

## **IACUC Protocol Review Process**

8-27-2013

Animal Use Protocols are submitted to the Office of Regulatory Research Compliance (ORRC). Projects involving animal subjects may not begin until approved by the Committee, regardless of the type of the project or its source of funding. Prior to IACUC review, each protocol is reviewed by the veterinarian, the IACUC chair, and IACUC administrator. Questions raised by these reviews are sent to the PI via email. The PI is required to respond and make changes before the IACUC review.

In addition to the veterinarian, two members of the IACUC are assigned as a primary reviewer and secondary reviewer and present their reviews at the meeting. However, all protocol materials are available to all IACUC members for review. The IACUC reviews each submission at a convened meeting of the full committee (Full Committee Review, FCR) at which a quorum is present. IACUC decisions are made by a vote of a simple majority (51%) of the quorum. Any member may abstain from participating in a protocol review.

Members must recuse themselves (i.e., abstain from voting and be absent from the room during deliberation and vote) if there is a conflict of interest. The Chair of the IACUC and the Senior Compliance Officer determine if a member has a conflict of interest. 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 and there is no perceived conflict of interest.

The IACUC determines through deliberation whether the research project conforms with the institution's assurance and meets the following requirements: 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 sacrificed at the end of the procedure or, if appropriate, during the procedure. An oral vote is taken following the discussion of the protocol.

The vote indicates the IACUC's decision to approve, require modifications to secure approval, defer or withhold approval. Protocols that are deferred are generally missing key information for the IACUC to assess the application and will be reviewed as a new submission at the next convened meeting. Within five business days following the IACUC meeting, the PI is notified in writing (via email) of the IACUC's decision. If approval is withheld, the PI is informed of the reasons for its decision. When substantive information is lacking from a protocol, and the committee has questions requiring a response from the PI, the IACUC may use designated member review (DMR) subsequent to full committee review (FCR). All IACUC members have consented in writing that the quorum of members present at a convened meeting may decide by unanimous vote to use DMR subsequent to FCR when modification is needed to secure approval. However, any member of the IACUC may, at any time, request to see the revised protocol and request FCR of the protocol. In certain circumstances DMR alone may be utilized. In this case, the application is made available to each member of the Committee with an opportunity, generally 5 business days, for any member to call for a full Committee review. If any member requests FCR, the application is held for the next scheduled meeting with a full quorum. If no member requests a FCR, the DMR process may commence.

In either case, the Chair and the IACUC administrator assign at least two IACUC member as a designated reviewer for any proposal reviewed by DMR. Veterinary review and compliance pre-review is conducted and any questions or comments are forwarded to the principal investigator. Once the PI has satisfactorily responded to the veterinarian's concerns, then the research project will advance for further review. DMR may result in approval, a requirement for modifications (to secure approval), or referral to the full committee for review. If a protocol is assigned to more than one designated reviewer, the reviewers must be unanimous in any decision. They must all review identical versions of the protocol and, if modifications are requested by any one of the reviewers, the other reviewers must be aware of and agree to the modifications.

Whether in full-committee review or designated member review, the IACUC or designated member reviewer(s) evaluates all components related to the care and use of animals to determine that the proposed research and for teaching protocols will be conducted in accordance with institutional policies. In making this determination, the IACUC confirms that the research project will be conducted in accordance with the PHS Policy and the Animal Welfare Act insofar as it applies to the research project, and the research protocol is consistent with the "Guide," unless an unacceptable justification for a departure is presented in writing.

The PHS Policy requires that a complete IACUC review of PHS-supported protocols be conducted at least once every three years. This triennial review is interpreted by OLAW as a requirement for de novo review, meaning that the criteria and procedures for review specified in IV.C. of the PHS Policy must be applied not less than once every three years. The three-year period must begin on the actual date of IACUC approval. The IACUC is not allowed to administratively extend approval beyond the three years. To assist investigators, the ORRC will provide adequate and repeated warning (3 month and 1 month) of pending protocol expiration (via email). It is the responsibility of the investigator to submit the third-year resubmission by the appropriate deadline date for a scheduled Full Committee Review (FCR) prior to protocol expiration. Third Year Resubmission must be submitted as a new proposal, using the most recent version of the application.

This three year review is sometimes called a de novo review because the protocol receives the same scrutiny by the committee as it would if it were a brand-new submission. Lead Researchers should not assume that their three-year renewal protocol will automatically receive approval. Many factors may have changed since the last full committee review, including federal animal welfare regulations, societal expectations, and the composition of the committee. As is the case with annual renewals, the protocol expires on its expiration date if a three-year renewal application has not been reviewed and approved by the IACUC. During the lapse in approval, animals are moved to the Veterinary Service holding protocol and are off limits to investigators and research personnel and may not be used for experiments or observation. Per federal regulations and HU's Animal Welfare Assurance, there are no exceptions and no extensions of approval granted by the IACUC.

All animal use protocols and modifications require IACUC approval. However, minor amendments to already approved protocols with no or minimal direct animal welfare and well-being concerns may be reviewed by a DMR. Criteria set forth for protocols to be eligible to undergo DMR as established under a quorum meeting of the IACUC are as follows:

### **Modification of Protocols**

Investigators must submit amendments to protocols for changes in animal activities.

- a. Minor amendments to already approved proposals with no or minimal direct animal welfare/well-being concerns may be reviewed by a DMR.
- b. The Chair and/or the Veterinarian will make the determination as to whether a modification is major or minor.

Examples of changes considered to be significant include, but are not limited to, changes

- in the objectives of a study
- from non-survival to survival surgery
- in survival time
- in duration of surgical operations
- resulting in greater discomfort or in a greater degree of invasiveness
- in the species or in approximate number of animals used
- in Principal Investigator
- in anesthetic agent(s) or the use or withholding of analgesics
- in the method of euthanasia
- in the duration, frequency, or number of procedures performed on an animal
- in the specimens collected (e.g., protocol says measure blood levels, you want to measure urine levels)
- in drugs to be used
- in drug dose
- in strain, sex or age of the same species
- in diet

The IACUC handles proposed significant changes in previously approved activities in the same manner as new protocol applications, including the methods used for submission, review and approval. Written notification by the investigator to the IACUC for approval is required before significant changes can be made to an approved protocol. Evaluation of amendments to protocols originally subjected to full-committee review are handled in the same way as new protocols and may be subjected to designated review if no committee member requests full review. Amendment applications for protocols originally subjected to designated review for which no member calls for full-committee review are assigned to the member(s) that originally conducted the designated member review where possible.

USDA Animal Welfare Regulations require that the IACUC conducts continuing reviews of activities involving live animals not less often than once per year, but do not require that this annual review be conducted by the full IACUC at a convened meeting. The Public Health Service Policy requires that the IACUC conducts a complete review of all previously-approved ongoing activities at least once every three years. The HU-IACUC complies with these requirements by allowing two annual continuing renewals that are performed by a subcommittee of the IACUC, and a complete resubmission of the full protocol for full committee review every three years.