

Protocol Review Process

Investigators complete and submit their protocols (new, fourth year renewals, annual review, or amendments) electronically via a web-based protocol management system to RICRO. These may be submitted at any time for Designated Member Review. To be considered for Full Committee Review, a schedule of the deadlines for protocol submission and meeting dates is posted on the Research Integrity and Compliance Review Office (RICRO) website.

Protocol Pre-Review

A pre-review prior to dissemination of the protocol to the IACUC for the formal review is conducted by the veterinary staff and RICRO staff. The primary focus of the veterinary review is on issues related to

1. The appropriateness of the model,
2. Appropriate sample collection and/or administration procedures,
3. Appropriate surgical procedures and aseptic technique, anesthetic monitoring, post-operative care, adverse effects, endpoints and euthanasia techniques.
4. RICRO staff may also conduct a pre-review of the protocol to address personnel training issues, lay summary, numbers justification, alternative searches, and completeness prior to IACUC review of the protocol.

Clinical Trials and Clinical Research

Clinical trials conducted at the Veterinary Teaching Hospital (VTH) are reviewed by the VTH Clinical Review Board (CRB) prior to or at the same time as IACUC Protocol review. The purpose of VTH CRB review is to examine the scientific rationale of the clinical trial, as well as the client consent form.

IACUC Review

Protocols are reviewed either at a convened meeting (full committee review, FCR) or by the designated member review process (DMR). The review process is the same whether it is a new protocol, a 4th year renewal, annual renewal, or an amendment to a previously approved protocol.

During its deliberations the IACUC considers the potential adverse effects of the study vis-à-vis the potential benefits of the research in order to determine whether or not to approve the proposal. The IACUC works with the investigators to minimize the potential adverse effects and to determine early endpoints whenever possible. The most common end point criteria used is the Behavioral Scoring assessment used by LAR; however, project specific criteria have also been developed. For studies that are USDA category D and E, veterinarians are frequently consulted prior to submission of the protocol for review. The committee is diligent at reviewing and assuring appropriate analgesia is provided unless otherwise justified and that the animal numbers are appropriately justified using statistical analysis or other appropriate means.

Full Committee Review (FCR)

FCR takes place at a convened meeting with at least a quorum of the members present. No member may participate in the review of a protocol in which the member has a conflict of interest (e.g. personally involved in the project) except to provide information requested by the IACUC; and may not contribute to a quorum. Determination of the outcome is by a simple majority of the members present.

Designated Member Review (DMR)

For DMR to occur committee members are provided access to the protocol, and then polled to acquiesce to DMR. All members have 3 business days to respond to the request. Members who do not respond by the end of 3 business days are deemed to have acquiesced to DMR.

After the 3 business days have passed, at least one suitably qualified member is appointed by the IACUC Chair to conduct DMR.

The members assigned DMR may ask questions regarding the protocol without calling it to FCR. IACUC members that acquiesce to DMR may also submit comments for the PI to address during the review process, without calling to FCR. Any IACUC member may provide these comments during the 3 business day period.

Outcomes of protocol review.

Investigators are notified in writing of the outcome of the review of their protocols. For FCR, outcomes include:

1. approval,
2. requires modifications to secure approval,
3. withhold approval.

For DMR, outcomes include:

1. approval,
2. requires modifications to secure approval,
3. call to FCR.

If the application requires modifications to secure approval or approval is withheld, the Principal Investigator (PI) is provided with the reasons for the decisions in writing, and the opportunity to respond to the feedback.

Protocols requiring modifications to secure approval after FCR are automatically routed to DMR unless a call for FCR review of the responses is made during the meeting. The IACUC adopted an updated "SOP for Reviewing Modifications to Protocol Applications or Amendments Requested for Currently Approved Protocols after Full Committee Review" on June 24, 2014, which was then signed by all IACUC members, pursuant to NOT-OD-09-035.

Annual review of protocols

Investigators are reminded prior to annual review date to renew, amend or close the protocol. The annual review includes documenting how many animals were used during that period, the perceived pain category, and the opportunity to propose changes to previously approved activities. A list of upcoming annual reviews for the month is circulated to committee members with opportunity to call for FCR. Annual reviews are reviewed by DMR, unless the protocol is called to FCR.

Review of Significant Changes to previously approved protocols (Amendment Requests)

Requests to modify previously approved protocols are submitted electronically to the IACUC via RICRO. Such requests are handled similarly to the process for review new protocols i.e. by FCR or DMR.

Examples of significant changes include:

- a. change in PI,
- b. change in procedure resulting in greater pain/distress and invasiveness,
- c. change from non-survival to survival surgery,
- d. in housing location that is not IACUC approved,
- e. in species,
- f. in study objectives,
- g. impact personnel safety (e.g. change in biosafety level)

Review of Significant Changes to previously approved protocols that may be handled administratively

The following significant changes to the IACUC protocol may be handled administratively without review by FCR or DMR.

The Attending Veterinarian or Alternates to the AV may administratively verify changes through Veterinary Verification and Consultation (VVC). These changes include:

- a. Anesthesia, analgesia, sedation, or other clinically relevant medication that use referenced dosages for the species. Reference material may include: textbooks (such as Harkness and Wagner's Biology and Medicine of Rabbits and Rodents; Flecknell's Laboratory Animal Anesthesia; Plumb's Veterinary Drug Handbook; Hawk and Leary's Formulary for Laboratory Animals; Fowler's Zoo and Wildlife Medicine; Lumb and Jones Veterinary Anesthesia and Analgesia; Quesenberry and Carpenter's Ferrets, Rabbits and Rodents Clinical Medicine and Surgery; Fish and Danneman Anesthesia and Analgesia of Laboratory Animals); journal publications (peer reviewed from PubMed and CAB database), personal communications with veterinary anesthesiologists at CSU; LAR and CSU Formularies.
- b. Experimental substances administration that does not exceed guidelines published by Diehl et al. A good practice guide to the administration of substances and removal of blood, including routes and volumes. J App Tox. 2001; 21:15-23.
- c. Changes in experimental substances or clinical medications within a similar class of substances to the original protocol approval, for example:
 - i. Chemotherapeutics, antibiotics, hormones, vehicles, etc.
 - ii. Changes in instrumentation that do not alter the objectives of the original proposal.
 - iii. Administration of over-the-counter (OTC) products used to facilitate research may be used with veterinary approval.
 - iv. Change in the frequency or dosage of an experimental substance administration of previously approved parameters, to meet experimental goals. These changes would not result in increased pain/distress or invasiveness.
- d. Euthanasia to any method approved in the AVMA Guidelines for the Euthanasia of Animals.
- e. Change in final disposition of animal, including change from euthanasia to adoption, or transfer to another protocol. Transfer to more invasive protocols such as survival surgery or infectious disease studies require IACUC review.

- f. Duration, frequency, type (e.g. blood collection site or volumes, route of administration, volumes, and dosages) of procedures contingent upon them not exceeding IACUC guidelines.
 - i. Blood collection site or volume
 - ii. Route of administration, volumes, and dosages
 - iii. Increasing food/fluid restriction prior to a procedure to more than 12 hours with adequate justification
 - iv. Change in timing of collections, as long as there is no additional welfare concerns and other guidelines are followed.
- g. Number of procedures performed on an animal, excluding surgical procedures contingent upon them not exceeding IACUC guidelines.
 - i. This may include repeating previously approved experiment(s) on the same protocol.
- h. Additional strains or sources of animals
- i. Changes to space requirements if restriction is justified and not excessive based on veterinary consultation, including scientifically justified changes in bedding type, in order to meet the study objective.
- j. Change in diet or water composition as long as remainder of diet maintains the proper nutritional needs of the animals. Alternative feeding strategies may also be reviewed such as placing feed on the floor of the cage.

These approvals are communicated to the IACUC.

Significant change that may be handled administratively by RICRO staff:

- k. Increase in animal number:
 - i. not to exceed 20% of the original approved protocol number.
 - ii. for breeding activities, not to exceed 50% of original approved protocol number.
- l. Change in housing or procedure location within an IACUC approved facility.

These approvals are communicated to the IACUC.

Other Changes that may be administratively approved by RICRO Staff:

- m. Change in personnel (not PI),
- n. Updated contact information,
- o. Typographical errors, including but not limited to grammatical errors, change in title, language changes that do not alter the scientific objective outlined in the protocol.
- p. Change in funding information.

These approvals are communicated to the IACUC.