IRB may consider, but is not limited to, the following possible range of actions:

- Modification of the protocol.
- Modification of the consent document or process for obtaining consent.
- Modification of the information disclosed during the consent process.
- Providing additional information to current participants. This must be done whenever the information may relate to the participant's willingness to continue participation.
- Providing additional information to past participants.
- Requiring current participants to re-consent to participation.
- Alteration of the frequency of continuing review.
- Observation of the research or the consent process.
- Requiring additional training of the investigator.
- Notification of investigators at other sites.
- Termination or suspension of IRB Approval.
- Referral to other organizational entities.

- Obtaining additional information.
- Taking no action.

The IRB, IRB Chair, or IRB Vice-Chair considers whether any additional procedures need to be followed to protect the rights and welfare of current participants, before holding, terminating or suspending IRB approval. Such procedures might include:

- Transferring participants to another investigator.
- Arranging for clinical care outside the research.
- Allowing continuation of some research activities under the supervision of an independent monitor.
- Requiring or permitting follow-up of participants for safety reasons.
- Requiring adverse events or outcomes to be reported to the IRB and the sponsor.
- Notification of current participants; or
- Notification of former participants.

In the references to reporting events to OHRP or FDA or other federal department or agency in the table below, this includes any successor office or the equivalent office within the appropriate department or agency. Any event reviewed by an IRB member that are proposed to require reporting to a federal or state authority must be reviewed by the Downstate convened IRB for concurrence prior to reporting the event. The IRB will promptly notify the governmental agency of all such events. In instances where additional time is required to gather necessary information, an initial report may be submitted, followed by a comprehensive supplemental report once all relevant details are obtained. Any event that requires reporting to a sponsor is referred to Sponsored Programs Administration for reporting to the sponsor.

When indicated, call the IRB at (718) 613-8480 or write to IRB@downstate.edu.

To report any events in writing, please do so in the electronic IRB submission and reporting system, using the Reportable Event Form.

The IRB reviews all other reportable events by an expedited reviewer; however, an IRB Member who is a Medical Doctor or Credentialed Clinician must review any event related to the health care of a participant. The reviewer may consult with other IRB Members when conducting the review or defer the review to the full board at any time. Full Board review is required to confirm a determination of an unanticipated event or to suspend or terminate IRB approval of a study.

Event Type	**Deadline from when the investigator first learns of an internal event for reporting to IRB for an internal event** (e.g., those that occurred with within the Downstate IRB's jurisdiction)	**Comments**
Government inspection (or audit)	Report findings within **24 hours**, if any serious or continuing non-compliance was found or proposed; otherwise within **5 days**.	The study team should alert the IRB when the inspection is scheduled or if an inspector arrives unannounced, so the IRB may help as needed.

Potential Privacy Violation, Incident, or Breach. A *privacy violation (or breach)* is, generally, an impermissible use or disclosure under the Privacy Rule that compromises the security or privacy of the protected health information such that the use or disclosure poses a significant risk of financial, reputational, or other harm to the affected individual. Certain exceptions may apply. The Downstate Privacy Officer has the ultimate authority to determine whether a *breach* has occurred, after it is reported and reviewed. Consider whether the event may also be a potential information security violation and reported as such.	**Immediately** report this to IRB **and** to the Privacy Officer via confidential email to compliance@downstate.edu or to the Compliance Hot Line at 877-349-SUNY (7869) or via the Web-based Reporting Compliance Line.	The Privacy Officer determines if a Breach occurs, whether notification to the research participant is required, and completes any necessary reports to the HHS Office of Civil Rights. General Counsel may assist in the way a breach is addressed.
Potential Information (Data) Security Violation, Incident, or Breach. An *information security* incident is, generally, an impermissible use or disclosure under the Privacy or Security Rules that compromises the security of the protected health information such that the use or disclosure poses a significant risk of financial, reputational, or other harm to the affected individual. Certain exceptions may apply. The General Counsel has the ultimate authority to determine whether a *breach* has occurred, after it is reported and reviewed. Consider whether the event may also be a potential privacy violation and reported as such.	**Immediately** report this to IRB **and** to the Information Security Officer via email to securityops@downstate.edu or to the Compliance Hot Line at 877-349-SUNY (7869) or via the Web-based Reporting Compliance Line.	The Information Security Officer in collaboration with Chief Information Officer and General Counsel determines if a Breach occurs and whether to complete any necessary reports to the HHS Office of Civil Rights. General Counsel may assist in the way a breach is addressed.
Incarceration of a research participant	**Immediately**, if participant is actively incarcerated and research interventions must take place while under incarceration; otherwise within 5 days.	If an already-enrolled research participant becomes incarcerated, all research interventions and interactions cease (except those required for the well-being of the research participant) until the IRB has made the prisoner determinations. For more information, see OHRP Prisoner Research FAQs.
Any FDA Actions to a Humanitarian Use Device (HUD) or FDA changes to a HUD.	Report **immediately**.	

Lapse in Continuing Review	Report **immediately, if the expired study places the research participant's safety, wellbeing, or welfare at risk; otherwise, report within 5 days.**	The PI or CI must report a lapse in continuing review to the IRB as a reportable event and describe corrective measures to prevent future lapses.
(Unanticipated) Serious Adverse Event (SAE). *NOTE: This term applies to Clinical Investigations and to* in vitro *bioavailability or bioequivalence studies in humans (including specimens) that are exempt from IND requirements. FDA regulations use different terms when referring to an adverse event, including, for example, adverse effect, adverse experience, unanticipated problems, and unanticipated adverse device effect.* *An Adverse Event (AE) or an SAE may also meet the definition of an Unanticipated Problems Involving Risks to Participants or Others (UPIRPO), Unexpected AE* **(***UAE), or Unanticipated Adverse Device Effect (UADE), or an Unanticipated Incidental Finding (UIF).* A *Serious Adverse Event* (SAE) is an *adverse event* (AE) that results in any of the following: • **Death.** Meets the criteria of an SAE when the death is suspected to be attributable to an outcome of a research AE. • **Life-threatening experience**. Meets the criteria of SAE if the research participant was at substantial risk of dying at the time of the AE, or the use or continued use of the device or other medical product might have resulted in the death of the participant. • **Initial hospitalization.** Meets the criteria of SAE if the admission was the result of the AE. Emergency Department visits that do not result in admission to the hospital should be evaluated for one of the other serious outcomes (e.g., life-threatening, required intervention to prevent permanent impairment or damage; other serious medically important event).	**24 hours** if an internal AE meets the following criteria: • serious (or alarming), **AND** • unanticipated (unexpected), **AND** • would have implications for the conduct of the study (e.g., requiring a significant and usually safety-related, change in the protocol such as revising inclusion/exclusion criteria or including a new monitoring requirement, informed consent, or investigator's brochure).	*CAUTION: If the IRB approves a protocol that has more strict SAE reporting requirements (e.g., required by the sponsor), the PI must report those SAEs to the IRB as described in the IRB approved protocol.* In general, consider AEs observed during the conduct of the study. The term "alarming" is not defined by the FDA, so it is up to the PI's or Sponsor's discretion on how to interpret this term. An individual AE occurrence ***ordinarily*** does not meet these criteria because, as an isolated event, its implications for the study cannot be understood. Reporting requirements to the sponsor of AEs for clinical trials conducted under IND are stricter. Examples of AEs that FDA considers "unanticipated problems" include: • A single occurrence of a serious, unexpected event that is uncommon and strongly associated with drug exposure (such as angioedema, agranulocytosis, hepatic injury, or Steven-Johnson syndrome). • A single occurrence, or more often a small number of occurrences, of a serious, unexpected event that is not commonly associated with drug exposure, but uncommon in the study

• **Prolongation of hospitalization.** Meets the criteria of SAE if the hospitalization of the research participants was prolonged because of the AE. • **Persistent or significant disability or incapacity**. Meets the criteria of SAE if the AE resulted in a substantial disruption of the research participant's ability to conduct normal life functions, i.e., the AE resulted in a significant, persistent or permanent change, impairment, damage or disruption in the participant's body function/structure, physical activities or quality of life. • **Congenital anomaly or birth defect.** Meets the criteria of SAE when it is suspected that exposure to a medical product prior to conception or during pregnancy may have resulted in an adverse outcome in the child. • **The need for medical, surgical, behavioral, social, or other intervention to prevent outcomes such as the above**. Meets the criteria of SAE when it is believed that medical or surgical intervention was necessary to preclude permanent impairment of a body function, or prevent permanent damage to a body structure, due to the use of a medical product. See related: *adverse event.* *Note: Any instance of an Unanticipated Problem should be assessed to determine whether it qualifies as non-compliance*. The IRB Chair or Vice Chair may determine that the event is "serious"; however, the event must be referred to the IRB for concurrence.		population (e.g., tendon rupture, progressive multifocal leukoencephalopathy) • Multiple occurrences of an AE that, based on an aggregate analysis, is determined to be an unanticipated problem. There should be a determination that the series of AEs represents a signal that the AEs were not isolated occurrences and involve risk to human subjects (e.g., a comparison of rates across treatment groups reveals a higher rate in the drug treatment arm versus a control).
Research related injury involving provision of healthcare.	**24 hours**, if serious. Report within the current approval period if minor.	The PI or IRB may consult with general counsel regarding recommended action.
Apparent Non-Compliance (including any serious or continuing non-compliance).	**24 hours**, if serious or continuing.	Downstate expects any employee or agent or investigator to report any apparent non-compliance to

Non-compliance occurs when conducting human research in a manner that intentionally or unintentionally disregards or violates regulations, policies, or procedures governing human research. *Non-compliant* actions may range from minor to serious, be unintentional or willful, and may occur only once or several times. Examples may include (but are not limited to): • Protocol deviations • Modifications to the research without IRB approval • Non-Exempt human research conducted without prior IRB approval • Research interventions conducted when participants have not provided their legally effective informed consent (unless this requirement was waived by the IRB) • Failure to properly obtain informed consent by using an invalid or outdated consent form that does not contain all the information that might affect an individual's willingness to participate in the research • Misadministration of an investigational drug or biologic • Misuse of an investigational device • Significant privacy or information security breaches such as accessing, obtaining, or reviewing PHI without proper approvals, and losing or misplacing files including PHI or failure to implement information security policies or technical safeguards for PHI • Implementing more than minor protocol changes without IRB approval, except when necessary to eliminate apparent immediate hazards or to protect the life or physical well-being of the research participant • Enrollment of an ineligible research participant into a clinical trial without prospective IRB approval and, if applicable, sponsor approval	Report within the current approval period, if minor (e.g., protocol deviation)	the IRB or to the Compliance Hot Line at 877-349-SUNY (7869) or via the Web-based Reporting Compliance Line. An anonymous report may be made using the web-based system, if desired. Only the convened (full) Downstate IRB may confirm a determination of "serious" or "continuing" non-compliance. Such determinations require prompt reporting to OHRP and funding Department or Agency when the study is federally funded and/or to the FDA when the research is a clinical investigation regulated by the FDA, and to the sponsor when applicable. The Executive Director works with the IRB Chair to report serious or continuing non-compliance to OHRP or FDA, the Downstate IO, and when indicated to the institution under which the research was reviewed under an IRB Reliance Agreement. The Executive Director completes the OHRP reporting form and sends it to OHRP. Typically, a Reviewing IRB which oversees multi-site research (i.e, Single IRB (sIRB) or Central IRB) will report events on behalf of all sites conducting the research; however, the process may depend on the details of the IRB Reliance Agreement. Sponsored Program Administration is responsible for reporting any issues to a department or agency head regarding a study funded by a Grant/Award.

• Failure to monitor the research participants for safety • Failure to report a significant adverse event (SAE) or unanticipated problem involving risks to participants or others (UPIRPO), or • Failure to obtain prospective IRB approval of a substantive change in the conduct of human research, except when necessary to eliminate apparent immediate hazards or to protect the life or physical well-being of the research participant. In general, serious *non-compliance* is n*on-compliance* that adversely affects the rights and welfare of the research participants. Such events may include, for example, an action or omission that • Substantively increases the risk of harm or causes adverse harm to a research participant or another individual. • Substantively decreases the safety, rights or welfare of a research participant or another individual. • Substantively decreases potential benefits to a research participant or another individual. • Substantively adversely alters the risk/benefit ratio of the research. • Substantively compromises the integrity of the research. • Substantively compromises the integrity or effectiveness of the Downstate Human Research Protections Program. • Substantively adversely impacts ethical principles; or • Meets other criteria, provided by OHRP, FDA, the Funding Department/Agency, or the Sponsor. In general, *continuing non-compliance* is a pattern of repeated *non-compliance* when an individual demonstrates inability, unwillingness, irresponsibility or a disregard for compliance with the regulations, Downstate policies, or the IRB requirements or determinations of research, particularly after an individual		The investigator should propose corrective actions in their submission to the IRB. The IRB, IRB Chair or Vice Chair will determine if any additional corrective actions, are needed.

has received notice by the IRB that an action must be taken to correct a previous, similar, or related non-compliance concern. In general, *minor (non-serious) non-compliance* is n*on-compliance* that does not adversely affect the research participant's rights or welfare. See also: *protocol deviation*. In general, *examples* may include, but are not limited to the following: • Failure to obtain IRB approval of a minor protocol change. • Unplanned deviation from the approved research protocol that does not affect the welfare of or pose potential risk to a single study participant. • Over-enrollment of a small number of research participants in a study that is no greater than minimal risk. • Failure to document informed consent with the signature of the investigator obtaining informed consent; or • Clinical staff accessing, obtaining, or reviewing any protected health information (PHI) for research purposes without first obtaining the appropriate research approvals, provided that 1) the activity did not involve any interventions or interactions with the individuals about whom the data pertains; 2) the records were only reviewed by healthcare personnel; and 3) the data remained secure. The IRB Chair or Vice Chair may determine that the event is "serious" or "continuing"; however, the event must be referred to the IRB for concurrence. *Note: Any instance of non-compliance should be assessed to determine whether it qualifies as an Unanticipated Problem.*		
New Information that Indicates a Change to the Risks or Potential Benefits of the Project.	**24 hours** if serious; otherwise within **5 days.**	

Unanticipated (Unexpected) Incidental Finding.	If serious, notify the IRB within **24 hours**; otherwise, submit to the IRB within **30 days** of discovery.	
Significant New Finding.	If serious, notify the IRB within **24 hours**; otherwise, submit to the IRB within **30 days** of discovery.	During research, significant new knowledge or findings about the medication or test article and/or the condition under study may develop. The PI should report any significant new findings to the IRB, and the IRB will review them regarding the impact on the research participants' rights and welfare. Since the new knowledge or findings may affect the risks or benefits to research participants' willingness to continue in the research, the IRB may require, during the ongoing review process, that the PI contact the currently enrolled research participants to inform them of the new information. If the change to the risk/benefits ratio is adverse, the informed consent should be amended and submitted to IRB for approval. The informed consent should be updated, and the IRB may require that the currently enrolled research participants be re-consented, acknowledging receipt of this new information and for affirming their continued participation.
Changes Initiated to Eliminate an Apparent Immediate Hazard.	**5 days**.	Include an amendment, to propose any additional or permanent changes.
Emergency Use (for Expanded Access, Compassionate Use, or Preapproval Access) of an Unapproved Drug, Unapproved Biologic or Unapproved Device.	Notify IRB Chair **as soon as possible**. Notify the IRB within **5 days** of drug administration or device use	Requires approval of the Department Chair and Chief Medical Officer before administration.
Protocol Deviations (including minor modifications made without IRB approval), Violations, or Complaints.	**5 days**, if it adversely affects the rights, safety, or welfare of the research participant; or the research participant's willingness to continue participation; or the integrity of the research data, including information	Include an amendment, to propose any additional or permanent changes, as a corrective action.

**Must be reported to the full board if the event meets the requirements to be reported within 5 days.* In general, a *protocol deviation* is an unplanned excursion from the protocol that is not implemented or intended as a systematic change. A *protocol deviation* could be a limited prospective exception to the protocol (e.g., agreement between sponsor and investigator to enroll a single subject who does not meet all inclusion/exclusion criteria). Examples: • An investigator fails to perform a test or examination as required by the protocol • A research participant fails to complete scheduled visits as required by the protocol See also: *non-compliance*.	security requirements; Otherwise report to IRB before continuing review or project closure.	Report complaints involving translations or interpretations to Patient Relations.
Termination, Suspensions, Pause, Administrative Hold, FDA Clinical Hold, Enrollment Hold. An A*dministrative Hold* is a voluntary action by an investigator to stop temporarily or permanently some or all approved research activities. Administrative holds are not suspensions or terminations. Protocols on administrative hold remain open and require continuing review. When the PI places an administrative hold on a study it is considered a voluntary action. An *FDA clinical hold* is an order issued by FDA to the sponsor of an IND application to delay a proposed clinical investigation or to suspend an ongoing investigation. All or some of the investigations conducted under an IND application may be placed on clinical hold. An *Enrollment Hold (partial suspension) is* an action by the IRB, IRB Chair, IRB Vice Chair, sponsor, or PI, or senior leadership, which prohibits the enrollment of new research participants. When the PI places an enrollment hold on a study it is considered a voluntary action.	5 days	The IRB may suspend or terminate approval or pause enrollment (partial suspension). These actions must be promptly reported to OHRP and the funding agency for federally funded research, to the FDA for clinical investigations, and to the sponsor if applicable. The Executive Director works with the IRB Chair to report serious or continuing non-compliance to OHRP or FDA, the Downstate IO, and when indicated to the institution under which the research was reviewed under an IRB Reliance Agreement. Typically, a Reviewing IRB which oversees multi-site research (i.e, Single IRB (sIRB) or Central IRB) will report events on behalf of all sites conducting the research; however, the process may depend on the details of the IRB Reliance Agreement.

Termination or Suspensions or Pauses are administrative actions that can be taken by the IRB Chair, IRB Vice Chair, Principal Investigator, Senior Leadership, or the Sponsor and these must either be reported to the IRB. Senior Leaders may direct the IRB to suspend, pause, or terminate a study for any reason; however, such actions are not a suspension or termination of IRB approval. The IRB however can suspend or terminate IRB approval as a follow-up action. Examples of activities that may warrant suspension or termination of IRB approval include failure to report activities to ClinicalTrials.gov website, Unanticipated SAEs, Serious or Continuing noncompliance, research misconduct, and similar types of events. A *Suspension or Termination of IRB approval* occurs when the Full Board IRB halts or ends a study. The IRB Chair or Vice Chair is authorized to suspend or terminate part or all of research study at any time; however, such actions shall be reviewed at the next scheduled convened IRB meeting and the IRB may suspend or terminate IRB approval. The IRB is required to provide the reasons for suspending or terminating IRB approval in the determination letter sent to the PI.		Sponsored Program Administration is responsible for reporting any issues to a department or agency head regarding a study funded by a Grant/Award. The investigator should propose corrective actions in their submission to the IRB. The IRB, IRB Chair or Vice Chair will determine if any additional corrective actions, are needed.
All <u>Local</u> Unanticipated Problems Involving Risks to Participants or Others (UPIRPO). **Must be reported to the full board if the event meets the requirements to be reported within 5 days.* An *unanticipated problem involving risks to participants or others* (UPIRPO) in general is to include any incident, experience, or outcome that meets **<u>ALL</u>** the following criteria: • unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and	**5 days**, if serious; otherwise, within **30 days.**	If the IRB concurs or determines that an event is an UPIRPO, such determinations require prompt reporting to OHRP and funding Department or Agency when federally funded and to the sponsor when applicable. The Executive Director works with the IRB Chair to report serious or continuing non-compliance to OHRP or FDA, the Downstate IO, and when indicated to the institution under which the research was reviewed under an IRB Reliance Agreement.

(b) the characteristics of the research participants population being studied. • related or possibly related to participation in the research (possibly related means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and • suggests that the research places the research participants or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized. An UPIRPO generally will warrant consideration of substantive changes in the research protocol or informed consent process/document or other corrective actions to protect the safety, welfare, or rights of research participants or others. Examples of corrective actions or substantive changes that might need to be considered in response to an unanticipated problem include: • changes to the research protocol initiated by the investigator prior to obtaining IRB approval to eliminate apparent immediate hazards to research participants. • modification of inclusion or exclusion criteria to mitigate the newly identified risks. • implementation of additional procedures for monitoring research participants. • suspension of enrollment of new research participants. • suspension of research procedures in currently enrolled research participants. • modification of informed consent documents to include a description of newly recognized risks; and • provision of additional information about newly recognized risks to previously enrolled research participants.		Typically, a Reviewing IRB which oversees multi-site research (i.e, Single IRB (sIRB) or Central IRB) will report events on behalf of all sites conducting the research; however, the process may depend on the details of the IRB Reliance Agreement. Sponsored Program Administration is responsible for reporting any issues to a department or agency head regarding a study funded by a Grant/Award. The investigator should propose corrective actions in their submission to the IRB. The IRB, IRB Chair or Vice Chair will determine if any additional corrective actions, are needed.

For more information, see the OHRP guidance on Problems Involving Risks and Adverse Events. *Notes: Other types of internal events as described within this table (e.g., SAE, AE, UIF, UADE, UAE, etc.) may also be an UPIRPO. Any instance of an Unanticipated Problem should be assessed to determine whether it qualifies as non-compliance.*		
Unexpected AE (UAE). An *unexpected adverse event* is defined as any adverse event in which the specificity or severity of which is not consistent with the current investigator brochure; or, if an investigator brochure is not required or available, the specificity or severity of which is not consistent with the risk information described in the general investigational plan or elsewhere in the current application. For example, under this definition, hepatic necrosis would be unexpected (by virtue of greater severity) if the Investigator Brochure only referred to elevated hepatic enzymes or hepatitis. Similarly, cerebral thromboembolism and cerebral vasculitis would be unexpected (by virtue of greater specificity) if the investigator brochure only listed cerebral vascular accidents. *Unexpected*, as used in this definition, refers to an AE that has not been previously observed (e.g., included in the investigator brochure), rather than from the perspective of such experience not being anticipated from the pharmacological properties of the pharmaceutical product. See also SAE and UPIRPO.	**5 days**, if serious; otherwise, within **30 days**.	If the IRB concurs or determines that this event is also an UPIRPO, follow the policy requirements for an UPIRPO.
Audit or Monitoring Activities.	**5 days** if findings identify apparent serious or continuing noncompliance; otherwise at continuing review or study closure.	
Unanticipated Adverse Device Effect (UADE). See also SAE and UPIRPO. A UADE is any serious adverse effect on health or safety or any life-threatening problem or death caused by, or	**As soon as possible**, but no later than **10 days.**	**Report to sponsor and IRB within 10 days.** If the IRB concurs or determines that this event is also an UPIRPO, follow the

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 research participants.		policy requirements for an UPIRPO.
Interim Analysis Reports, Data Monitoring Committee Data and Safety Monitoring Board (DSMB) reports.	Submit to the IRB within **30 days** of discovery.	
Adverse Event (AE). *NOTE: This term applies to Clinical Investigations and to* in vitro *bioavailability or bioequivalence studies in humans (including specimens) that are exempt from IND requirements.* See also *(Unanticipated) Serious Adverse Event (SAE), or Unexpected Adverse Event (UAE)* for related information. The FDA regulations use different terms for AEs, including "adverse device effect," "adverse drug event," "unanticipated problems" and "unanticipated adverse device effect". An *adverse event* (or *AE*) is any untoward physical or psychological occurrence in a research participant. An AE can be any unfavorable and unintended event including an abnormal laboratory finding, symptom, or disease associated with the research or the use of a medical investigational test article. An A*E* does not necessarily have to have a causal relationship with the research.	Maintain a record of AEs in the research record for clinical investigations and provide any information related to AEs to the IRB, upon request. Although not required, the PI may provide a summary of internal AEs to the IRB at the time of continuing review, when continuing review is required, or within one year of the occurrence if continuing review is not required.	Report to the sponsor, as required by the sponsor. Sponsor determines deadline.
External reportable events (e.g., those that occurred with participants that were enrolled outside of the local site of the IRB jurisdiction).	N/A	Report to IRB, if required by the Sponsor, but no later than the time of continuing review during the approval period for which the event occurred, or within one year if continuing review is not required.
Sponsored required reporting.	N/A	Sponsor determines deadline.

AMENDMENTS

The PI **MUST** submit **ANY** proposed changes to non-exempt human research to the IRB.
Note: For changes to exempt research to the IRB, see the following subsection.

IMPORTANT: Do not wait until the time of Continuing Review to request approval of an amendment. Do not initiate changes to approved research without first obtaining IRB approval except when necessary to eliminate apparent immediate hazards or to protect the life or physical well-being of the research participant.
NOTE: The Downstate IRB reserves the right to require annual Continuing Review/Progress Report submissions, when not otherwise be required under this policy, if the PI does not submit amendments in a timely manner.

The IRB Office, in consultation with the IRB Chair when needed, will determine if the amendment can be expedited (i.e., minor changes, additional research staff, no change to risk/benefit ratio, etc.) or whether it needs to be reviewed by the full board (more than minor changes, increase in risk/benefit ratio, etc.).

The IRB considers the following examples as minor, which may undergo expedited review:

- Adding or removing research staff, that is consistent with maintaining the level of expertise during the prior approval period. However, if the expertise changes in a study that is greater than minimal risk, the amendment be reviewed by the full board.
- Making changes that do not affect the risks of the research or the risks/benefit ratio,
- Administrative corrections or clarifications,
- Non-substantial changes in the research design or methodology,
- A proposed change in the number of research participants enrolled in the research, or
- Multiple minor changes.
- Study closure. The completion of the study is a change in activity and must be reported to the IRB. Although subjects will no longer be "at risk" under the study, a final report/notice to the IRB allows it to close its files as well as providing information that may be used by the IRB in the evaluation and approval of related studies.

The following examples are of changes that must go to the full board:

- A change in the qualifications of the research team,
- A change in the CI for an FDA regulated trial, when the qualifications and experience of the CI are different than the original CI.
- A change in the facilities available to support the safe conduct of the research, or
- Any other factor that may increase the risk to research participants or others.

Addition of study staff always requires an amendment, prior to the study staff conducting any research. Submit relevant COI disclosures and training documents with the amendment, if the documentation is not available to the IRB (e.g., documents for external investigators).

An amendment may not necessarily need to be promptly reviewed and approved by the IRB, when a change is necessary to eliminate apparent immediate hazards or to protect the life or physical well-being of the research participant; however, such a change must be reported to the IRB within 5 business days. Promptly submit amendments to the IRB to prevent a future hazard or protect the life or well-being of research participants.

The PI signature is always required for an amendment; and the Department Chair's signature required if there is a change in the PI. On a case-by-case basis, the IRB may require the

signature acknowledgement by the Department Chair or Dean when there is a change in funding, resources, or budget.

Although a PI may submit an amendment at the time of continuing review, the IRB recommends prompt amendment submission as a separate event, as soon as the PI recognizes the need for the amendment, so the reviews do not interfere with one another.

Submit amendment requests in the electronic IRB submission and reporting system. The instructions are included on the Amendment request form and include a list of required materials needed for the amendment.

Whether or not the amendment includes changes to an IRB-approved informed consent form, the IRB will review the amended or current informed consent document carefully to determine if it requires any additional revisions based on the submitted amendment, current IRB policy and practices, and current informed consent templates.

In general, amendments related to patient care undergo review by an IRB Member who is a clinician. The reviewer may consult with other IRB Members when conducting the review or defer the review to the full board at any time.

Those research participants who are presently enrolled and actively participating in the study should be informed of the change if it might relate to their willingness to continue their participation in the study. In general, the IRB does not require reconsenting of research participants that have completed their active participation in the study, or of those who are still actively participating when the change will not affect their participation, for example when the change will be implemented only for subsequently enrolled participants.[61]

To request an amendment, submit one or more of the following as applicable:

- Form 20-B2A: Application for Amendment
- Form 20-B2B: Application for Amendment - STAFF CHANGES ONLY
- Revised materials for reviewed by the IRB

AMENDMENTS RELATED TO THE TERMINATION OF INVESTIGATORS

RESERVED: This section will be updated in a future revision. Contact the IRB if guidance is needed, prior to the revised update.

AMENDMENT TO TRANSITION EXISTING IRB APPROVED RESEARCH TO THE 2018 COMMON RULE

A PI may submit an amendment to transition previously approved research grandfathered under the Pre-2018 Common Rule to comply with the 2018 Common Rule under this policy; however, the PI should provide a compelling reason when submitting such an amendment. The PI must ensure the amendment meets all the requirements of this policy, including a plan to transition to sIRB review when required for federally funded multi-site research.

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For such amendments, the IRB will determine whether the investigators must re-obtain consent of all currently enrolled research participants using an amended consent form to comply with any new requirements under the new policy.

To request an amendment, submit one or more of the following as applicable:

- Form 20-B2A: Application for Amendment
- Form 20-B2B: Application for Amendment - STAFF CHANGES ONLY
- Revised materials for reviewed by the IRB

CHANGES IN EXEMPT RESEARCH OR IRB DETERMINATIONS

The IRB does not require review of most changes to **exempt research** or IRB Determinations; however, submit an amendment to the IRB for prospective approval, prior to the initiation of the change, for any of the following reasons:

- Reporting a new or revised Significant Financial Interest in a conflict-of-interest disclosure for anyone who is considered an *investigator for the purposes of COI*, for a federally funded or supported research study,
- Proposed change in investigative staff,
- Proposed change to the research that places the research in a different exempt category,
- Proposed changes to a HIPAA waiver or HIPAA Authorization,
- Proposed changes to information security or privacy protections, or
- Proposed change to the research that requires a higher level of review (e.g., expedited, or full board review).

To request an amendment, submit one or more of the following as applicable:

- Form 20-B2A: Application for Amendment
- Form 20-B2B: Application for Amendment - STAFF CHANGES ONLY
- Revised materials for reviewed by the IRB

If the proposed changes to exempt research require expedited review, please contact the IRB to determine if an expedited IRB application form is required, as additional information may be required.

ACKNOWLEDGEMENT REQUESTS AND OTHER CONSIDERATIONS

In general, the IRB will conduct an administrative review and acknowledge events and documents that do not require review by the IRB. Examples of such activities may include:

- External reportable events (e.g., SAEs that occur at external sites),
- Letters from sponsors,
- Administrative corrections,
- Publications and presentations, or
- Notices from external IRBs.

In general, the IRB reviews acknowledgement requests and other considerations by an administrative or expedited reviewer; however, any clinical event must be reviewed by an IRB Member who is a Clinician. The reviewer may consult with other IRB Members when conducting the review or defer the review to the full board at any time.

To request an acknowledgement, submit “Form 20-B1: Application for Acknowledgment”.

ADMINISTRATIVE CORRECTIONS

Contact the IRB to request a minor administrative correction, such as a typo, or incorrect date on an IRB approved document. The IRB office can process administrative changes without additional IRB approval; however, if needed, the IRB may request the research team initiate the request in the electronic IRB submission and reporting system.

CHECK-IN REPORT

If annual continuing review is not needed, the PI must confirm every three years that the research remains unchanged by submitting a Check-In report (Form 20-B4) to the IRB, including for exempt research. The IRB may require more frequent Check-Ins and will inform the PI in writing with reasons. This three-year rule also covers research initially approved via expedited review under the Common Rule, but it does not apply to FDA-regulated studies.

CONTINUING REVIEW

Effective on January 21, 2019, IRB approval for non-exempt human research is valid for a maximum of twelve (12) months from the date of the initial approval for the following types of research and therefore require an annual continuing review (progress report):

1. Research regulated by the FDA or DOJ.
2. A study requiring full board review, unless otherwise noted in this policy.
3. A study initially approved by an expedited review process prior to January 21, 2019, unless otherwise noted in this policy or transitions to the requirements of the 2018 Common Rule.

The IRB requires a 3-year check in period for any research that does not require annual review to track the research and ensure local requirements are up to date. IRB Determinations do not expire and do not have a check-in period. The IRB will document any rationale for conducting continuing review of any non-FDA regulated or non-DOJ regulated research that would not otherwise require a continuing review or 3-year check-in an IRB letter to the PI.

Depending on the nature of the study, the investigator, or in cases were reportable events or amendments are consistently not submitted in a timely manner; the IRB may require more frequent reviews by approving the protocol for periods of less than one year or requiring a progress report update after a certain number of participants are enrolled.
Failure to receive continuing review and approval before the end of the current approval period will result in the expiration of IRB approval of the study.
When applicable, the IRB may approve studies at the time of continuing review with a contingency that certain investigators cannot continue to do the research, until they submit any delinquent requirements (e.g., conflict of interest disclosures, training requirements, etc.).

For more information, see the OHRP guidance on continuing review and FDA guidance on continuing review for clinical investigations.

Annual continuing reviews (progress reports) are not required for the following types of research, provided the research is not FDA or DOJ regulated:

1. IRB Determinations that state IRB approval is not required.

2. Research approved with an exemption, including exemptions approved under limited IRB review.
3. Research initially approved by the IRB when it qualifies for expedited review on or after January 21, 2019, even if the Downstate IRB requires the initial review by the full board review of certain research that qualifies for expedited review under the federal regulations.
4. Research initially approved through an expedited review process prior to January 21, 2019, after transitioning to the requirements of this policy, as determined and documented by the IRB.
5. Research initially approved by the full board on or after January 21, 2019 (or research which has transitioned to the new policy), after or upon investigator notification to the IRB (through an amendment, notice, or progress report) that the research has progressed to the point where it involves one or both of the following:
    a. Data analysis only, or
    b. Accessing follow-up clinical data from clinical care.

CONTINUING REVIEW APPLICATION

The IRB must receive a continuing review application ("Form 20-B4: Application for Continuing Review/Check-In/Study Closure/Re-Activation") and all required materials in sufficient time to permit continuing review and approval.

Provide all required materials for a convened (full) IRB review at least three (3) weeks in advance of the scheduled meeting for which the study requires review. If the continuing review is eligible for expedited review, provide all required materials at least three (3) weeks in advance of the expiration date. If a Check-In is required, submit all required materials at least two (2) weeks in advance of the expiration date.

The IRB may request modifications or directed changes, when the submission is incomplete and cannot otherwise receive full approval by the expiration date; otherwise, the study's IRB approval automatically expires.

When approving research with directed changes at the time of continuing review, the IRB's letter should state whether any conditions need to be satisfied before an investigator can continue specific research activities related to those conditions. For example, if at the time of continuing review, the IRB requires the investigator to change the research protocol to include a specific new procedure for screening prospective research participants, the IRB could approve the research with the following directed change: research activities involving currently enrolled research participants may continue, but no new research participants may be enrolled until a designated IRB member reviews a revised protocol and verifies that the protocol includes the new screening procedure. *Please note that a suspension of enrollment at the time of continuing review is NOT considered to be a suspension of IRB approval that needs to be reported to appropriate institutional officials, the head (or designee) of the agency conducting or supporting the research, or FDA/OHRP.*

If a study fails to meet COI and CITI requirements in time for approval, the IRB or PI may close the study. Alternatively, the IRB or PI may modify the study to remove delinquent investigators or key personnel from the study, provided this does not negatively impact the risk/benefits to research participants or the research.

The IRB Chair, Vice-Chair, or another IRB Member review continuing reviews eligible for expedited review. All other submissions undergo review by the convened (full) IRB.

Expedited reviewers may consult with other IRB Members when doing the review or defer the review to the Full Board at any time.

LAPSE IN CONTINUING REVIEW/EXPIRED IRB APPROVAL

The Federal regulations make no provision for any grace period extending the conduct of research beyond the expiration date of IRB approval. A lapse in IRB approval of research occurs whenever a PI has failed to provide continuing review information to the IRB, or the IRB has not conducted continuing review and re-approved the research by the expiration date of IRB approval.

The PI must ensure continuing review and re-approval of research by the IRB before the current approval period ends. Lapses in IRB approval should be uncommon, but compliance with regulations remains the investigator's responsibility. To maintain IRB approval, investigators should submit all required information promptly and accurately. Submitting materials too early may result in outdated study details at the time of review, so timing is important.

If a study's IRB approval expires, the team will automatically be notified to stop all research. On the expiration date, every activity involving human subjects must halt, including interactions or interventions with participants, the analysis of any personally identifiable private data, and any use or sharing of protected health information (PHI) for research.

Persistent failure to complete timely reports may represent continuing non-compliance of a PI, and the IRB may hold approval of future studies submitted to the IRB until the PI submits all pending materials.

PREVENTING LAPSES

The electronic IRB system alerts the study team 60 and 30 days before approval expires. The PI must submit a timely progress report for continuing review.

The IRB Office monitors lapses, notifies investigators of missing applications, including the application for continuing review or closure reports, and an application for a reportable event to report the lapse. **If the study is not updated within 30 days, the IRB may suspend other research or require completion of outstanding submissions before approving future projects.** During review of new submissions, the IRB checks for prior review lapses and ensures they are addressed.

EXPIRATIONS IMPACTING THE SAFETY, RIGHTS, OR WELFARE OF ANY RESEARCH PARTICIPANTS

The PI must contact the IRB immediately if an expiration of IRB approval negatively affects the safety, rights, or welfare of any participants. If it benefits research participants to continue interventions during a lapse in IRB approval, the IRB may permit only those interventions to protect participants' safety, rights, or welfare until full approval is granted.

The IRB may approve the temporary continuation of participation of already enrolled research participants, if the IRB finds it is necessary or appropriate, for example, when the research interventions hold out the prospect of direct benefit to the research participants (e.g., investigational chemotherapy regimen in an oncology trial), or when withholding those interventions poses increased risk to the research participants.

If the IRB decides that already enrolled research participants should continue to receive the interventions that were being administered under the research protocol, data collection (especially safety information) should also continue for such research participants (e.g., implantable device requiring long-term follow-up).

If the PI is initially determining whether it is in the best interests of one or more already enrolled research participants to continue to participate in the research after IRB approval has expired, the PI should consult the treating physician (if the PI is not the treating physician). In all cases, the PI should verify that the IRB Chair, Vice-Chair, or designate agrees with this determination as soon as possible. The IRB Chair, or Vice-Chair, documents the determination in writing within the electronic IRB submission and reporting system, and request the IRB staff to issue a letter to address whether the PI's determination applies to one or more individuals and stipulate any other applicable information, such as the period for which the participants may continue in the research. In an emergency when there is no time to issue an IRB letter, the IRB Chair or Vice-Chair may provide an email to the PI with the necessary details, while the letter is being drafted. A copy of this email is shared with the IRB staff to save in IRBNet, and it may be used as a basis to draft the official notification letter.

RE-ACTIVATION OF EXPIRED OR CLOSED STUDIES

When IRB approval of an ongoing study lapses and the IRB subsequently re-approves (re-activates) the research, the IRB may approve the study for one year and establish a new anniversary date for the expiration date of subsequent approval periods. The IRB may also re-approve the research for a period of less than 1 year, either to retain the original anniversary date on which prior approval periods expired or to address study risks.

STUDY CLOSURE (FINAL REPORT)

The completion of a study is a change in activity and should reported to the IRB.[62] Study closure reports ("Form 20-B4: Application for Continuing Review/Check-In/Study Closure/Re-Activation") are required to close a study all research (including exempt research).

If IRB approval (or check-in period) expires, the study team should submit a closure re-port or request the study be re-opened.

To close a study, follow the form instructions and submit a "Final Report" Form before the deadline for continuing review or check-in.

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Analysis of identifiable data and the enrollment of new research participants in a protocol for which IRB approval has closed or is expired are not permitted; however, the PI is still obligated to fulfill reporting requirements.

If a PI plans to leave the Downstate and does not transfer the study to another PI, the PI MUST close the study before the PI departs.

The use, storage, de-identification, retention, and/ or destruction of data and specimens involved in the study must be consistent with the IRB approved protocol, Downstate policy, Federal requirements, and ALL relevant applicable IRB approved documents such as the informed consent document, information sheet, HIPAA research authorization, HIPAA waiver, and sponsor requirements.

Please provide IRB with copies of presentations or publications at the time of study closure. If presentations or presentations are available after the study closure, they PI may report these to the IRB for acknowledgement.
Obtain approvals to transfer research records or materials to another institution (e.g., Materials Transfer Agreement), when required.

If the PI anticipates premature closure of a funded study or a study that involves a contract, the PI must immediately report this to Pre- and Post- Award. Before a PI prematurely closes a study, (s)he and the IRB must consider whether any additional procedures need to be followed to protect the rights and welfare of current participants.

The IRB Chair, Vice-Chair, or another experienced IRB Member reviews the study closure request. Expedited reviewers may consult with other IRB Members when doing the review or defer the review to the Full Board at any time.

REQUEST TO RE-ACTIVATE (RE-OPEN) A STUDY

The PI may request a study be re-opened by submitting "Form 20-B4: Application for Continuing Review/Check-In/Study Closure/Re-Activation" and a cover letter indicating why the study expired or closed prematurely and any applicable measures to prevent re-occurrence. Research activities cannot start until the IRB provides approval of the study re-opening through an IRB approval letter. If the study is eligible for expedited review, it may follow the expedited review process. If it is not eligible for expedited review, it will follow the review process by the full IRB.

The PI must upload the last version of the protocol, if it is not available to the IRB (e.g., if the IRB has destroyed the materials in accordance with record retention and destruction requirements).

CARE-Q CERTIFICATION

The Downstate Institutional Review Board (IRB) shall obtain and maintain current certification through the Committee on Accreditation for IRB Quality (CARE-Q). This certification is intended to ensure that the IRB's policies, procedures, and review practices adhere to nationally recognized standards for quality, efficiency, and ethical oversight of human research. The IRB is responsible for maintaining documentation of certification status, monitoring renewal dates, and ensuring that all requirements for continued accreditation are met. Failure to maintain active

CARE-Q certification must be reported promptly to the Institutional Official and the SVP of Research along with a corrective action plan.

RETENTION AND DESTRUCTION OF RESEARCH RECORDS

Downstate faculty should consult with FDA regulations, State Retention Policies, Downstate guidance, and their departmental policies for additional information.

If research records are part of a legal hold or audit, hold the records **until the hold is lifted or they are no longer needed for an audit**. Please consult the SUNY Downstate Office of General Counsel or the group performing an audit if you have any questions.
The SUNY Downstate Office of General Counsel will notify the Department or IRB of any litigation holds and follow-up when records are no longer subject to a legal hold.

Research records and specimens must be securely stored in accordance with the research procedures.

Do not destroy any IRB records that may have important historical value.

Before destroying any research record, list the records on a Records Management Certificate of Destruction form and obtain approval by the Records Management Officer or Designee.

Research records and specimens may not be destroyed unless in conformity with Downstate policies, and when applicable other requirements of sponsors or external research sites. In general, research retention periods follow, but may differ depending on the details of the study. Some of the minimum retention periods are provided below; however, it is recommended all research records be retained securely for up to ten (10) years (including the minimum requirements indicated below), when practicable:

- Securely maintain records relating to a specific research activity, including research records collected by investigators for at least three (3) years after completion of the research. This minimum retention period applies regardless of enrollment of any research participants.
- Securely maintain records, if the research is FDA regulated, for at least two (2) years after approval of the investigational agent by FDA; if it is not approved, records should be retained at least two years after the study is terminated, and FDA is notified. However, the FDA requirements for record retention differ and the individual pharmaceutical or device manufacturing companies sponsoring the research may have their own policies on record retention to which the investigators may be subject. Consult with the sponsor before destroying any records.
- Securely maintain the research participants' signed HIPAA Research Authorization forms (or informed consent documents containing the HIPAA authorization) for a minimum of six (6) years after such authorization last was in effect.
- Securely maintain records concerning controlled substance research for five (5) years after completion of the study.
- When research takes place an external site, the PI must follow the longer specified retention period of either the external site or Downstate.

For the purposes of calculating the retention period for IRB records of non-exempt human research and FDA regulated research, the three-year retention period starts from the date of study closure or study expiration (if the PI failed to submit a study closure application).

ELECTRONIC SYSTEMS, ELECTRONIC RECORDS, AND ELECTRONIC SIGNATURES

RESERVED: This section will be updated in a future revision. Contact the IRB, if guidance is needed, prior to the revised update.

RETAINING CERTIFIED COPY OF CLINICAL INVESTIGATION ELECTRONIC RECORDS

The IRB complies with SUNY record retention and destruction policies.

For FDA regulated research, when Downstate intends needs to retain copies of electronic records, including IRB records, Downstate follows the FDA Guidance for Retaining Certified Copy of Clinical Instigation Electronic Records.[63]

When an original paper record or an original electronic record is copied for retention purposes, the copy maintained and retained should be a certified copy that includes the date and time when the copy is created. The certified copy of the original record must be verified with a data signature or by generation through a validated process. The person reviewing the copy must verify and confirm each page of the record is accurate and must sign a Certification Form to this effect. Copies of the electronic record must be stored in a secure manner approved by Downstate Information Security policies or by the Downstate Data Safety Officer.

NON-COMPLIANCE IN HUMAN RESEARCH

REPORTING POSSIBLE RESEARCH NON-COMPLIANCE TO THE IRB

Investigators and other research staff are required to report all suspected noncompliance to the IRB. A PI may voluntarily decide to suspend or terminate some or all the research activities that may be under current review or investigation and inform the IRB of this action.

Occurrences of noncompliance may come to the attention of the IRB through other sources, including new applications, continuing reviews/progress reports, internal audits, study monitoring, adverse event reporting, reports from Data Safety Monitoring Boards, or reports from collaborators, employees, staff, research participants, patients, family members, IRB Members, or others.

Research noncompliance may often be due to faulty communication or systematic error rather than the negligent actions of a single individual. Identification and investigation of noncompliance provides an opportunity for the improvement of faulty communication paths and systems, while honoring the respect of those who participate in human research. It is to this end that individuals are encouraged to identify, and report suspected occurrences of research noncompliance.

RESEARCH MISCONDUCT

63 FDA Guidance for Retaining Certified Copy of Clinical Instigation Electronic Records

Research misconduct means fabrication, falsification, or plagiarism in proposing, performing, or reviewing research, or in reporting research results, as indicated below:

- *Fabrication* is making up data or results and recording or reporting them.
- *Falsification* is manipulating research materials, equipment, or processes, or changing or omitting data or results such that the research is not accurately represented in the research record.
- *Plagiarism* is the appropriation of another person's ideas, processes, results, or words without giving appropriate credit.

Research misconduct does not include honest error or differences of opinion.

For more information, see related Policy OCA-4 Compliance Reporting, Inquires, and Investigations.

REPORTING ALLEGATIONS OF NON-COMPLIANCE TO THE IRB OR OTHERS

Report any allegation of non-compliance to the IRB, Office of Compliance and Audit Services (OCAS), or Institutional Official (IO). An allegation may be reported anonymously to the confidential Compliance Line (877-349-SUNY or via Compliance Line Website); however, anonymous reports must provide sufficient information to conduct an investigation, as the IRB or other officials may not be able to re-contact an anonymous resource.

Downstate refers allegations of research misconduct, privacy violations, or security violations to the appropriate departments for further investigation.

Downstate takes all allegations of non-compliance seriously. In the unlikely event that a PI is not willing to report an incident that requires reporting to the IRB, a study team member or anyone else, including a research participant, can report it to the IRB. The IRB may require additional actions or sanctions for a PI who was not willing to report the incident.

No one may retaliate against anyone making a report.

If an individual is uncomfortable with reporting apparent non-compliance through the above mechanisms, allegations of non-compliance or complaints may be made directly to the appropriate regulatory authority, such as the HHS Office for Human Research Protections, FDA, or Office of Civil Rights.

REVIEW OF POSSIBLE RESEARCH NON-COMPLIANCE

The IRB Chair or Vice-Chair may do any of the following:

- Take interim action as needed to eliminate apparent immediate hazards or protect the well-being of research participants.
- Determine whether the concern is non-compliance.
- Determine whether non-compliance is not serious and not continuing; or
- Determine whether non-compliance appears to be serious or continuing and as such, refer the review to the convened IRB for confirmation and promptly notify the IO and OCAS.

- Temporarily suspend part or all the research activities and refer the research to the full board to determine if the IRB approval of the study should be suspended or terminated. A temporary suspension by the IRB Chair, Vice-Chair, or IRB must be reported to federal authorities and the sponsor, when applicable.
- Request the PI voluntarily suspend or terminate part of all the research activities.

Only a convened IRB may determine serious non-compliance or continuing non-compliance. The convened IRB must review any apparent serious or continuing non-compliance that appears to be serious or continuing, at the earliest practicable opportunity.
The IRB must determine and document whether any non-compliance that may appear to be serious or continuing noncompliance occurred. In reviewing information to make a final determination of serious or continuing noncompliance, the convened IRB may consider:

- Whether any additional information is required.
- Whether an audit report and any other available information sufficiently supports a determination of non-compliance.
- Whether an audit report and any other available information supports the need to suspend or terminate the research to protect research participants or others.
- Additional actions to protect the rights and welfare of currently enrolled participants.
- Whether procedures for withdrawal of enrolled participants account for their rights and welfare; or
- Whether and how to inform participants of the noncompliance and/or any of the corrective actions.

For serious or continuing non-compliance, the IRB aims to:

- Correct the issue,
- Prevent recurrence, and
- Reduce any negative impact on research participants.

If the IRB determines that serious or continuing noncompliance occurred, the IRB must document the IRB determination and determine if remedial actions are needed to ensure present and/or future compliance, which may include, but not limited to, any of the following:

- Convene an investigation committee.
- Conduct or request a for-cause audit.
- Require follow-up audit(s).
- Suspension or termination of the study procedures/enrollment or IRB approval.
- Suspension of other projects conducted by the same investigator.
- Notification of current research participants (required when such information may relate to participants' willingness to continue to take part in the research).
- Modification of the study protocol or informed consent document.
- Require current research participants are re-consented to continue participation.
- Require monitoring of the research.
- Modification of the continuing review schedule.
- Require observation of consent procedures.
- Require more frequent review of the conduct of the research.
- Require additional training for the research team.
- Refer issues to other institutional entities (e.g., Institutional Official, applicable Dean, applicable Department Chairs, Legal Counsel, Risk Management, Privacy Officer, Data Security Officer, Performance Improvement, etc.)
- Imposition of restrictions as a condition for the continuation of research

- Destruction of data collected during the period of Noncompliance.
- Disallowance of the publication of data collected during the period of Noncompliance.
- Additional oversight monitoring
- Any other action deemed appropriate by the IRB to protect the rights and welfare of research participants.
- When appropriate, applying any corrective action to all similar protocols.

The IRB provides written notice of the IRB determination to the investigator, including the period for which corrective actions are required.

The IRB should notify an auditor or the complainant within 15 business days after its final notifying the PI of determinations, regardless of outcome, when the IRB is acting in response to a report of apparent serious or continuing noncompliance identified by an auditor or complainant. The IRB promptly notifies the IO, OCAS, and Sponsored Programs Administration (SPA, if sponsored) of any serious or continuing non-compliance, suspension or termination of IRB approval, or unanticipated problems. These parties may also inform relevant university leaders, such as the Dean, Department Chair, SVP of Research, General Counsel, Risk Management, Privacy Officer, or Data Security Officer. Additional investigations or reports to government agencies or sponsors may be conducted as needed.

The PI must initiate the corrective actions within the required deadline of the IRB and notify the IRB when the actions are complete. The deadline determined by the IRB should be no greater than 120 calendar days after any determination of noncompliance, except where remediation requires substantial renovation or fiscal expenditure, hiring, legal negotiations, or other extenuating circumstances. A failure to implement the corrective plan on time may require further action, including suspension or termination of IRB approval of the research protocol. When the PI cannot complete remedial actions within the required deadline, the PI must notify the IRB of the delay.

If the IRB action will affect participants in the protocol (e.g., requires withdrawal of participants), the IRB shall utilize a process that considers the impact on the health and safety of the research participants.

If anyone has concerns related to the integrity or objectivity of any aspect of an IRB determination or an investigation, (s)he should discuss such concerns with the IO.

INVESTIGATION COMMITTEE

The IRB, the IO, or OCAS may determine and warrant an additional investigation and whether the investigation should expand beyond the specific allegation or IRB determination (e.g., research misconduct). If any facts are at issue, the IRB, IO, or OCAS may contact any appropriate persons for verification of such facts.

The IRB, or an Investigation Committee appointed by the IRB, IO, or OCAS, may invite the PI or other research staff to a portion of the meeting to answer questions and to discuss the issue of noncompliance. The PI or other research may invite a faculty representative, legal counsel, union representative, or another member of his or her department; however, (s)he should notify the Chair of the meeting in advance. These inquiries/ investigations are internal processes under which all PI's and/or research staff must adhere to. The IRB allows PI's/ research staff to obtain, at their own expense, the advice of legal counsel or a personal advisor who is not otherwise

involved with the case. The counsel or advisor may be present at interviews with the PI/ research staff, but may not speak for, or on behalf of, the PI/ research staff during an inquiry or investigation. If the PI/ research staff wishes to direct all communication to the legal counsel or personal advisor, the PI/ research staff must submit a written notification to the Committee.

INSTITUTIONAL REVIEW OF HUMAN RESEARCH

The IRB functions independently when granting approval and disapproval of research. Research may be subject to further appropriate review and approval or disapproval by officials of the institution. However, these officials may not approve human research that the IRB has not approved.

APPEALING DOWNSTATE IRB DECISIONS

There is no regulation that requires a process for a PI to appeal an IRB decision, because the IRB has ultimate authority to approve the research. Under no circumstances, does the Downstate IRB permit an appeal of a suspension or a termination of IRB approval. However, when a PI is not satisfied with an IRB decision, the IRB recommends the PI take the follow progressive steps, within 60 days of receiving the IRB decision:

1. The PI should consult with an IRB Vice Chair to try to resolve the situation in an amicable manner.
    a. The Vice-Chair may require a written submission.
    b. At any time, the Vice-Chair may require additional supporting documentation, and/or consult with others regarding the matter.
    c. The Vice-Chair may agree to approve changes in the research if it qualifies for expedited review or could refer a controversial situation to the IRB Chair or the Full Board and/or may request additional supporting documentation from the PI.
    d. Unless referred to the Chair, the Vice-Chair informs the IRB members of the outcome preferably during or before the next convened (full) IRB meeting.
2. Unless the Vice Chair refers the situation to the Chair or a Full Board meeting, the PI may escalate an unresolved appeal to the IRB Chair to further consideration.
    a. The Chair may require a written submission.
    b. At any time, the Chair may require additional supporting documentation, and/or consult with others regarding the matter.
    c. The Chair may agree to approve changes in the research if it qualifies for expedited review or could refer a controverted situation to the Full Board and/or may request additional supporting documentation from the PI.
    d. The Chair informs the IRB members of the outcome preferably during or before the next convened (full) IRB meeting.
3. Finally, for an unresolved appeal not referred to the full board, the PI may submit a one-time written appeal (or a one-time amendment regarding the appeal) to the IRB via the electronic IRB submission and reporting system.

The IRB documents the outcome of any appeal in a written letter to the PI. Any discussions that take place at the full board meeting are documented within the IRB minutes.
Note: The PI, Vice Chair, Chair, or IRB may consult with the IO, Department Chair, or Dean to facilitate a resolution; however, only the IRB has the regulatory authority to grant approval of a study.

REPORTING AND INVESTIGATION OF ALLEGATIONS OF UNDUE INFLUENCE

If the IRB Chair, a member, or representative from the IRB's administrative staff feels that the IRB Committee has been unduly influenced by any party, they shall make a confidential communication to the Institutional Official or via confidential Compliance Line (877-349-SUNY or via Compliance Line Website) depending on the circumstances. The official receiving the confidential communication will conduct a thorough investigation to take any applicable corrective actions to prevent additional occurrences.

HARASSMENT TOWARD IRB STAFF AND MEMBERS

Any form of harassment, intimidation, or perceived harassment directed toward Institutional Review Board (IRB) staff or IRB members, whether verbal, written, physical, or electronic, is strictly prohibited and will be addressed according to institutional policies.

Such behavior undermines the integrity and functioning of the IRB and creates a hostile work environment. All incidents or concerns involving actual or perceived harassment should be promptly reported to Human Resources and/or the Office of Labor Relations for review and appropriate action, in accordance with institutional policy and applicable laws.

Retaliation against individuals who report such conduct in good faith is strictly prohibited.

The person or supervisor reporting any harassment should consult with Human Resources or Labor Relations with any questions of concerns about the process.

DISCLOSURE STATEMENT ON USE OF ARTIFICIAL INTELLIGENCE

This policy document was evaluated and edited with the assistance of artificial intelligence (AI) tools, specifically OpenAI's ChatGPT, and Microsoft Co-Pilot. These tools were used to support drafting, formatting, and refinement of content. However, all substantive decisions regarding content, accuracy, and policy were made by the authors and finalized through Institutional Review Board (IRB) review and approval. The final document reflects the professional judgment and oversight of the IRB and its designated representatives.

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- FDA Guidance on Expanded Access to Investigational Drugs for Treatment Use
- FDA Guidance on IRB Continuing Review after Clinical Investigation Approval
- FDA Guidance on Marijuana research with Human Subjects
- FDA guidance on SR and NSR Medical Device Studies
- FDA ICH Guidance Documents
- FDA Information Sheet: IRB FAQs
- FDA Investigator Responsibilities for Investigator-Initiated IND Applications
- FDA Investigator's Responsibilities for INDs
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- U.S. Department of Education, Title 34 Part 350: Disability and Rehabilitation Projects and Centers Program
- U.S. Department of Education, Title 34 Part 356: Disability and Rehabilitation research
- U.S. Department of Health and Human Services (HHS) Regulations for Protection of Research Participants under 45 CFR 46 (including Subparts A, B, C, D, and E)
- https://www.pmddtc.state.gov/ddtc_public?id=ddtc_kb_article_page&sys_id=24d528fddbfc930044f9ff621f961987U.S. Food and Drug Administration (FDA) regulations under 21 CFR 11, 50, 56, 312, 320, 812, and 814

REVIEW HISTORY

Supersedes:

- Investigators Manual (2004)
- IRB Policies and Procedures Manual (2015)
- Human Research Protections Program (IRB-01) (March 30, 2017)
- Human Research Protections Program (IRB-01) (January 19, 2018)
- Human Research Protections Program (IRB-01) (December 20, 2018)
- Human Research Protections Program (IRB-01) (November 22, 2019)
- Human Research Protections Program (IRB-01) (February 03, 2021)