Protocol Review Process[1]

Investigators complete and submit their protocols (new, continuing 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. Appropriate sedatives, analgesics, or anesthetics.
5. 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.

Veterinary Clinical Trials and Clinical Research

In cooperation with the CSU IACUC, the CSU VTH Clinical Review Board assists in the review and approval process for all CSU research or teaching activities involving privately-owned animals. VTH CRB reviews the study, including review of client consent form(s), when research or teaching activities involve the use of privately-owned animals. VTH CRB review shall be conducted in accordance with the AVMA Policy on Veterinary Clinical Studies Committees (VCSC).

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, continuing review, 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 to determine whether or not to approve the protocol. 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. 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. The veterinary staff is available for consultation, if requested, prior to submission of the protocol for review.

[1] Relevant NIH OLAW Notices: NOT-OD-09-035, NOT-OD-14-126

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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. Any IACUC member may provide comments during the 3 business day period without calling to FCR, and these comments will be included in the protocol review process.

After the 3 business days have passed, at least one committee member is appointed by the IACUC Chair to conduct DMR. The DMR assignee may ask questions regarding the protocol without calling it to FCR, by submitting comments for the investigator(s) to address; however, if issues are not resolved satisfactorily, DMR assignees may call the protocol to FCR.

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.

Reviewing modifications to protocols, or amendments for currently approved protocols, after FCR, and continuing review of protocols

Protocols requiring modification to secure approval after FCR are automatically reviewed by the IACUC following the DMR process outlined above according to OLAW NOT-OD-09-035 “Guidance to IACUCs Regarding Use of Designated Member Review (DMR) for Animal Study Proposal Review Subsequent to Full Committee Review (FCR).” CSU IACUC agrees that if all members of the IACUC are not present at a meeting, the committee may use DMR after FCR according to the following stipulations:

- All IACUC members agree in advance in writing that the quorum of members present at a convened meeting may decide by unanimous vote to use DMR after FCR when modification is

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needed to secure approval. However, any IACUC member may, at any time, request to see the revised protocol and/or call the protocol to FCR.

The IACUC also conducts continuing review of each previously approved protocol at appropriate intervals as determined by the IACUC. This includes USDA-regulated protocols require continuing review no less than annually, or a complete review at least once every 3 years according to PHS Policy IV.C.1.-5. These reviews are done by DMR, as outlined above.

Continuing review includes an assessment of the animals used in the previous year of approval, the perceived pain category, any unanticipated adverse impacts of the procedures, and an opportunity to amend the protocol. Investigators are reminded when their protocol is up for continuing review or expiration.

Review of Significant Changes to previously approved protocols (Amendments)

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 (VVC Amendments)

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:

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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, or type 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 procedures, 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 guidelines stated in CSU IACUC Performance of Repeat Procedures.
    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 changes 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.
    iii. for CSU holding protocol only[2], adding animal numbers as needed.
l. Change in housing or procedure location within an IACUC approved facility.

These approvals are communicated to the IACUC.

[2] CSU holding protocol is approved for all species; amendments to add species and increase animal numbers is an administrative task to generate cage cards, facilitating tasks in the electronic systems related to animal census and management. This is based on guidance provided in Lab Animal Protocol Review Article, "Management of a holding protocol."

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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.
q. Administrative addition of animal species to CSU holding protocol only, facilitating administrative tasks related to animal census and financial transactions.

These approvals are communicated to the IACUC.

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