

University of Louisville
Institutional Animal Care and Use Committee
Policies and Procedures

Proposal Review

Scope

Any use of live vertebrate animals for teaching or 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* has been submitted by the Project Director and reviewed by the IACUC.

Although continued approval of each IACUC *Proposal* may be granted during the Annual Review process, a new *Proposal* to use laboratory animals in teaching or research must be submitted at the end of three years. The use of animals for pilot and/or internally funded research must also have IACUC approval. During *Proposal* review, the significance of study goals are 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.

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.

Submission and Administrative Review

The review process is initiated when a *Proposal* is received by the IACUC Office. Incoming *Proposals* are examined to ensure that the Project Director has provided all pertinent information required for Committee review. Manual and computer files are created for each *Proposal* and an IACUC identification number is assigned.

The IACUC administrative office will address *Proposals* that have not been completed according to the instructions. Project Directors will be contacted and asked to supply missing information. With the exception of required signatures, information may be provided verbally or by email and added by the administrative staff to complete the *Proposal*. Information added to the *Proposal* by administrative action must be designated by an initialed notation identifying the authority for making changes. Completed *Proposals* will be assigned for IACUC review.

Proposal Type and Classification

New Proposal:

A new *Proposal* to use animals in research and/or teaching is one that does not have current IACUC approval. Previously approved *Proposals* which have been resubmitted to comply with the IACUC mandate for three-year review are also considered in this category.

Modified Proposal:

A modified *Proposal* is one in which the Project Director requests permission to make 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."

Classification:

Animal use is classified according to the following scheme:

Class I - Studies in which animals will experience *no pain or distress* greater than that produced by routine injections or venipuncture and will therefore receive *no pain-relieving agents*.

Class II - Studies in which there is a *potential for pain or distress* which is *minimized or eliminated by anesthetics, analgesics, and/or tranquilizers*. Examples include biopsy, endoscopy, vascular cut-down, implantation of chronic catheters as well as *non-survival and survival surgery*.

Class III - Studies in which animals will *experience pain or distress* greater than that produced by routine injections or venipuncture and will *not receive pain-relieving agents*. Examples include exposure to agents or radiation levels that cause serious illness, research involving significant stress or procedures involving prolonged restraint.

NOTE: Studies characterized by the likelihood of *severe* unrelieved pain or stress **will not be considered** by the IACUC without comprehensive and explicit scientific justification. Class III *Protocols* will be approved only when detailed scientific justification is provided for: a) the purpose of the study, b) the inappropriateness of less “severe” alternatives, and c) the incompatibility of pain/distress relief and the goals of the research. The Project Director 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. When this threshold is reached, project participants or veterinary staff will intervene and euthanasia may occur.

The Project Director 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 monitor high-risk animals. Should the staff identify animals requiring immediate attention, attempts will be made to contact the Project Director 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.

Veterinary Pre-Review

All *Proposals* receive a pre-review by a RRF veterinarian. Although this review concentrates on animal husbandry and veterinary care issues, the pre-review also ensures *Proposal* accuracy and completeness.

Proposals shown by veterinary review to lack clarity will be referred back to the Project Director. Through personal, telephone, or email contact with the project Director, the veterinary staff member performing the initial review will identify *Proposal* sections that may require clarification and suggest additions and/or corrections. Depending on the extent or nature of the suggestions, the Project Director may elect to clarify the *Proposal* through resubmission or may choose to make changes on the originally submitted *Proposal*. When suggestions involve simple changes related to additions or corrections (anesthetic agents/doses, study classification, a clarifying word, *etc.*) the veterinary reviewer may agree to make change(s) in the *Proposal* for the project director based on telephone or email contact. Such changes must be designated by the veterinarian’s initialed notation identifying the authority for the changes. *Proposals* with the clarity required for complete understanding will be assigned for IACUC review. Copies of correspondence between the veterinary pre-reviewer and the Project Director may also be used to document *Proposal* changes.

Reviewer Assignment

Proposals will be assigned to a subcommittee composed of a Primary Reviewer and one or more Secondary Reviewers. The Primary Reviewer will be chosen from the IACUC membership. The Secondary Reviewers are generally IACUC committee members, but may also be non-member expert

consultants. Non-member consultants may not approve or withhold approval of a *Proposal* or vote with the IACUC. Responsibility for serving as a Primary Reviewer, which serves as the “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. Reviewers are notified of assignment by the **Reviewer Assignment Letter** (Attachment 1) and all receive a copy of the *Proposal* and other pertinent information submitted by the Project Director.

A summary of the scheme for IACUC *Proposal* review assignment is shown below:

Class I	<i>Primary Reviewer</i>
Class II	
Non-surgical procedures:	<i>Primary Reviewer + 1 Secondary Reviewer</i>
Surgical Procedures:	
Non-survival surgery:	<i>Primary Reviewer</i>
Single Survival Surgery	
Minor:	<i>Primary Reviewer + 1 Secondary Reviewer</i>
Major:	<i>Primary Reviewer + 2 Secondary Reviewers</i>
Multiple Survival Surgery:	<i>Primary Reviewer + 2 Secondary Reviewers</i>
Class III	<i>Primary Reviewer + 2 Secondary Reviewers</i>

IACUC Activity Report and Requests for Full Committee Review

All new *Proposals* are listed on the **IACUC Activity Report** (Attachment 2). The report includes the *Proposal’s* Lay Summary and is forwarded weekly to all members of the IACUC via e-mail, facsimile, or other expeditious form of delivery. Any committee member 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.

The entire review process generally requires several weeks, which gives reviewers and other committee members ample opportunity to request FCR. If, however, a Project Director requests accelerated review (*i.e.*, within one week), then the IACUC Office will forward the specific summary and lay abstract to all committee members, who are given three working days to request FCR. If a PI requires approval within 3 working days, a special convened meeting of at least a quorum of the committee must be held for *Proposal* review.

Review Considerations

Subcommittee members will examine each *Proposal* in accordance with *PHS Policy*, USDA Regulations, and the *Guide for the Care and Use of Laboratory Animals*. Although all aspects of the proposed use of animals must be clearly delineated and justified, the reviewers will pay particular attention to the following issues.

1. *Lay research summary*. The summary must be written for the understanding of persons not trained in biomedical science (see *Proposal*, Section XI).
2. *Study classification*. If classification appears to be inaccurate, the reviewer notifies the IACUC Office, whereupon the classification may be reconsidered. If classification is changed, reviewers are re-assigned accordingly (see *Proposal*, Section IX.A.-page 6).
3. *Alternative models*. The methods and reference sources used to address the issue of alternative animal models must be outlined (see *Proposal*, Section V.C.-page 3).
4. *Project Participants*. The qualifications and training of personnel who will conduct procedures on the species to be studied must appropriately prepare them for their specific role in the study (see *Proposal*, Section VI.-pages 3-4).
5. *Hazardous agents*. If applicable, a detailed protocol for the use of hazardous agents must be reviewed and approved by the appropriate safety personnel/committee (see *Proposal*, Section VII.B.-page 5).
6. *Unnecessary duplication*. A written assurance that the proposed activities do not unnecessarily

- duplicate previous experiments must be included (see *Proposal*, Section V.B.-page 3).
7. *Consideration of alternatives.* A written description of the methods and reference sources used to address the issue of alternatives to painful procedures must be included (see *Proposal*, Section X.C.-page 8).
 8. *Pain-relieving agents.* If applicable, a list of the sedative, analgesic and/or anesthetic agents to be used in the study must be included and appropriate (see *Proposal*, Section X.F.-page 9). The *Proposal* should also address other procedures that will be used to avoid or minimize discomfort, distress, and pain to animals used in non-surgical procedures (see *Proposal*, Section X.D.3.-page 8 and X.E.2.-page 8).
 9. *Prolonged restraint.* If applicable, the use of any devices used to restrain animals for prolonged periods of time must be thoroughly described and justified (see *Proposal*, Section X.D.2.-page 8).
 10. *Multiple survival surgery.* If applicable, justification for multiple survival surgery performed on a single animal must be included (see *Proposal*, Section X.E.4.-page 9).
 11. *Peri-operative care.* If applicable, plans for pre- and postoperative care and a description of aseptic surgical techniques must be included (see *Proposal*, Section X.E.1- page 8; X.E.5 - page 9).
 12. *Euthanasia.* A description of euthanasia procedures and the clarification of a study endpoint must be included (see *Proposal*, Section X.G.1-page 10).

Subcommittee Review Process and Actions/Recommendations

The IACUC office will maintain the original *Proposal*, all appropriate attachments, including the grant application (if applicable), and forward copies of all submitted materials to (a) Secondary Reviewer(s) who will complete the review within 10 working days. Reviewers will forward their comments to the IACUC office. Although an e-mail may be used to continue *Proposal* processing, a signed "Reviewer Assignment Letter" must follow. The office will use a log as a prompt for telephone or e-mail contact with Secondary Reviewers to assure a 2-week (10-working day) *Proposal* review turnaround.

The IACUC office will assemble and forward a copy of the complete *Proposal*, all appropriate copies of attachments including grant applications and all Secondary Reviewer comments to the Primary Reviewer. The Primary Reviewer will review the *Proposal* and Secondary Reviewer comments within 5 working days of receipt and contact the Project Director if clarification or changes are required. Verbal clarification by the Project Director may be acceptable or written changes to the *Proposal* may be required. In the latter case, all communications will clearly indicate that further action by the IACUC may not take place until the Project Director's written response has been received by the Primary Reviewer. Responsibility for a response lies with the Project Director. The Primary Reviewer is expected to exercise due diligence in obtaining timely written responses.

Written changes or corrections submitted by the Project Director may be accepted by the Primary Reviewer or may be referred to the Secondary Reviewer(s) to verify that problems or issues raised have been sufficiently addressed. Once all issues have been satisfactorily addressed, the Primary Reviewer will make a formal recommendation and inform the IACUC office of this action. Although e-mail may be used to continue *Proposal* processing, a signed copy of the "Reviewer Assignment Letter" must follow. The Primary Reviewer will return all reviewer comments and all other materials related to the review process to the IACUC office.

The entire review process for new *Proposals* is generally completed within 1 month. Should the Project Director fail to respond to request(s) for written clarification of review issues within 22 working days (1 calendar month), the Primary Reviewer may return the *Proposal* to the IACUC office. The *Proposal* will be classified as "Withdrawn From Review (WFR)" and no further action will be taken by the IACUC.

The following actions/recommendations may be made by the Primary Reviewer:

Proposal Approval: *Proposal* approval is recommended when: 1) all subcommittee members agree to

accept a *Proposal* as submitted or, 2) subcommittee questions regarding protocol or procedures that may have been raised during review have been satisfactorily addressed by the Project Director.

Contingent Approval: When the subcommittee requires minor changes in the protocol (such as a change in caging systems, route of anesthesia administration, *etc.*), a *Proposal* may be recommended for approval contingent upon the Project Director's stated willingness to make protocol revision(s). Projects that involve the use of hazardous substances in living animals may also receive approval contingent upon safety office/committee review and approval. The Primary Reviewer must clearly outline approval contingencies in the Reviewer Assignment Letter. The Chair is then responsible for ensuring that the contingencies outlined have been met.

Request for Full Committee Review: The Primary Reviewer, as any member of the IACUC, may request Full Committee Review of a *Proposal*. Because a subcommittee may not "disapprove" a *Proposal*, any decision other than "approval" or "contingent approval" must involve a Full Committee Review.

Full Committee Review

Any member of the subcommittee or any other committee member who has reviewed the *Proposal* may request a Full Committee Review (FCR). In such an instance a copy of the *Proposal* is forwarded to all IACUC members and the Primary Reviewer notifies the Project Director that review by the full Committee is necessary. The Project Director may be asked to participate in Committee discussions related to the proposed research. The IACUC may invite consultants to assist in the review of complex issues arising out of its review of proposed activities. Consultants may not approve or withhold approval of an activity, and may not vote with the IACUC unless they are also members of the IACUC. IACUC members with a conflict of interest will not participate in the review process or contribute to the constitution of a quorum. FCR may occur only at a convened meeting of a quorum.

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

Proposal Approval: After discussion, the committee may determine that the *Proposal* is suitable for approval as submitted.

Approvable with Contingencies: This action follows a determination that the *Proposal* is suitable for approval once certain contingencies are met and the committee is comfortable with delegating the review of the response. Such contingencies must be clearly outlined and forwarded to the Project Director by either the Primary Reviewer or Chair, who is then also responsible for ensuring that the contingencies outlined have been met.

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 Project Director by either the Primary Reviewer or Chair; the responses by the Project Director are then brought back to the next IACUC meeting for deliberation.

Proposal Disapproval: 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 is recommended. Before final action is taken, however, the Chair may discuss subcommittee comments and recommendations with the Project Director after which s/he may elect to withdraw the *Proposal* from further Committee consideration. If not withdrawn, the *Proposal* is *disapproved* with the basis for such action clearly stated on the Reviewer Assignment Letter. The Project Director is notified of disapproval by a letter (**Proposal Disapproval Letter** - Attachment 3) in which the basis for Committee action is clearly stated. The signed original *Proposal*, including subcommittee comments, is returned with the letter.

IACUC Chair Review and Action

After subcommittee, full committee, and other relevant correspondence (e.g., review results of various safety committees) are received by the IACUC Office, the *Proposal* is prepared for final review by the IACUC Chair. Depending upon subcommittee and safety committee comments and recommendations, the Chair may approve, approve with contingencies, or request Full Committee Review of the *Proposal*. In the Chair's absence, the Vice-Chair serves as Chair for this review. Alternatively, the Chair may authorize a scientist member of the IACUC to review and take final action on a *Proposal*.

The Project Director is notified of *Proposal* approval or contingent approval by letter (***Proposal Approval Letter, Contingent Approval Letter*** - Attachments 4 and 5). The signed original *Proposal* including any comments or contingencies is returned with the letter.

Proposal Ratification

A list of all *Proposals* approved by the subcommittee 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 review and discussion by the entire committee, and does not preclude the IACUC from requesting additional information or clarification from the Project Director to ensure continued approval.

Review Frequency

IACUC approval to use laboratory animals in research and teaching is granted for a period of three (3) years subject to Annual Review. Although continued approval may be granted annually, a new application must be submitted at the end of three years.

IACUC *Proposal* approval expires at the end of three years. Ninety days prior to *Proposal* expiration, the Project Director is notified by letter (***Three-Year Renewal Notice Letter*** - Attachment 6) in order to continue the study, a new *Proposal* must be submitted. Review is conducted according to the procedures given for new *Proposals*.

Appeal Process

The Project Director may appeal IACUC action. An appeal must be made in writing to the IACUC Chair and/or the Institutional Official. If it is determined that the IACUC will reconsider its action, Full Committee Review of the *Proposal* is required.

IACUC Records

All *Proposals* and related review correspondence are filed in the IACUC office. *Proposal* information, including approval status, is also recorded in the IACUC database which is accessible to the Research Resources Facilities through a Local Area Network (LAN).