Institutional Animal Care and
Use Committee (IACUC) Office
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INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE POLICY
Review and Approval of IACUC Submissions
Approval Date: February 7, 2022

SUBMISSION REVIEW PROCESS BACKGROUND

- All vertebrate animal use for research, teaching, or testing at SUNY Downstate Medical Center must be reviewed and approved by the Institutional Animal Care and Use Committee (IACUC).
- The Principal Investigator (PI) is responsible for providing sufficient information to the IACUC about the purpose and plan to use laboratory animals so that the Committee may make a reasonable evaluation of the impact of the research activities on the welfare of the animal subjects.
- Additional information or clarifications may be requested from the PI during the review process in an effort to facilitate the approval process. The PI is encouraged to email, call, or meet with IACUC Office staff and/or the IACUC Chair to clarify any comments or suggested edits if the comments or suggested language is unclear. The reviewer(s) may communicate with the PI as well.
- A simultaneous administrative review is conducted to evaluate:
  - whether personnel listed have required training for the species and procedures proposed.
  - whether personnel listed have required occupational health clearance for the species proposed.
  - whether review and approval of any associated Institutional Biosafety Committee review are needed.

This policy offers direction on the following topics:

- Protocol and Amendment Pre-review
- Protocol Review Process
- Amendment Review Processes
  - Designated Member Review (DMR)
  - Administrative with Verified Veterinary Consultation (VVC)
  - Administrative
- Annual Review Process

REGULATORY GUIDANCE

- Animal Welfare Act (AWA) and Regulations (AWR)
- Guide for Care and Use of Laboratory Animals (Guide)
- PHS Policy on Humane Care and Use of Laboratory Animals (PHS Policy)
- OLAW FAQ D9
- NOT-OD-14-126: Guidance on Significant Changes to Animal Activities
- OLAW FAQ F4: Use of non-pharmaceutical grade substances in animals

PROTOCOL and AMENDMENT PRE-REVIEW

Consultation with the Attending Veterinarian (AV) or their designee is required during the planning phase of the study for PIs using USDA-covered species involving procedures that have the potential for pain and/or distress (category D or E procedures). The AV and the Institutional Animal Care and Use Committee (IACUC)are available for consultation with PIs to discuss any concerns during preparation of the protocol, design of the study and protocol review. A protocol preparatory meeting with the AV and IACUC Office staff is encouraged for new animal models and pilot studies for all species.

Upon submission of protocols and amendments to the IACUC and prior to distributing the submission to the committee members, the Institutional Animal Care and Use Committee (IACUC) Office conducts a pre-review in consultation with veterinary pre- and primary reviewers. This feedback is presented to the PI to allow changes to be made to the protocol prior to full committee review and facilitate a more efficient approval of the submission.

Using this process:

- Comments and suggested edits are captured in the notification email is sent to the PI. The IACUC Office may forward a Word version of the document including the comments and suggested edits depending on the number of comments and if time allows.
- Revisions made to address the comments are requested using the 'track changes' feature in MS Word.
- Comments that do not require revision to the document can be addressed within the comment bubble or in the body of the email response by the PI. If grant congruency is needed at the time of review for a new award or change in scope to an existing award, it can be performed in conjunction with the IACUC review. The grant congruency review process occurs independent of the IACUC review and does not impact approval of the protocol. Any modifications that are needed to make the protocol congruent with the grant can be made during the course of the IACUC review of the protocol or by amendment after the protocol has been approved.
- Additional reviews are performed for the following items:
  - Institutional Biosafety Committee (IBC) Approval: Submissions are assessed to determine if IBC review and approval is needed. If needed, the PI is advised to submit an IBC application (or amendment to existing application if appropriate based upon IBC feedback to the PI) to the IBC for review. The IBC and IACUC reviews can occur in parallel. The IACUC approval cannot be processed until the necessary IBC approvals have been obtained.
  - Training Completion: Training requirements are assessed relative to the species being used and procedures performed. Any training that is needed is communicated to the PI and the personnel to complete the training. The IACUC protocols and amendments cannot be approved until training requirements have been fulfilled.
  - Facility Use Agreements: IACUC protocols for non-Downstate PIs (PIs who are not paid Downstate employees) cannot be approved until a signed and executed Facility Use Agreement is in place.

PROTOCOL REVIEW PROCESS

FULL COMMITTEE REVIEW (FCR)

All initial and three-year renewal protocols are reviewed by FCR. In addition, any member of the IACUC may request FCR of any protocol or amendment at any time. FCR takes place at a convened meeting with at least a quorum of the members present. No member may participate in the review of a protocol in which the member has a conflict of interest (e.g. personally involved in the project) except to provide information requested by the IACUC. Members with a conflict of interest do not contribute to quorum and depart the meeting during the vote.

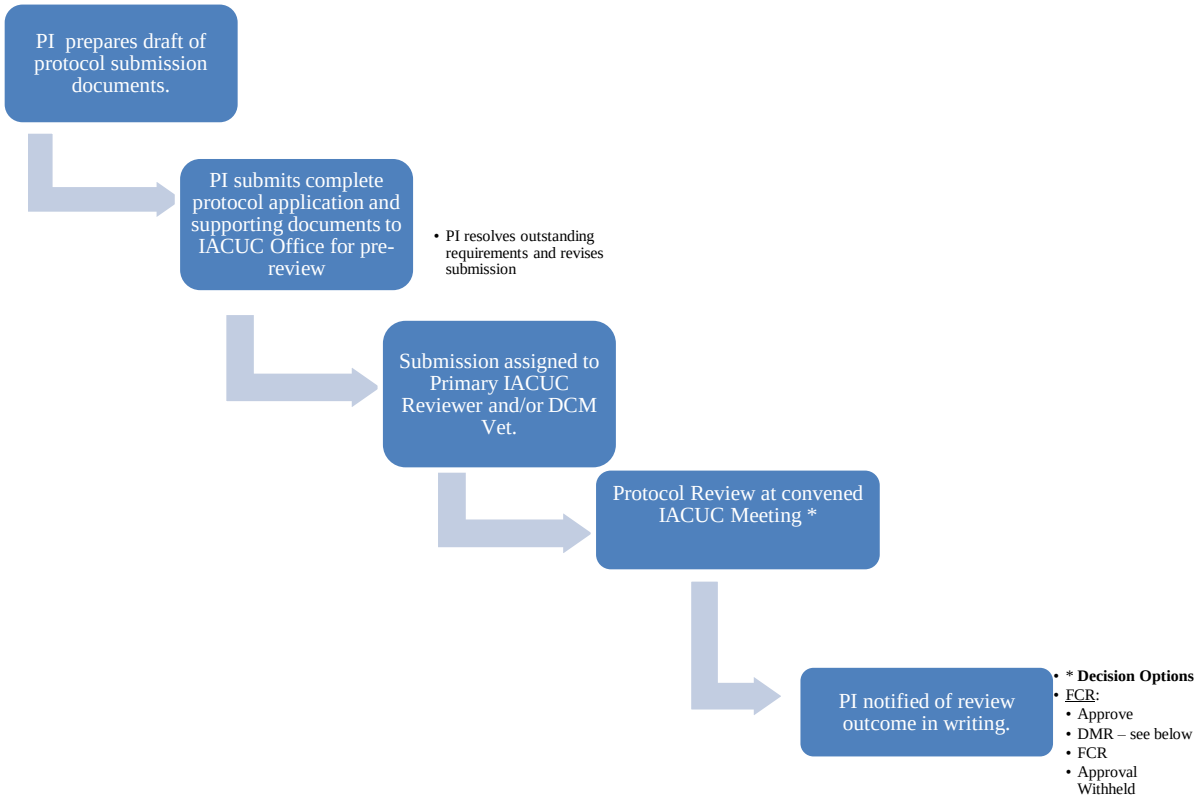
The PI has the opportunity to attend the IACUC meeting during review of their protocol to provide members with clarifications and better understand any additional clarifications that may be needed prior to approval of their protocol. Investigators are notified in writing of the outcome of the review. For FCR, the outcomes include:

- *Approval*: requires a majority vote by the members. Protocols are approved for a maximum of 3 years, with some requiring annual review prior to the first and second anniversaries of the initial approval date. Protocols

not requiring an annual review will expire on the day prior to the third anniversary of the initial protocol approval date. Protocols requiring an annual review due to funding requirements will expire if the annual review is not submitted prior to the first and second anniversaries of the initial protocol approval date. See Annual Review Process below.

- *Modifications Required to Secure Approval* –
  - Deferred to Designated Member Review (DMR): requires a unanimous vote of the members; if the vote is not unanimous, the submission is returned to FCR. When protocols are deferred to DMR subsequent to FCR, the IACUC Chair designates the IACUC member(s) to review the response to the concerns. Once the DMR(s) agree that the concerns have been addressed and any outstanding training completed or associated IBC approvals obtained, the protocol is approved.
    If the concerns cannot be resolved, the submission is returned to FCR.
    Returned to FCR: requires the request of at least one member or the PI.
- *Approval withheld* - disapproval: requires a majority vote by the members.

Note: PI must respond to all IACUC comments and submit a revised application



AMENDMENT REVIEW PROCESS

Amendments are changes to existing and active protocols. Amendment reviews must be conducted as per the SUNY DMC Assurance and the USDA Animal Welfare Act and Regulations, and must be consistent with PHS policy and OLAW expectations (NOT-OD-14-126). Amendments are now no longer required to be reviewed by the full Committee at the monthly meeting. In most cases amendments can be processed in a timely manner by either by DMR or administrative review.

DESGINATED MEMBER REVIEW

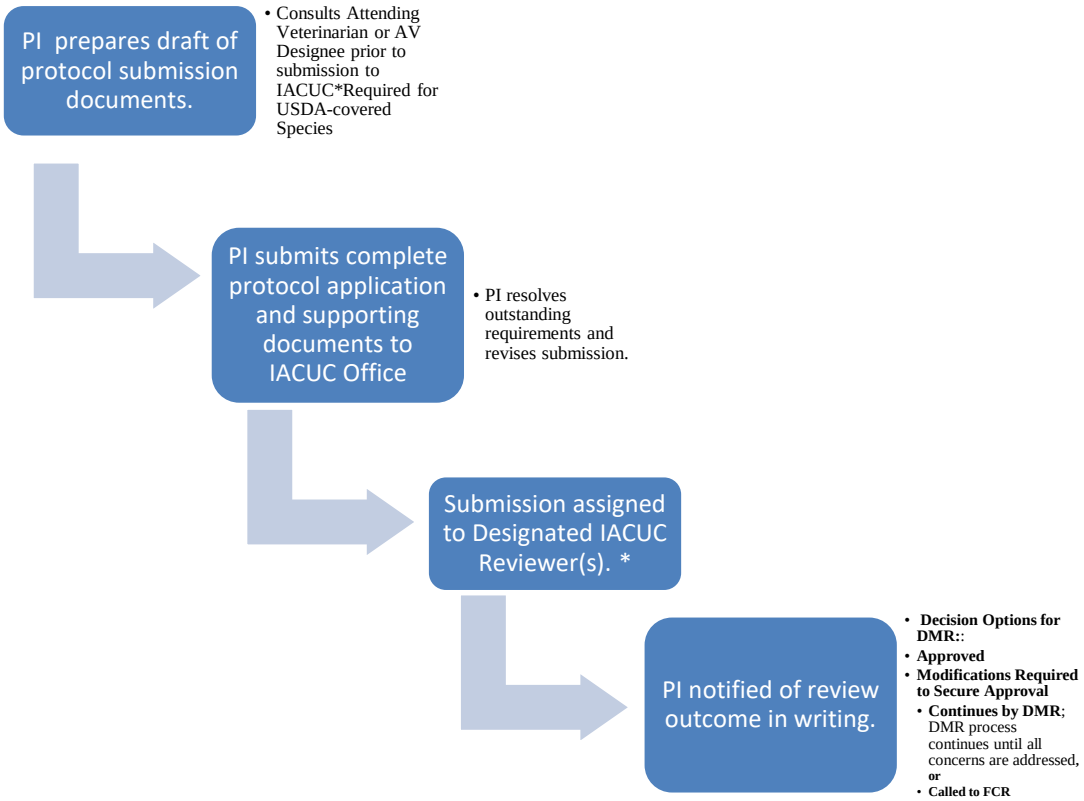
Amendments (submitted as a protocol amendment form or as a revised version of the approved protocol in track changes format) that are processed by DMR include:

- changing from non-survival to survival surgery;
- changes resulting in greater pain, distress, or degree of invasiveness, such as:
  - Addition of survival surgical procedure.
  - Addition of a painful procedure.
  - Change in protocol that would require an animal to undergo more than one survival surgery.
  - Change in protocol that would require animals to be fed, housed or cared for in a way that is not standard for that species, or does not meet that species' minimum requirements.
  - Increase in the degree of invasiveness of a procedure or discomfort to an animal.
  - Change in protocol that would eliminate or restrict an animal's access to veterinary care.
  - Change to withhold analgesics.
  - Change in protocol where death becomes the experimental end point.
- changes in housing and or use of animals in a location that is not part of the animal program overseen by the IACUC;
- changes in purpose, specific aim or study objectives;
- change in species;
  - Some changes in species require a separate animal protocol – i.e., changing from mouse to rat, or changing from pigs to sheep.
  - Some changes in species can be accomplished by amendment – i.e., addition of another species of rat (addition of *Rattus norvegicus* to a protocol that is approved for the use of *Rattus rattus*), or addition of another species of macaque (addition of *Macaca radiata* or *Macaca fascicularis* to a protocol that is approved for the use of *Macaca mulatta*).
- an increase in number of USDA-regulated animals needed;
- a greater than 30% increase in the number of non-USDA regulated animals needed;
- use of a non-pharmaceutical-grade substance for a reason or preparation other than those detailed below (see Administrative Amendments with Verified Veterinary Consultation);
- changes in Principal Investigator (PI);
- addition of personnel involving USDA-covered species
- changes to personnel responsibilities including new and existing procedures involving USDA-covered species; and
- changes that impact personnel safety.

These are examples of amendments that are reviewed by DMR. All IACUC members receive the submission by email, indicating that they have 72 hours to request clarifications or call for FCR. The IACUC Chair assigns specific DMR(s) to review the submission. Any clarifications requested by the DMRs are communicated to the PI.

For DMR, the outcomes include:

- *Approval*: if no member calls for FCR within the 72 hour time frame detailed in the email, any outstanding training requirements completed or IBC approvals obtained for the amended activities, and the DMR(s) agree that any concerns have been addressed, the amendment is approved.
- *Modifications Required to Secure Approval* –
  - If the concerns cannot be resolved, the submission is added to the next full committee agenda for FCR.
  - Call to FCR: requires the request of at least one DMR or the PI.



Administrative Amendments with Verified Veterinary Consultation (VVC)

To minimize review time and reduce regulatory burden, certain protocol changes may be handled administratively in consultation with an IACUC authorized veterinarian (Attending Veterinarian (AV), or AV designee). This review process implements veterinary performance standards and professional judgment together with IACUC-reviewed and -approved policies (e.g., guidance documents, standard operating procedures, drug formularies) for the conduct of animal activities. The veterinarian serves as a subject matter expert to verify that compliance with IACUC policy is appropriate for the animals affected by the proposed changes. Amendments that result in increased pain or distress to the animal, impact approved endpoint criteria, or impact approved personnel safety considerations may not be reviewed by this method. The veterinarian may refer any request to the IACUC for review for any reason and must refer any request that does not meet the parameters of IACUC polices. The PI may also request IACUC review.

Amendments that may be processed by VVC include changes in:

- Anesthesia, analgesia, or sedation.
  - *Anesthesia, analgesia, or sedation* – Reference material for anesthesia, analgesia, or sedation dosages may include textbooks (such as Harkness and Wagner's Biology and Medicine of Rabbits and Rodents; Flecknell's Laboratory Animal Anesthesia; Plumb's Veterinary Drug Handbook; Hawk and Leary's Formulary for Laboratory Animals; Lumb and Jones Veterinary Anesthesia and Analgesia; Quesenberry and Carpenter's Ferrets, Rabbits and Rodents Clinical Medicine and Surgery; Carpenter's Exotic Animal Formulary; Fish, Brown, Danneman and Karas Anesthesia and Analgesia of Laboratory Animals); journal publications (peer reviewed from PubMed and CAB database), personal communications with a veterinary anesthesiologist; or IACUC Formularies.
- Experimental substances.
  - Changes in ***substances that are the same class of compounds*** (ex. Novel peptides, chemotherapeutic drugs) currently approved in the protocol and which are not expected to increase pain or distress, impact the approved endpoint criteria, or impact the approved personnel safety considerations.
  - Changes in ***substances that are different types of compounds*** than those currently approved in the protocol but which are not expected to change the objectives of the study, increase pain or distress, impact the approved endpoint criteria, or impact the approved personnel safety considerations - examples of the type of compounds includes: antibiotics, colloidal fluids, diluents/ vehicles (e.g., DMSO, diluted ethanol, corn oil, peanut oil, sesame seed oil, commonly formulated physiologic saline and buffer solutions, distilled water), imaging contrast agents, gene expression modulators (e.g., tamoxifen, tetracycline), etc. with published doses referenced in materials listed above for "Anesthesia, analgesia, or sedation".
  - Injection with new tumor cell lines provided the tumor size and condition endpoints are consistent with the originally approved protocol but which are not expected to increase pain or distress, impact the approved endpoint criteria, or impact the approved personnel safety considerations.
- Use of non-pharmaceutical-grade substances, when pharmaceutical-grade alternatives are not available, for the following reasons:
  - An equivalent veterinary or human pharmaceutical-grade compound does not exist or it is unavailable.
  - The equivalent veterinary or human pharmaceutical-grade compound is not available in the appropriate formulation or concentration required.
  - Although there is an equivalent veterinary or human drug available, the chemical grade is required to replicate methods from previous studies.
  - The equivalent veterinary or human pharmaceutical-grade compound contains preservatives or inactive ingredients which may confound the research goals of the study.
  - with pH 6-8, and purity and sterility requirements are met:
    - Onsite manipulation with standard laboratory precautions using aseptic procedures
    - Use of sterile diluents
    - Use of sterile containers if prepared/maintained for >24 hours prior to use
    - >95% purity documented from vendor
- Euthanasia to any method approved in the AVMA Guidelines for the Euthanasia of Animals.
- Change to animals of a different sex.
- Addition of another strain or breed of the same species.
- Duration, frequency, or type (e.g., blood collection site or volumes, route of administration, volumes, and dosages), or number of approved procedures contingent upon them not exceeding IACUC guidelines or resulting in increased pain or distress to the animal, impacting approved endpoint criteria, or impacting

approved personnel safety considerations. *This cannot be used to add new procedures, but instead to make specific modifications to approved procedures*.

These reviews are documented and communicated to the IACUC.

Administrative Amendments

Specific protocol changes may be handled administratively by IACUC designated staff without additional consultation or notification. Examples include:

- Increase in numbers ≤30% of non-USDA regulated species.
- Addition or removal of personnel (other than the PI) after verifying training requirements are complete.
- Change in procedure locations that are part of the animal program overseen by the IACUC.
- Correction of grammar or typographical errors.
- Contact information.
- Change in protocol title.
- Change in funding source.

The PI may request IACUC review.

ANNUAL REVIEW PROCESS

Annual reviews are required for all protocols that meet any of the following criteria: use of Veterans Affairs (VA) funding, use of Department of Defense (DOD) funding, or any protocol that uses USDA regulated species and requires Animal Care and Use Review Office (ACURO) review by the funding agency. Investigators are reminded prior to the annual review date that they are required to renew or close the protocol. The annual review includes providing a brief summary of the progress made over the past year towards the research goals, documenting any unanticipated adverse events or animal deaths prior to experimental endpoints, request to continue currently approved scientific reasons for single housing of social species, and requests to continue currently approved scientific justifications for not providing environmental enrichment. Annual reviews and approvals are performed only by IACUC members, such as the AV or AV designee. Members are notified at monthly convened IACUC meetings of upcoming annual reviews and have the opportunity to call for FCR. The PI may also request FCR review.

IACUC Meeting Dates and Protocol Submission Deadlines

Due to the time involved in preparing the materials for distribution to the IACUC members for review, all submissions must be received by noon on the deadline date listed on the IACUC webpage.

No late submissions will be accepted. Submissions received after the deadline will be processed for the next meeting date.

PI must respond to IACUC comments and requests for modifications within 90 days of notification via email.