
Guidelines for the Review of Animal Care and Use Protocols

Information that must be evaluated as part of the review process. The Public Health Service (PHS) and the United States Department of Agriculture (USDA) include the following topics among those that should be considered as part of the preparation and review of animal care and use protocols.

- Training and experience of personnel with the procedures to be used*
- Rationale and purpose of the proposed use of animals
- Justification of the species and the number requested
- Consideration of non-animal, less invasive, or less painful alternative procedures, and the use of species phylogenetically lower than the species that is proposed for use (the 3 R's: Reduction, Refinement, & Replacement).
- Unnecessary duplication of experimentation
- Nature of the proposed use of animals
- Housing and husbandry requirements
- Appropriate use of sedation, analgesia, and anesthesia
- Are multiple survival surgeries planned and justified?
- Criteria and process for intervening to reduce stress or discomfort of animals
- Plans for post-procedural care
- Method of euthanasia or other dispositions of animals
- Safety of the working environment for personnel

*Administratively reviewed by the PACUC office – no need for PACUC Member Review.

Items considered to be significant changes to an approved protocol. Per federal regulations, approval by the PACUC is required prior to the implementation of any “significant” changes to a protocol. The PACUC uses the following list as a guide to determine what types of changes should be considered significant. Rather than being exhaustive, this list is used to indicate the general range of changes that should be considered for approval by the PACUC.

- Change in the Principal Investigator on the protocol.
- Changes in the overall objectives of the approved studies.
- Changes from non-survival to survival surgery or vice-versa.
- Changes that increase the pain or discomfort experienced by animals (e.g., increased restraint, restrictions on food or water intake, exposure to noxious or hazardous stimuli or materials).
- Changes in the anesthetic agent(s) or dose(s) or the method(s) of administering of anesthetic agents.
- Changes in the use of analgesics.
- Changes in the use of sedatives or tranquilizing drugs.
- Changes in the method of euthanasia.
- Changes in the species used.
- Increases in the number of procedures performed on an animal.

- Modifications to a surgical procedure.
- Changes in the duration of a procedure that is performed on an animal (e.g., chronic rather than acute procedures or vice-versa, length of a behavioral test session).
- Changes in the housing or husbandry of animals.
- Changes in the frequency of procedures (e.g., blood sampling, drug administration, tissue biopsy, exposure to stimuli, number of repeated behavioral tests).
- Changes in the invasiveness of a procedure (e.g., utilized a catheter rather than a needle to obtain fluid samples, injected rather than administered as an oral form of a drug).

Types of review for new protocols, amendments, annuals, and triennials.

1. Designated Member Review (DMR) of protocol applications (Outcome #1): Review is conducted via the Coeus system by the Chair (or designee) and a LAP veterinarian. The responsibility for the third review is divided among the remaining members of the PACUC, with different members performing this function on a monthly basis. **This review is to be completed within 10 working days of receiving the protocol for review.** This review has one of three potential outcomes.
 - a. *Approval on a designated basis.* This outcome is reserved for protocols that do not raise questions about animal care and use or about regulatory compliance and are received in approval-ready form.
 - b. *Consider comments before recommending approval on a designated basis.* Reviewers may ask for additional information before determining whether a protocol application can be approved. The questions or comments of reviewers will be summarized in a question memo that is prepared by the PACUC Administrative Assistant (or designee) and forwarded to the PI or to his or her designate via Coeus. Further consideration of the protocol application will be suspended until a response to the question memo is returned. The response is sent to the DMR's for review and to determine whether the protocol is ready for approval via DMR.
 - c. *Recommendation for review at a meeting of the full PACUC.* If an IACUC member performing DMR recommends full committee review (even after the full PACUC recommended DMR), the protocol application will be reviewed at a meeting of the full PACUC. The protocol application, along with the response to the memo, will be forwarded to each member of the PACUC at least one week prior to the meeting at which approval will be considered.
 - The PACUC Administrative Assistant (or designee) forwards all questions and comments of the reviewers to the PI *unless the PACUC Administrator consults with the reviewer about withdrawing a question or comment.* The Administrator would consider withdrawing a question or comment only under a very limited set of circumstances. One circumstance would be if the issue raised by the reviewer seemed to already be addressed adequately within the protocol application. Another circumstance would be if a question or comment posed by the reviewer seemed to instruct the PI to perform a practice or procedure that is unsatisfactory or that is less satisfactory than the practice or procedure proposed by the PI. It is hoped that through discussion, the reviewer and the Administrator would either agree to withdraw or to rephrase the question or comment. If such an agreement cannot be reached, the Administrator (in consultation with the Chair) retains the right to withdraw the question. However, in this situation, the protocol will automatically be

scheduled for review by the full PACUC.

2. Procedures for Full Committee Review (FCR) [Outcome #2]: The PACUC meets once per month on a 12-month basis unless there is no business to discuss. Under special circumstances, the PACUC may meet more often than once per month. Review of protocols at a meeting of the full PACUC can only begin if there is a quorum of the voting members of the PACUC present at the meeting. The Chair will also ask those present to indicate any potential conflicts of interest they may have pertaining to protocols listed on the agenda for the meeting. If a quorum exists after any person who has a potential conflict of interest is excused, consideration of a protocol can begin. At the conclusion of the discussion, a motion is formulated concerning the action the committee will take on the protocol. The members of the PACUC are then asked to vote on that motion. The PACUC may vote to adopt any one of the following categories of action:

- a. *Approval*: A protocol will be approved only when the PACUC considers that all significant points and potential concerns have been addressed satisfactorily by the PI. Granting approval means that the PI has permission to conduct the project that was described, with the number of animals that were indicated, in the protocol, or in other communications from the PI that were considered by the members of the PACUC. The Committee may instruct the Administrator to communicate to the PI comments or remarks made during the discussion of the protocol. However, approval of the protocol is not conditional upon the response of the PI to this communication, nor is the PI required or expected to respond.
- b. *Withhold approval pending modifications*: This action will be taken when the PACUC deems that specific aspects of the protocol may be problematic and require further explanation, justification, documentation, or information. The Administrator (or designee) will communicate, as clearly as possible, these problematic areas to the PI. The Chair (or designee) and a LAP veterinarian (appointed designated member review) will review the response of the PI to this communication. This procedure is in agreement with the PACUC-approved Policy on DMR review after FCR review. Approval to conduct the activity described in the protocol will be withheld until the response of the PI has been judged to satisfy the conditions set forth previously by the committee. If the two PACUC members (designated member reviewers) agree that the response of the PI addresses satisfactorily the issues raised at the PACUC meeting, the protocol will be approved. In cases where consensus among the two PACUC members cannot be obtained, evaluation of the response and the decision to approve will be made, based on a majority vote at the next meeting of the full PACUC.

Approval will also be withheld when the PACUC considers that all significant points and potential concerns have been addressed satisfactorily by the PI, but that, specific administrative details, such as signatures of responsible parties, phone numbers, and information about submission to funding agencies are missing or need clarification. Approval will be granted when this type of information has been provided to the satisfaction of the PACUC Administrator. No further review by the Chair, LAP veterinarians, or other PACUC members is required.

- c. *Deferral/Table*: The Committee may decide to defer action on, or table, a protocol until a later date. The reason for deferring action usually involves having

insufficient information upon which to make a judgment about the protocol. A protocol may be deferred until the information needed by the committee is available.

- d. *Disapproval*: The PACUC may vote to disapprove a protocol application. To appeal a decision to disapprove, the PI must present the PACUC with pertinent evidence or expert opinions in addition to those that were available when the decision to disapprove was made. This presentation shall be made by the PI, in writing or in person, at a regular meeting of the PACUC where a quorum of the voting members is present. The intention to appeal must be announced no less than ten (10) days prior to the PACUC meeting where the option to appeal will be executed.

Situations that automatically require full committee review include the following:

- Death as an Endpoint.
- Pain Category E.
- Heat- or cold-stress protocols.
- No analgesia being provided post-surgery/procedure.
- Multiple Survival Surgery (if both surgeries are considered major).
- Use of greater than 10,000 animals on a protocol (mammalian species only).
- Other (i.e., Exceptions to the Guide, protocol that a committee member marks FCR, etc.).

Re-review of Approved Protocols: All protocols are approved by PACUC for a period of three (3) years. However, both the USDA and the HS have requirements pertaining to the continuing review of previously approved activities involving the care and use of animals. According to the USDA, the PACUC is required to conduct “continuing reviews” of activities covered by approved protocols at intervals “not less than annually.” The PHS policy requires a “complete review” of previously approved activities “at least once every three years.” To meet these requirements, the PACUC has developed policies and procedures for conducting re-reviews of approved protocols.

- a. Annual Review of Approved Protocols. This review requires that PIs submit information about personnel changes, the number of animals used, the health status of animals, and about unexpected complications or difficulties that may have occurred during the previous 12-month period of approval. The Annual Review process is the same as for protocol review described above. **This review is to be completed within 10 working days of receiving the Annual for review.**
- b. Triennial resubmission and review of previously approved protocols. Protocols are approved by the PACUC for a period of three years. To continue a project beyond this three-year approval period, the PI must submit a complete protocol application that is subject to the same review and approval process as is a new application (see above). The triennial resubmission will retain the same identification number as the original protocol. **This review is to be completed within 10 working days of receiving the Triennial for review.**

The Protocol Review Process

