IACUC POLICY
PROTOCOL AND AMENDMENT REVIEW

The University of Pennsylvania’s Institutional Animal Care and Use Committee (IACUC) and the Office of Animal Welfare (OAW) have developed a review process for animal research protocols that involves a comprehensive pre-review from several institutional departments. The IACUC has adopted the following policy to help clarify all steps of the initial review process and all subsequent reviews of ARIES protocols and amendments.

AGENDA

Once a protocol is submitted for pre-review it is placed on the IACUC agenda. The protocol will remain on the agenda for 5 days during which time any IACUC member can call for a full committee review (FCR). Protocols must remain on the agenda for the full 5 day period and cannot be approved before then. If the protocol is not requested for a FCR then the protocol is assigned to a designated IACUC reviewer. There is no need for the protocol to be reviewed during the monthly IACUC meeting. Amendments are placed on the agenda on Monday, Wednesday, and Friday. The amendment cannot be approved until the next agenda date.

PROTOCOL PRE-REVIEW

An extensive pre-review is conducted on initial submission of a new animal research protocol (Form A), privately owned animal protocol (POAP), offsite application, or during a three year renewal.

- Prior to submission of an animal research protocol (Form-A), principal investigators (PIs) should consult with University Laboratory Animal Resources (ULAR) veterinarians for all laboratory animal research activities performed at Penn requiring more than momentary or slight pain or distress for USDA-regulated species.

APPROVED
11/25/14
Prior to being submitted to the IACUC, the protocol is routed to the PI’s Department Chair for certification. The Chair may return it to the PI if there are any comments regarding the scientific merit of the project.

Upon submission of protocols and amendments, Office of Animal Welfare (OAW) protocol specialists conduct an administrative pre-review. The pre-review includes a federally-mandated grant-protocol congruency check, an evaluation of the content relative to institutional guidelines and policies, verification of the completion of required trainings, and otherwise assures that the protocol is complete.

During the pre-review, expertise outside of IACUC membership may be necessary. Individuals with experience in specific fields are assigned as adjunct reviewers (Guide, p. 26). Depending on protocol content, adjunct reviewers may include:

- ULAR Diagnostic Services evaluates the transportation of rodents between facilities and results of pathogen screenings of cells and tissue used in rodents.
- Animal Program Veterinarians evaluate surgical and potentially painful or distressful procedures performed on animals for Form-A submissions.
  - ULAR veterinarians evaluate (for USDA-regulated species):
    - Procedures that involve the use of anesthesia, analgesia, sedation
    - Procedures that involve the use of neuromuscular blockers
    - Procedures that are potentially painful/distressful procedures (USDA pain category D or E)
  - OAW veterinarians evaluate:
    - All procedures that involve non-USDA regulated species
    - Procedures that involve Penn pain category A (USDA pain category C) procedures in USDA-regulated species not involving anesthesia, analgesia, or sedation
- OAW compliance liaisons evaluate the use of areas outside of a ULAR-managed animal facility, e.g., surgery and satellite housing areas.
- Environmental Health and Radiation Safety (EHRS) evaluates the use of potentially hazardous biologicals, chemicals, and other materials, as well as vectors, transgenic animals, and procedures involving radiation or radioactive materials.
- The Hospital of the University of Pennsylvania Department of Healthcare Epidemiology, Infection Prevention and Control (HEIPC) evaluates transportation of animals through human patient areas.

The IACUC Chair has discretion to not assign (or un-assign) secondary reviewers to a protocol or amendment.
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• After the initial pre-review, comments are returned to the PI and subsequent revisions are managed by OAW staff until all reviewer comments have been addressed. Whenever submissions are returned for revisions during the pre-review process, the PI is notified within ARIES and by email of the decision for “withheld approval”.

The extensive pre-review managed by OAW staff serves as a convenient way of refining protocols so that designated IACUC member reviews can be completed more quickly and efficiently.

DESIGNATED MEMBER REVIEW (DMR)

Following the pre-review, the protocol is then assigned to an IACUC member for review. All protocols receive a review from one or more designated members of the IACUC upon completion of the pre-review. After the pre-review, protocols should be very well organized and refined for a more efficient IACUC member review.

• IACUC members have the opportunity to contribute comments to the DMR of all protocols and amendments.

• Outcomes of a DMR may be “approval”, “requires revisions by DMR”, or “request full committee review”.

• If there are comments from the DMR(s), they are returned to the PI so that revisions to the protocol can be made. The PI is notified within ARIES and by email of the decision of “withheld approval” (requires revision by DMR).

• Subsequent revisions are returned to the same designated IACUC member(s) for review until all reviewers unanimously recommend “approval”.

• Once any required training has been completed and the IACUC DMR(s) have recommended approval, the submission will be approved. The PI will be notified within ARIES and by email of the decision for “approval”.

FULL COMMITTEE REVIEW

Any member of the IACUC may request full committee review (FCR) of any protocols and/or amendments at any time (OLAW Correct Conduct of Full-Committee and Designated-Member Protocol Reviews). All IACUC members have the opportunity to submit comments for FCR. FCRs are assigned at least two IACUC members as “primary” reviewers.

• At the convened monthly IACUC meeting with a quorum of members, the assigned primary reviewers present a summary of any protocol or amendment brought to the full committee.

• Any outstanding comments or questions are discussed and questions from the Committee are recorded.

• Following each discussion, a recommendation is made, a vote is taken, and decision recorded.
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- If further revisions are required to the protocol, the PI is notified within ARIES and by email of the decision for “withheld approval” (requires revision by DMR) or tabled for future FCR.

- Once any required training has been completed and the IACUC (either at FCR or by subsequent DMR review) has recommended approval, the submission will be approved. The PI will be notified within ARIES and by email of the decision for “approval”.

- If the protocol is considered unacceptable, the PI is notified of the decision for “disapproval”.

AMENDMENTS

Amendments are changes to existing and active protocols. Amendment reviews must be conducted as per the University Assurance and the USDA Animal Welfare Act and Regulations, and must be consistent with PHS policy and OLAW expectations (NOT-OD-14-126).

- Administrative review amendments do not require an official IACUC review. Administrative amendments are evaluated and approved by OAW protocol specialists or other designated OAW staff.
  - Correction of grammar or typographical errors.
  - Addition or removal of personnel (not including the PI – this requires IACUC review) after verifying appropriate qualifications, training, enrollment in an occupational health and safety program, and any other necessary IACUC criteria.
  - Change in the funding source(s) associated with a protocol after assuring congruency of the grant with the protocol.
  - Transportation of animals along acceptable traffic routes by acceptable means or movement of animal source materials between facilities to allow for effective biologic containment.
  - Change in procedure locations or housing locations.
  - Update to the literature search.
  - A Program Veterinarian may also be assigned as a subject expert (not a DMR) for the following types of amendments, and the veterinarian’s review will be documented within ARIES. The veterinarian may refer any submission to the IACUC for review and must refer submissions to the IACUC for review if they contain changes that are inconsistent with IACUC-approved guidelines and policies. The Program Veterinarian may use specific IACUC approved formularies, published formularies, and current literature when reviewing an amendment to determine appropriateness and dosing of any drugs.
    - Changes in anesthesia, analgesia, sedation, and experimental substances that may impact animal welfare.
    - Changes in euthanasia that are approved (or approved with conditions when conditions have been met) in the AVMA Guidelines for the Euthanasia of Animals.
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- Changes in duration, frequency, type, or number of approved procedures performed on an animal.

- Amendments that must be reviewed by the IACUC through DMR or FCR are detailed below.
  - Change in PI.
  - Addition of animal numbers, including addition of breeding activity.
  - Change in the study objectives (Experimental Design).
  - Addition of species.
  - Changes in hazardous materials that impact personnel safety.
  - Addition of procedures or changes to existing procedures that result in greater pain, distress, or degree of invasiveness (USDA C→D→E).

Any other changes not detailed above will also be reviewed by the IACUC (DMR or FCR). In addition to these specific review assignments, adjunct reviewers (EHRS, Program Veterinarians, ULAR diagnostic services, OAW compliance, HUP HEIPC) are assigned based upon the details of the protocol changes.

CONTINUING REVIEW

The “Continuing Review” is used for the annual continuing renewal of protocols which involve research of species covered by the USDA Animal Welfare Act & Regulations (CFR 2.31 (d) (5)). The IACUC conducts continuing reviews of protocols by DMR at appropriate intervals, at least annually. In addition to the designated IACUC reviewer, the OAW compliance staff reviews all continuing reviews. As with any IACUC submission, all members have the opportunity to make comments or request that any submission be sent to the full committee for review. OAW compliance staff may contact PIs if protocol revisions are necessary as one mechanism of the post-approval monitoring process.

PIs will submit a progress report describing how the USDA-regulated species were used and an explanation of any unexpected adverse events or deaths that occurred in the previous year. In order to comply with federal regulations, if the annual renewal has not been submitted by the yearly anniversary date of the protocol, the protocol will be terminated and animal work must cease until a new protocol is approved.

Continuing reviews for offsite collaborations (see below) are performed based upon the collaborator’s IACUC process. While Penn only requires continuing reviews for USDA-regulated species, the collaborator may require it for all species. Once the collaborator’s IACUC has approved the continuing review, it can be uploaded and submitted with the Penn offsite application continuing review.

THREE-YEAR RENEWAL

Three-year protocol renewals are required to update the protocol, including modifications or a new scope of the project, and are resubmitted at appropriate intervals, but at least every 3 years as outlined by PHS policy (PHS policy IV.C.5). Satellite housing applications (see below) must also be renewed every three years. These resubmissions will undergo a de novo review as described previously. Email
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reminders are sent 120 days prior to expiration with periodic reminders up until expiration. We recommend that the renewal should be submitted at least six weeks prior to the expiration date. If the protocol is not approved by the 3-year renewal anniversary date of the initial approval period it will be considered expired and no animal work can be done on that protocol. Any animals currently on the protocol must be transferred prior to its expiration to another active protocol with similar work being done (Request to Transfer Animals Form) or to the ULAR holding protocol (contact ULAR Training Division). If a protocol has expired, the study has been concluded, and a 3-year renewal is not needed and/or desired, then animals can only be euthanized by ULAR (not by protocol personnel since the protocol has expired).

SATELLITE HOUSING

A satellite facility is a room or area where animals are maintained for more than 12 hours and where ULAR does not perform daily observations, regardless of the room’s inclusion in or proximity to the vivarium. A satellite housing application must be submitted if satellite housing is being used on a protocol. The satellite housing application is reviewed by DMR in conjunction with the Satellite Housing Subcommittee and OAW compliance staff. Part of the submission may include inspection of the site by the IACUC to determine if the area is appropriate for animal housing. A strong scientific justification and documented communication with ULAR for the need to use satellite housing will be required for approval. All personnel listed on the satellite housing application will need to complete training for the species being housed and the requirements for managing a satellite housing facility. Animals may not be housed in the satellite housing area until approval is granted by the IACUC, in writing. Satellite housing application must be renewed every 3 years.

Prior to submission, the PI must confirm with ULAR that housing requirements cannot be met in a ULAR-managed vivarium. Once the housing application is submitted, this application can be linked on a Form A protocol. This can be done on a new Form A, 3-year renewal, or amendment. The housing location should be linked to all protocols where animals will be housed in the satellite housing location. The review of a request to renew or create a new satellite area is performed separately from the review of the protocol or amendment to which it is linked; the two documents are reviewed separately so that review of the satellite housing request does not delay approval of the protocol or amendment. Please see the IACUC policy on satellite housing for more in-depth detail.

OFFSITE Collinsations

Work being performed at another institution that is receiving funding associated with the University of Pennsylvania requires an offsite application (formerly Form D). OLAW requires that the awardee institution be responsible for ensuring that all terms and conditions of the award, including the PHS animal welfare policy, are met (OLAW PHS Policy FAQs). This includes:

- Collaborations with other academic institutions.
- Custom antibodies generated offsite.
- Contract labs performing a Penn PI’s research.
- Offsite animal housing.

Confirmation of this work is required by the Office of Laboratory Animal Welfare (OLAW) (NIH Grants Policy Statement). This includes an IACUC-to-IACUC memorandum of understanding (MOU) to clarify the
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regulatory aspects of the collaboration (Guide for the Care and Use of Laboratory Animals). Basic regulatory information submitted with the offsite application includes the species and number of animals associated with the offsite work, the registration/assurance/accreditation status of the other institution, the funding source, and the offsite protocol and associated IACUC or ethics review board approval letters.

The offsite application is reviewed by DMR with a grant-protocol congruency check. It is important to note that the approval period of the offsite application is contingent upon the review period and cycle required by the IACUC or ethics review board at the collaboration site. For example, non-USDA-regulated species protocols at Penn do not require annual review, but if the offsite location requires annual review for non-USDA-regulated species (which is often the case) then documentation of continued review will need to be submitted to the Penn offsite application annually. The offsite approval letter may be submitted to the OAW with the continuing review of the offsite application after approval by the collaboration site’s IACUC or ethics review board as described above.

EXEMPTIONS

When deviating from the federal regulations and guidance or University policies regarding the care and use of vertebrate animals in testing, research, and educational activities, a request for an exemption must be submitted to the IACUC for review. Exemptions are reviewed by the IACUC (through DMR), a veterinarian, and any relevant adjunct reviewers. This exemption, if granted, may be reported to the USDA and/or the Office of Laboratory Animal Welfare as required by law. Some examples of an exemption include scientifically justified modifications to space requirements, light cycles, exercise plans for dogs, food/water restriction, and specific IACUC guidelines.

Exemptions will be reviewed on the same cycle as continuing reviews (USDA-regulated species) and 3-year renewals (all species). Exemptions are submitted automatically in ARIES for all continuing reviews but must be submitted manually for 3-year renewals.

REFERENCES