University of Delaware
Institutional Animal Care and Use Committee (IACUC)
Standard Operating Procedure
Protocol Review

**Types of Protocols:**
1. New Protocol
2. Three-Year Renewal
3. Annual Review
4. Amendment to an Existing Protocol
5. Teaching Protocol

The IACUC currently meets on the first Monday of each month.

In the interest of expedient review of protocols, IACUC has established the following operating procedure concerning protocol submission and review.

**Protocol Submission.** The Principal Investigator (PI) submits the protocol electronically and the signed signature pages by campus mail, to the IACUC Coordinator (IC), at least eight weeks prior to the IACUC meeting. Upon receipt, the protocol is assigned a protocol number and logged into the system by the IC, then sent to the Attending Veterinarian (AV) and the Protocol Facilitator (PF). The AV is specifically responsible to review procedures concerning surgery, pain and anesthesia on the protocol. The PF ascertains that the protocol provides all required information. These two members of the IACUC perform their initial review of the protocol within two weeks of receipt. Should any changes and/or corrections be required, the Veterinarian and/or Facilitator communicate them to the IC who then informs the PI. The PI has one week to make the requested changes and/or corrections and return the revised protocol to the IC. One week prior to the meeting, the protocols are then sent to members of the IACUC for their review. All protocols are discussed and voted on at the monthly IACUC meeting. Upon approval, the protocol is signed and dated by the IACUC Chair or any other member of the IACUC. This date becomes the due date for the next annual review or three-year renewal. If the IACUC determines that substantive outstanding information prevents “approval” outright or the IACUC is unable to dictate specific “modifications” necessary to secure approval, and in the absence of a call for Full Committee Review (FCR) from any member present, the IACUC may agree to send the protocol to designated review (DR). The Designated Reviewer is a member of the Committee selected anonymously by the Chair to gather the information requested by the Committee regarding a particular protocol. Take note, however, that before the protocol can go to DR, all voting members including members who are absent from the convened meeting must be provided the opportunity to request FCR. If a voting member is absent from a convened meeting, the DR process cannot be initiated until that member has been asked if DR is acceptable or not; only if no Committee member requests FCR, can the protocol be turned over to the DR process. Once the IACUC agrees to the designated reviewer method, the IACUC officially delegates its authority for protocol approval to the designated reviewer or designated review team. The IC
forwards the approved information to each PI with a copy sent to the IACUC Chair. The PI is responsible for making all requested changes/corrections on the protocol. This revised protocol must be returned to the IC within one week. The DR will review a protocol when the PI has satisfied all requested modifications. Upon approval from the DR, the Chair or any member of the IACUC will sign the protocol. Individual members of the IACUC shall not disclose or comment upon Committee deliberations or decisions unless requested by the Chair.

If the protocol requires clarification in order for the IACUC to make a judgment, committee members with certain expertise are not present, the IACUC wishes to seek external consultation, or any of a number of other reasons prevent the IACUC from conducting its review, then the IACUC may defer or table review.

Teaching Protocols must have IACUC approval prior to the start of the semester in which they are to be implemented. Teaching Protocols will not be renewed by IACUC in the semester in which they are being taught. This restriction does not apply to Amendments to Teaching Protocols; they may be reviewed at any time.

**Approved Protocols:** The PI will receive an e-mail from the IC notifying that the protocol has been approved. The PI will receive a .pdf copy of this approved protocol. The Office of the Vice Provost for Research will also receive a copy of this notification as well as the .pdf copy. Pls should maintain an electronic version of their current, approved protocol.

**Protocol Renewal Notification:** The IC sends an e-mail reminder to each PI at least three months in advance of due date, notifying of the due date for either an annual review or three-year renewal of their protocol. The forms required for renewal are included with the notification. If applicable, the Pls are also asked to submit a termination form at the completion of their project.

**Expired Protocol:** The Public Health Service (PHS) Policy mandates a complete review of each protocol once every three years. However, to comply with the Animal Welfare Regulations (AWRs), Pls must submit reviews for IACUC approval annually. (Please refer to page 7 – “Frequency of Review of Approved Protocols” for complete details.) If approval of the annual review or three-year renewal has not been secured by its due date, the protocol will be considered EXPIRED.

If a PI fails to renew a protocol and the approval expires, OLAM will transfer the animals associated with that protocol to an IACUC-approved “holding protocol”. The PI will be informed that the animals are no longer approved for use unless a new protocol or renewal is submitted and approved by the IACUC. If the PI uses the animals under an expired protocol, the IACUC will report the event to OLAW. There will be no exceptions to this rule.

**Protocol Review Procedures (ARENA\(^1\)/OLAW\(^2\) IACUC Guidebook)**

The procedural review requirements of the *PHS Policy* or the AWRs take precedence even though they may differ from some commonly used

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\(^1\) Applied Research Ethics National Association  
\(^2\) Office of Laboratory Animal Welfare
parliamentary procedures. Institutions may develop their own meeting procedures as long as the procedures do not contradict or are not inconsistent with the requirements of the PHS Policy or the AWRs.

If a proposed protocol may cause more than momentary or slight pain or distress to animals, the AWRs specifically require investigators to consult with the AV or his or her designee during protocol development. Some committees find it helpful to assign a member a given proposal for in-depth review and liaison with the investigator prior to committee review. Still other committees assign this task to professional IACUC staff. The investigator may choose to consult with these individuals and request a preliminary review before formally submitting a protocol.

The PHS Policy and AWRs recognize two methods of protocol review: full committee review and designated member review. The following pertains to review of initial protocols as well as to review of proposed significant changes in previously approved protocols.

- **Full committee review**

  Full committee review of protocols requires a convened meeting of a quorum of the IACUC members. The PHS Policy and AWRs are explicit that proposals reviewed by the full committee must receive the approval vote of a majority (>50%) of the quorum present in order receive approval.

  Some committees designate a specific member or members to serve as primary or primary and secondary reviewers. These individuals, usually chosen for their expertise or familiarity with a given topic, are responsible for an in-depth review of a proposal and sometimes take responsibility for describing the proposal to the full committee and answering questions about the proposal during review by the Committee. Primary and secondary reviewers can also take the initiative to contact the investigator prior to the meeting for clarifications, additional information, or in anticipation of questions the IACUC may raise. The use of primary reviewers facilitates full committee review by distributing the workload among IACUC members so that each member has responsibility for in-depth review of only a portion of the proposals the IACUC will review. It differs from designated member review (see below), which invests authority to approve a proposal in one or more members.

  Review of proposals by the full committee method invokes a deliberative process, and the PHS Policy and AWRs require that minutes of IACUC meetings reflect committee deliberations. Minutes should include records of attendance, a summary of the issues discussed and the resolution of issues, and the results of IACUC votes on protocols.
Participation by investigators in meetings in which their proposal is being reviewed is not addressed by either the PHS Policy or the AWRs. The participation of the investigator can facilitate the review in a number of ways. Obviously, questions can be addressed as they are raised rather than after the meeting, allowing the review process to proceed rather than be interrupted for this exchange of information. Another benefit is the opportunity for the investigator to give a broad overview of how the proposal under review fits into the larger research picture, thus providing additional information regarding the justification and scientific merit. Invariably, both the investigator and the IACUC benefit from such an exchange. The greatest deterrents to participation by investigators in the IACUC meeting are that it may make the meeting last longer, and problems arise if this is an adversarial rather than collegial exchange of information. In any event, the investigator should leave before the final committee deliberations and if he or she is a committee member may not contribute to a quorum or vote.

- **Designated member review**

To utilize designated member review, each IACUC member must be provided with at least a list of the proposed research protocols or proposed significant changes to previously approved protocols prior to the review. Most committees provide members with an abstract of proposals; in all cases, written descriptions of the research proposals must be made available to IACUC members upon request. All members must have the opportunity to request full committee review of any proposal. If no member requests full committee review, the Chair designates one or more qualified members to review the proposal (or proposed amendment). These designated members have authority to approve, require modifications in (to secure approval), or request full committee review.

IACUCs with a large volume of proposals to be reviewed find the designated member review option may allow for efficient management of the IACUC workload as well as timely turn-around of requests from investigators for protocol review. Some committees prefer to reserve the designated member review option for certain classes of protocols or amendments; conversely, some IACUCs have devised categories of research activities that must be reviewed by the full committee, e.g., nonhuman primate studies, survival surgeries, etc. If the designated member review method is to be used by PHS-supported institutions then the IACUC’s specific procedures for using the method should be described in its PHS Assurance.

**Categories of IACUC Actions**

As a result of their review of protocols, an IACUC may take one of several different actions depending upon the findings of the committee: approval,
modifications required to secure approval, and withhold approval. An IACUC may also defer or table review if necessary.

The *PHS Policy* and AWRs require the IACUC to notify investigators and the institution in writing of its decision to approve or withhold approval, or of modifications required to secure approval. If approval is withheld the IACUC must provide the reasons for its decision and give the investigator an opportunity to respond.

- **Approval**

  When the IACUC has determined that all review criteria, based on the *PHS Policy* and AWRs, have been adequately addressed by the investigator, the IACUC may approve the project, thus providing the investigator permission to perform the experiments or procedures as described.

  An IACUC-approved proposal may be subject to further appropriate review and approval by institutional officials due to financial, policy, facility, or other institutional or administrative considerations. However, those officials may not approve an activity if it has not been approved by the IACUC.

- **Modifications required to secure approval**

  An IACUC may require modifications to the protocol before granting approval. If the IACUC determines that a protocol is approvable contingent upon receipt of a very specific modification (e.g., receipt of assurance that the procedure will be conducted in a fume hood), or clarification of a specific point, the IACUC may handle these modifications or clarifications as administrative details that an individual, such as the Chair, could verify.

  If a study is unusually complex or involves untried or controversial procedures the IACUC may wish to impose restrictions, (e.g., approval for the use of a limited number of animals as a pilot study with a written report of interim results, or close monitoring by veterinary or other qualified personnel.) If such modifications represent significant departures the IACUC can ask the investigator to revise the protocol to reflect the modifications imposed by the IACUC.

  If the protocol is missing substantive information necessary for the IACUC to make a judgment, or the IACUC requires extensive or multiple modifications, then the IACUC can require that the protocol be revised and resubmitted. If the IACUC wishes to shift to the designated reviewer mode for the approval of the modified protocol, that shift should be explicitly noted in the minutes and the requirements for designated review must be met.
IACUCs sometimes use terms such as "conditional approval," "provisional approval" or "approved pending clarification." Anything less than full IACUC approval via one of the accepted methods described above is not adequate for initiation of animal activities or for submission of an IACUC approval date to PHS in conjunction with a grant application. Therefore, OLAW and USDA recommend that IACUCs either avoid using these terms, or describe them (e.g., in IACUC minutes, Assurance documents, etc.) in sufficient detail to be fully understood.

Withhold approval

When the IACUC determines that a proposal has not adequately addressed all of the requirements of the PHS Policy and AWRs as applicable, the committee may withhold approval. A designated reviewer may not withhold approval; this action may only be taken if the review is conducted using the full committee method of review.

As indicated above, a higher institutional authority may not administratively overrule an IACUC decision to withhold approval of a proposal.

- Defer or table review

If the protocol requires clarification in order for the IACUC to make a judgment, committee members with certain expertise are not present, the IACUC wishes to seek external consultation, or any of a number of other reasons prevent the IACUC from conducting its review, then the IACUC may wish to defer or table review. Good communication between the IACUC and the investigator can ensure that this action is needed infrequently. However, should it be necessary, the investigator should be informed so that he or she can respond or plan accordingly.

Review of Changes to Approved Protocols

Significant changes to an IACUC-approved protocol must be reviewed and approved by the IACUC before they occur (PHS Policy IV.C.1., and AWR §2.31[d][1]). It is prudent for an IACUC to develop a policy on the kinds of changes that are considered significant in order to avoid ambiguity. OLAW has identified the following kinds of significant changes that may serve as examples to guide the IACUC in its determinations:

- change in objectives of a study;
- proposals to switch from nonsurvival to survival surgery;
- change in degree of invasiveness of a procedure or discomfort to an animal;
- change in species or in the approximate number of animals used;
- change in personnel involved in animal procedures;
• change in anesthetic agent(s) or in the use or withholding of analgesics;
• change in methods of euthanasia, or
• change in duration, frequency, or number of procedures performed on an animal.

Review of significant changes may be conducted using either the full committee review or the designated member review method described above.

**Frequency of Review of Approved Protocols**

The *PHS Policy* requires that a complete IACUC review of PHS supported protocols be conducted at least once every three years. This triennial review is interpreted by OLAW as a requirement for *de novo* review, meaning that the criteria and procedures for review specified in IV.C. of the *PHS Policy* must be applied not less than once every three years. The three-year period begins on the actual date of IACUC approval; IACUCs may not administratively extend approval beyond the three years. The triennial review may be conducted using either the full committee review or the designated member review method described above.

AWRs require an annual review, which may be a monitoring mechanism whereby the IACUC requires the investigator to annually report on the status of the protocol, verify that completed activities were conducted in accordance with the approved protocol, describe any proposed departures from the approved protocols, and solicit information about activities projected for the upcoming year. (Proposed significant changes would require IACUC review prior to initiation.) This kind of a monitoring system will satisfy the AWR requirement for annual review, but would not be sufficient for the complete IACUC review required on a triennial basis.