Title: Animal Care and Use Study Review Process

The intent of this Standard Operating Procedure (SOP) is to describe the review process of animal care and use protocols at Illinois State University (ISU). This SOP is for use by anyone, who reviews animal care and use protocols at ISU. This SOP is approved by the ISU Institutional Animal Care and Use Committee (IACUC). Any deviation from an approved SOP must be included in a Study or Amendment request and approved by the IACUC prior to its implementation.

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1. Introduction

This SOP sets out to establish the approved practice and procedures for review of animal care and use studies and modifications by the Illinois State University Institutional Animal Care and Use Committee (IACUC).

While the criteria that must be met before an IACUC can approve a proposed research study is covered under Public Health Service Policy (IV, c,1,a-IV,c,1g;IV,d1,-IV,d,1e) and the Animal Welfare Act (2.31,d; 2.31,e), the method to accomplish this is left up to each individual institution.

2. Scope

Principal Investigators are responsible for insuring that they and their personnel follow the steps required in this SOP. All trained personnel, working with animals are responsible for knowledge of the content of the SOP and for following the prescribed course of action. IACUC members are required to sign the agreement statement yearly.

All teaching, research, research training, experimentation, biological testing, and related activities involving live vertebrate animals require IACUC approval prior to conducting the work.

To avoid the perception of conflict of interest, committee members who are participants or immediate family members of the PI in the protocol being reviewed do not participate in the review, deliberations, and decisions on those protocols. Additionally, any IACUC member may ask to be recused from review of a particular protocol due to perceived conflict of interest.

3. New Animal Use Studies and 3 year de novo Study reviews

Meeting dates and corresponding submission deadlines are posted on the IACUC website at https://research.illinoisstate.edu/ethics/animal/schedule/. Studies must be submitted and authorized by the PI via Cayuse IACUC before review can begin.

For all studies, regardless of the review process, the IACUC will determine applicable regulations in accordance with, as well as the ISU Policies and Procedures and Assurance.

The specific requirements for approval as defined in PHS Policy include:

a. Procedures with animals will avoid or minimize discomfort, distress, and pain to the animals, consistent with sound research design.
b. Procedures that may cause more than momentary or slight pain or distress to the animals will be performed with appropriate sedation, analgesia, or anesthesia, unless the procedure is justified for scientific reasons in writing by the investigator.

c. Animals that would otherwise experience severe or chronic pain or distress that cannot be relieved will be painlessly killed at the end of the procedure or, if appropriate, during the procedure.

d. The living conditions of animals will be appropriate for their species and contribute to their health and comfort. The housing, feeding, and nonmedical care of the animals will be directed by a veterinarian or other scientist trained and experienced in the proper care, handling, and use of the species being maintained or studied.

e. Medical care for animals will be available and provided as necessary by a qualified veterinarian.

f. Personnel conducting procedures on the species being maintained or studied will be appropriately qualified and trained in those procedures.

g. Methods of euthanasia used will be consistent with the recommendations of the American Veterinary Medical Association (AVMA) Panel on Euthanasia, unless a deviation is justified for scientific reasons in writing by the investigator.

There are two methods used for study review depending on the USDA pain classification, Designated Member Review (DMR) or Full Committee Review (FCR), as described below. For more information on USDA pain classifications, see http://oacu.od.nih.gov/ARAC/documents/USDA_Reports.pdf. Review by the AV is required on all protocols, regardless of method.

- **DMR for new studies**

For studies submitted with a "C" pain classification (no pain, distress, or use of analgesics), DMR may be used.

All members of the IACUC committee receive identical copies of the study and are given two business days to call for FCR. If FCR is not indicated in Cayuse IACUC, the IACUC chair will act as the designated reviewer or contact one or more appropriately qualified IACUC member(s) for DMR. The IACUC chair may also appoint additional IACUC members to assist in the review. Designated reviewer(s) may approve or require modifications to the study. IACUC members
can also submit comments or questions to be considered during the DMR process. The AV’s review is required for all studies approved under DMR.

If a study is assigned to more than one designated reviewer, the reviewers must be unanimous in any decision. They must all review identical versions of the study and if amendments are requested by any one of the reviewers, then the other reviewers must be aware of and agree to the amendments. If the reviewers cannot agree, the study must be reviewed by FCR.

The designated reviewer(s) cannot deny a study; only the full IACUC has that authority. If the designated reviewer(s) wants to consider denying a study, the study needs to be moved for FCR.

Any IACUC member at any time during this process may request FCR.

- **FCR for new studies**

Studies submitted with either a “D” (pain/distress with appropriate analgesic/anesthesia/tranquilizers) or “E” (pain/distress without appropriate analgesic/anesthesia/tranquilizers) pain classification must be reviewed at a convened meeting of the IACUC, defined as a quorum of the total membership. A majority of the quorum is required to either approve the study as submitted, withhold approval pending minor revisions, or deny the study with recommendations for major revisions (if appropriate). The IACUC may deny a study if it determines that any of the previously identified approval criteria are not met.

IACUC members have agreed in advance in writing that the quorum of members present at a convened meeting may decide by unanimous vote to use DMR subsequent to FCR when minor modifications are needed to secure approval. DMR will then be conducted by the IACUC chairperson or by one or more appropriately qualified IACUC members to serve as the designated reviewer(s) and appointed by the IACUC chair.

Should the Designated Reviewer not be satisfied with the revisions as submitted, the study will be maintained as withheld pending and presented for discussion at the next regular IACUC meeting. If a study is assigned to more than one designated reviewer, the reviewers must be unanimous in any decision. If the reviewers cannot agree, the study must be returned to the IACUC for discussion at the next regular meeting. However, any member of the IACUC may at any time request to see the revised study and/or request FCR of the study. For major modifications, the revised study would undergo a second round of FCR at the next convened meeting.
The IACUC’s determination is communicated in writing to the PI. If revisions are required to secure approval, the study will be administratively withdrawn if the PI has not submitted revisions within 30 days after notification.

For approved studies, the starting and ending dates of the approval period will be stated on the approval letter sent to the PI. Approval is limited to no more than three years, in periods not to exceed one year (see below for further details). In certain cases, the IACUC may require a shorter approval period. If DMR is used, the approval date is the date that the designated member approved the study. No activity involving animals can occur prior to the approval of the protocol.

4. Annual Reviews to Animal Use Studies

An annual review of all studies is required by the USDA. PIs are responsible for tracking the annual renewal date; however, automated reminders are sent through Cayuse IACUC at 30, 60, and 90 days prior to the studies annual review date.

PIs should complete the Annual Review submission in Cayuse IACUC, which verifies the active status of the study, verifies that completed activities were conducted in accordance with the approved study, describes any proposed departures from the approved studies, and solicits information about activities projected for the upcoming year. Inadequate or incomplete responses on the Annual Review submission will result in follow-up communication from the IACUC as necessary. For all protocols, the completed Annual Review submission is reviewed as soon as possible by the DMR process. Consequently, the completed Annual Review submission must be submitted to REC at least 30 days prior to the expiration date in order to allow time for review and possible FCR. Once approved, REC will provide the study with an updated approval date. The renewal date will be effective for one year and always on the anniversary date of the original approval date, unless there is cause for interim review.

Failure to complete the annual review process before the annual expiration date indicated in the approval letter will result in termination or suspension of the study. If termination occurs, the research approved under the study must cease, and the animals must be either euthanized or transferred to another approved study. A new study will need to be submitted and approved by the IACUC prior to resuming any animal activity related to the study. If suspension occurs and the PI does not meet conditions for continuation as expressed by IACUC, the study will be terminated.

5. Modifications to Animal Use Protocols
PIs are informed in their approval letter that they must submit an Amendment submission in Cayuse IACUC and receive IACUC approval prior to instituting any amendments (Only the PI is authorized to submit this request). The submission distinguishes between minor and significant amendments. OLAW guidance allows for various processes for approval of significant amendments based on severity.

**Significant Amendments**

1: Significant amendments

The majority of significant amendments require approval by one of the valid IACUC approval methods- DMR or FCR by the IACUC (Submission deadlines for amendment requests that require FCR are the same as for submission of a new study; amendments considered for DMR but submitted near a scheduled IACUC meeting may be reviewed at that meeting). Those changes marked by an asterisk require FCR. These include:

- Changes in the objective of the study as originally submitted and approved by the IACUC
- Changes from non-survival to survival surgery*
- Changes resulting in greater pain, distress, or degree of invasiveness*
- Change in the species
- Change in Principal Investigator
- Change in impact of personnel safety
- Change in housing to or use of animals in a location that is not part of the animal program overseen by the IACUC

Significant amendments designated as FCR will be reviewed by the full IACUC committee at a convened meeting. As with an initial review, the requested amendment may be approved, withheld pending minor revisions (with subsequent DMR), or denied. If approved, the revised study will carry the same approval period as the original approval.

2: Significant amendments that may be administratively approved with Veterinarian Consultation

Some significant amendments may be approved by the Director of REC in consultation with the Attending Veterinarian (AV). The AV in these instances is serving as a subject matter expert in interpreting this and all other IACUC approved policies in reviewing the amendment request.
(The AV may refer any request to the IACUC for further review for any reason.) These are limited to changes:
   - in anesthesia, analgesia, sedation, or experimental substances;
   - in euthanasia to any method approved by the AVMA Guidelines for the Euthanasia of Animals; and
   - in duration, frequency, type, or number of procedures performed on an animal.

3: Significant amendments that may be administratively approved by the IACUC Chair (or alternate)

An increase in previously approved animal numbers may be approved by the IACUC Chair (or alternate) without additional consultation or notification. Modification requests for an increase in number must include a justification for the increase.

Minor amendments

1: Minor amendments that may be approved by the IACUC Chair or Alternate Chair include, but are not limited to:
   - Change in location of research;
   - Change in source of animals;
   - Change in animal strain.

2: Minor amendments that may be administratively approved by the Director of REC include:
   - Correction of typographical errors;
   - Correction of grammar;
   - Contact information updates; and
   - Change in personnel, other than the PI. (There must be an administrative review to ensure that all such personnel are appropriately identified, adequately trained and qualified, enrolled in occupational health and safety programs, and meet other criteria as required by the IACUC.)

Alteration of training

Requests for alteration of training typically accompany a new protocol but may also be submitted via the Amendment submission in Cayuse IACUC. All alteration of training requested via the Amendment submission will be reviewed by DMR with option to call for FCR. Please refer to the SOP on Training for more information on alteration.