Proposal Review and Approval

Policy: Any use of live vertebrate animals for teaching or research, including pilot and/or internally funded research, at the University of Louisville must be reviewed and approved by the Institutional Animal Care and Use Committee (IACUC) prior to the start of related research or teaching activities. Approval may be granted only after a Proposal to Use Laboratory Animals in Research and Teaching (“Proposal”) has been submitted by the Principal Investigator and reviewed by the IACUC. Principal Investigators must be University faculty or otherwise meet criteria defined in applicable University policies (e.g., Research Handbook).

Continued approval of each IACUC Proposal may be granted during the Annual Review process (if applicable); however, Proposal approval expires three years following the date of approval. A new Proposal to use laboratory animals in teaching or research must be submitted for review and approval at the end of three years.

Studies characterized by the likelihood of pain or stress will not be considered by the IACUC without comprehensive and explicit scientific justification. Such Proposals will be approved only when detailed scientific justification is provided for the purpose of the study and the inappropriateness of less “severe” alternatives. Class III Proposals must also detail the incompatibility of pain/distress relief and the goals of the research.

In the Proposal, the Principal Investigator must also provide a detailed description of the objective criteria that will be used to determine when an unacceptable level of pain or distress is reached and the intervention that will occur when this threshold, or “humane endpoint” is reached. The Principal Investigator will be responsible for monitoring high-risk animals to ensure that the specified criteria for determining unacceptable levels of pain or distress are met. The RRF staff will also assist in monitoring high-risk animals. Should the RRF identify animals requiring immediate attention, attempts will be made to contact the Principal Investigator or a suitable designee. In the event that these individuals cannot be reached, RRF veterinarians will intervene on behalf of the animal. This intervention may include euthanasia.

The IACUC also requires a written protocol for the use of vertebrate animal tissue(s), using a form entitled, Request to Use Fresh or Frozen Animal Tissues in Research and Teaching. The use of plants, bacteria, protozoa, or invertebrate animals is excluded from the IACUC review process. However, in accordance with the Guide for the Care and Use of Laboratory Animals, the IACUC expects that the use of invertebrate animals (e.g., cephalopods) will be conducted using comparable ethical considerations.

Proposals for which the PI has not responded to reviewer(s) comments or resolved safety contingencies for over 12 months will be provided a 30-day deadline for response, after which the Proposal will be administratively withdrawn.
**Rationale:** Federal regulations and guidelines require the IACUC to review and approve all anticipated animal use. Review and approval of the Proposal form provides this mechanism. During Proposal review, the significance of study goals is weighed against the pain and/or distress that may be imposed on animals which serve as models. Decisions involving Proposal disposition are made only after consideration has been given to other research methods which may not involve animals and/or cause pain or distress. The Committee gives ethical consideration to animal use as well as to the benefits related to the improvement of animal or human health or other societal good.

**Procedures, Guidelines, and Exceptions:**

1. **Definitions Used**
   a. *New Proposal.* A new Proposal to use animals in research and/or teaching is one that does not have current IACUC approval.
   
   b. *Three-Year Renewals* are previously approved Proposals which have been resubmitted to comply with the IACUC mandate for three-year de-novo review.
   
   c. *Modified Proposal.* A modified Proposal is one in which the Principal Investigator requests protocol change(s) in a currently approved project. The procedures for reviewing requests to modify existing Proposals are described in “Modification of an Approved Proposal.”
   
   d. Experimental groups are categorized based on the anticipated amount of pain and distress associated with the procedure used. Refer to the IACUC policy “Pain and Distress Class Categorization.”

2. **Submission and Administrative Pre-Review**
   Incoming Proposals are examined by IACUC Office staff to ensure that the Principal Investigator has provided all pertinent information required for Committee review. IACUC Office staff may also conduct a thorough pre-review to ensure that the Proposal is suitable for review.

3. **Veterinary and Safety Pre-Review**
   All Proposals are assigned to an RRF veterinarian for review. The IACUC Office will also notify the appropriate safety unit representative for Proposals involving the use of biological, chemical, or physical hazards. Veterinary and Safety Reviewers may require revisions to the Proposal (“stipulations”) before completing their review and may provide review comments for consideration by the Designated Reviewer.

4. **Reviewer Assignment**
   Proposals will be assigned to a Designated Reviewer and up to two Review Consultants. The IACUC Chairperson has delegated the authority to assign the Designated Reviewer to the IACUC office. The Designated Reviewer will be chosen from the IACUC membership. The Review Consultants are generally IACUC committee members, but may also be non-member expert consultants. Responsibility for serving as a Designated Reviewer, as described in Public Health Service “Policy on Humane Care and Use of Laboratory Animals” and USDA Animal Welfare Regulations, is rotated among scientist members and conflict of interest is avoided.
The number of Review Consultants depends upon the pain/distress category:

- Class 0 or 1: No Review Consultants
- Class 2: 1 Review Consultant
- Class 3: 2 Review Consultants

Reviewers and Consultants are notified of assignment automatically by iRIS or via email; all receive or have web-based access to the Proposal and other pertinent information submitted by the Principal Investigator.

5. IACUC Activity Report and Requests for Full Committee Review

All Proposals undergoing review are listed on an IACUC Activity Report. The report includes information such as the PI, title, species, highest pain/distress category, and Lay Summary and is forwarded at least weekly to all members of the IACUC via e-mail, facsimile, or other expeditious form of delivery. All committee members have access to, or may request a complete copy of any Proposal should additional information be desired. Furthermore, any IACUC member may request Full Committee Review (FCR) of any Proposal. Once requested, final committee action must await FCR.

Committee members are allowed three days following submission of an IACUC Activity Report; lack of a response within three days is considered acceptance of a Proposal for Designated Review. If a PI requires approval within three days, a special convened meeting of at least a quorum of the committee must be held for Proposal review.

6. Designated Review Process and Actions/Recommendations

The Designated Reviewer will review the Proposal and any comments by other reviewers, if any. Note that lack of comments by (a) Review Consultant(s) within 7 days may be considered a recommendation for approval. The Designated Reviewer then has the authority to:

a. Recommend approval, if no other revisions are required,
b. Require revisions to secure approval, or
c. Request Full Committee Review. Note that the Designated Reviewer may not “disapprove” or “table” a Proposal; any decision other than “recommend approval” or “require revisions to secure approval” must involve a Full Committee Review.

Approval for Proposals that involve the use of hazardous substances in living animals is contingent upon safety office/committee review and approval. The IACUC Office and Chair is responsible for ensuring that safety-related contingencies have been met.

7. Full Committee Review

Any committee member may request a Full Committee Review (FCR) of a Proposal. In such an instance, a notice, which may include a copy of the Proposal, is forwarded to all IACUC members and the assigned reviewers. The Designated Reviewer becomes the Primary Reviewer for the Proposal, assisted by the Veterinary and Review Consultants. The Principal Investigator may be asked to participate in Committee discussions related to the proposed research. The IACUC may invite additional consultants to assist in the review of complex issues arising out of its review of proposed activities, although consultants may not vote with the IACUC.
Discussion of the Proposal during a convened meeting of the IACUC, in which a quorum (>50%) of the voting membership is present, will be led by the Primary Reviewer and assisted by the Veterinary and Review Consultants. IACUC members with a conflict of interest will not participate in the review process or contribute to the constitution of a quorum.

Action on the Proposal is based on a majority vote. Possible Full Committee actions/decisions include:

a. Approval, if the Proposal is suitable as submitted.

b. Revisions required to secure approval, if contingencies must be met, yet the Committee is comfortable with delegating the review of the response. Such contingencies must be clearly outlined and forwarded to the Principal Investigator by either the Primary Reviewer or Chair, who is then also responsible for ensuring that the contingencies outlined have been met. In accordance with PHS Policy, this reverts the review to Designated Review, and therefore can only occur following a unanimous vote for this action (in other words, any dissenting vote requires that the Proposal be “tabled”). The IACUC Office will include the revised Proposal provided by the PI on the IACUC Activity Report.

c. Withhold approval.
   1) Tabled: When issues of concern exist such that the committee requests additional information for Full Committee Review, the Proposal is “tabled.” All such issues must be clearly outlined and forwarded to the Principal Investigator by either the Primary Reviewer or Chair, who are then responsible for ensuring that the issues outlined have been met. In accordance with PHS Policy, this reverts the review to Designated Review, and therefore can only occur following a unanimous vote for this action (in other words, any dissenting vote requires that the Proposal be “tabled”). The IACUC Office will include the revised Proposal provided by the PI on the IACUC Activity Report.

   2) Disapproved: When the committee determines that a proposed study protocol is unacceptable according to federal, state, and/or local regulations, or fails to meet University standards, disapproval may be recommended. The Principal Investigator is notified of disapproval by a letter in which the basis for Committee action is clearly stated.

8. IACUC Chair Review and Action
After Designated or Full Committee Review is completed and other relevant correspondence (e.g., results of various safety committee review) are received by the IACUC Office, the Proposal approval letter is prepared for the IACUC Chair. Should the Chair identify additional concerns, s/he may forward these concerns to the Designated Reviewer for resolution with the Principal Investigator. In the Chair’s absence, the Vice-Chair or another scientist member of the IACUC will take final action on a Proposal. The Principal Investigator is notified of final Proposal action by letter. The date on this letter is considered the Proposal initiation date; Proposal expiration is three years from this date.

9. Proposal Ratification
A list of all Proposals approved by Designated Review but not yet ratified is prepared for Committee action. The list is reviewed at a convened meeting of a quorum and ratification is based on a majority vote. Although approved Proposals may have been initiated at this point, ratification provides an additional means of discussion by the entire committee, and does not preclude the
IACUC from requesting additional information or clarification from the Principal Investigator to ensure continued approval.

10. Review Frequency
IACUC approval to use laboratory animals in research and teaching is granted for a period of three (3) years. Proposals using species covered by USDA Animal Welfare Regulations are subject to Annual Review at 12 months following the last IACUC approval, including requests for Modification of an Approval Proposal. A form to verify that the Principal Investigator wishes to retain the Proposal and that no changes have or will occur without submission of an appropriate Modification will be used. This form, and the Proposal itself, is reviewed by a Veterinary and Designated Reviewer as described above.

IACUC Proposal approval expires at the end of three years. Four, three, two, and one month(s) prior to Proposal expiration, the Principal Investigator is notified by e-mail in order to continue the study, a new Proposal must be submitted for review and approval. Review is conducted according to the procedures given for new Proposals.

11. Appeal Process
The Principal Investigator may appeal an IACUC action. An appeal must be made in writing to the IACUC Chair and/or the Institutional Official. The Institutional Official cannot approve a Proposal not approved by the IACUC, but can encourage the IACUC to reconsider its decision. If it is determined that the IACUC will reconsider its action, Full Committee Review of the Proposal is required.