Animal Care and Use Protocol Review Process

112.1. Purpose:

This document provides the approved practice and procedures for review of animal care and use protocol proposal by the University of Kentucky Institutional Animal Care and Use Committee (IACUC). While the criteria that must be met before an IACUC can approve a proposed research protocol is covered under Public Health Service Policy (IV, c,1, a-IV,c,1g;IV,d1,-IV,d,1e) and the Animal Welfare Act (2.31,d; 2.31,e), the method to accomplish this is left up to each individual institution. This document serves to document the practice and processes performed at the University of Kentucky to ensure proper reviews for each type of review.

112.2 Web-based Protocol Review Process:

The University of Kentucky uses a web-based Electronic Protocol Processing System to permit the investigator to submit their protocol to the IACUC on-line. The Electronic Protocol Processing System protocol form populates sections based upon the response to early questions by the investigator and protocols only contain sections related to the actual protocol being submitted.

The University of Kentucky reviews all protocols, regardless of funding source, on an annual basis and requires a de novo review of every protocol at an interval not to exceed 3 years.

112.3 New Animal Use Protocols and 3 year de novo Protocol reviews:

The University of Kentucky IACUC uses both the Full Committee and the Designated Reviewer methods for review and approval of new Animal Care and Use Protocols and submitted 3 year de novo protocol reviews. Protocols involving unalleviated pain or distress (USDA Category E), multiple major survival surgery, the use of paralytics, or prolonged restraint are automatically assigned to Full Committee Review (FCR) for final approval. All other protocols are assigned as eligible for Designated Member Review (DMR) by the IACUC Office staff.

112.4 Designated Member Review (DMR) Process:

Protocol submissions determined to be eligible for approval by the Designated Member Review method by the IACUC Office staff are initially routed to the full IACUC. These protocols are available to all IACUC members for review and comment for a minimum of 5 business days.

The IACUC Chairperson has delegated the authority to assign the primary reviewer to the IACUC office. The veterinary reviewer role is generally assigned to the veterinarian directly overseeing the facility involved. Both the primary and veterinary reviewers may request additional reviewers be assigned by the IACUC Office staff for specific expertise or assistance.

The IACUC members review the protocol and may request clarifications, additional information, protocol changes, modifications, etc. from the investigator. After the reviewers have completed their review, the protocol is returned to the investigator by the IACUC Office staff for their responses and changes. If no IACUC member requests Full Committee Review during the period of IACUC review, the review is completed by a primary and veterinary reviewer as a Designated Member Review. Complex protocols may be exchanged between the reviewers and the investigator several times for changes and clarifications prior to approval by the Designated Reviewers.
Any Full member of the IACUC can call for a Full Committee review of any protocol submitted for Designated Review at any time during the review process. Once requested, the protocol must be approved by Full Committee review which occurs during the regular convened meeting of the IACUC (usually the third Wednesday of every month).

Any approval decision by the Designated Reviewers must be a consensus decision. If the Designated Reviewers cannot reach a consensus decision, the protocol is sent for Full Committee review.

112.5 Full Committee Review (FCR) Process:

Protocol submissions are initially routed to a primary reviewer and a veterinary reviewer by the IACUC Office staff. The primary reviewer is assigned by the IACUC Office staff while the veterinary reviewer is assigned to the veterinarian directly overseeing the facility involved. The full committee (which includes the primary and veterinary reviewers) has five business days to review, comment on, make suggestions, or ask for additional information or clarifications online.

The IACUC Office staff then routes the protocol back to the investigator with all comments for consideration, responses, and changes listed. Reminders are sent by the IACUC Office staff periodically. After responding to the written concerns, the investigator resubmits the protocol to the IACUC Office staff.

The protocol is then rerouted to the primary and veterinary reviewers for additional review and to ensure the investigator has responded to the questions, requested changes, clarifications, etc. If questions or concerns remain, the primary or veterinary reviewers may return the protocol to the investigator for additional responses, information, clarification, etc. Complex protocols may be exchanged between the reviewers and the investigator several times before the protocol is considered ready for Full Committee Review and it is placed on the meeting agenda.

At the IACUC meeting the primary reviewer presents a synopsis of the protocol along with any comments and concerns that have not been resolved as of the meeting date. The IACUC discusses the protocol and related issues during the meeting. All protocol discussions are considered potentially confidential and are considered in an executive session. The final recommendations of the IACUC are voted upon in open session.

IACUC actions include:

- Approval
• Require Clarifications/Modifications to Secure Approval – When items are pending (e.g. clarification of animal numbers, drug doses, etc.) the IACUC may, by a majority vote, require clarifications or modifications to secure approval by either mechanism (FCR or DMR). By unanimous agreement of all voting and alternate members, the Committee has adopted the practice of allowing DMR subsequent to FCR when substantive additional information is required to properly evaluate proposals and requires modification to secure approval. DMR subsequent to FCR can only occur in these situations by the unanimous vote of the members present at a properly convened meeting. Committee member signatures are on file authorizing this practice. If this method is chosen, the IACUC Chairperson and Committee generally assign the designated reviewer during the discussion of the protocol.

• Withhold Approval – The IACUC may, by a majority vote, withhold approval for a protocol. In these cases, the investigator is notified in writing of the IACUC’s decision and the reasons for such a decision. The investigator is provided the opportunity to respond to the IACUC’s decision either in person or in writing. The IACUC may reconsider its decision following the investigator’s response.

Due to the extensive pre-review process, most protocols are either approved as written or require some minor clarifications or modifications to secure approval and are assigned to designated member review for final review and approval. While the IACUC generally strives for consensus, in cases where disagreements exist the majority vote determines outcome. The IACUC decision and any requested clarifications or changes are communicated to the investigator via e-mail and the web-based Electronic Protocol Processing System.

Protocols with numerous or serious flaws requiring extensive rewriting may not be considered for review and may be deferred (tabled). Investigators are provided with a list of concerns, comments, and questions for response and guidance in resubmitting the protocol for consideration. Deferred protocols must be reviewed (FCR or DMR) before approval may be granted.

In order to facilitate protocol approval and to allow adequate time for review, it is strongly recommended that protocols submitted to the IACUC adhere to the Guidance on Protocol Submission Deadlines as posted in the IACUC webpage.

112.6 Annual Animal Use Protocol Reviews:

The University of Kentucky uses the Designated Member Review method of protocol review for annual protocol reviews. The investigator completes a short questionnaire concerning any changes in the protocol and provides a brief progress report, which is distributed for review and consideration by all IACUC members. If no IACUC member requests Full Committee Review during the period of IACUC review, the review is completed by an IACUC reviewer as a Designated Member Review.

112.7 Amendments to Animal Use Protocols:

Amendments to protocols are submitted to the IACUC Office staff. Based on the criteria listed below, amendments are classified as either minor or major (significant). Major amendments require IACUC review as detailed in PHS Policy (IV,B,7) and AWAR (2.31,c,7). Further clarification on significant changes to animal activities is delineated in NOT-OD-14-126.

Major amendments involving unalleviated pain or distress (USDA Category E), multiple major survival surgery, the use of paralytics, or prolonged restraint are assigned to Full Committee Review.
(FCR) for final approval if the protocol was not approved previously by Full Committee Review (FCR).

All other major amendments are assigned for review by the Designated Member Review method and the review completed as described in 112.4 above. If no IACUC member requests Full Committee Review of a protocol assigned for review by the Designated Member Review method during the period of IACUC review, the review is completed by an IACUC member and a veterinarian as a Designated Member Review.

Examples of other major amendments include the following:
- Change in purpose or specific aim of study
- Change of principal investigator
- Change of species
- Addition of species
- 10% or more increase in animal numbers over the number approved on the initial protocol and any subsequent committee reviewed amendments
- Addition of any procedure not previously approved.
- Unanticipated marked increase in clinical signs or proportion of animal deaths

Minor amendments are processed through the IACUC Office staff as administrative changes. Minor amendments include the following:
- Correction of typographical or grammatical errors
- Changes to contact information or training updates of the PI or study personnel
- Addition or deletion of study personnel
- Decrease in the number of animals used
- Addition or deletion of animal usage location
- Changing the title of a protocol

Veterinary Verification and Consultation (VVC) is a method for approving significant changes to a previously approved protocol. It may not be used to add a new procedure that was not previously approved on the protocol. Examples of specific significant changes that may be approved administratively after consultation with an IACUC authorized veterinarian (both full and alternate veterinarian members) include the following:
- Change in anesthesia, analgesia, sedation as listed in:
  - Non-steroidal and Opioid Analgesics for Rodents and Rabbits,
  - Recommended Anesthesia for Some Laboratory Animal Species,
  - Formulary for Laboratory Animals (current and future editions),
  - Handbook of Laboratory Animal Science (current or future editions) and other accepted published veterinary drug formularies; or experimental substance to a substance in the same category (e.g. an antineoplastic drug to another antineoplastic drug).
- Change in euthanasia to any method acceptable/acceptable with conditions in the AVMA Guidelines for the Euthanasia of Animals (current and future editions). See UK IACUC Policy 103.
- Change to the duration, frequency, type or number of procedures performed on an animal as listed in
  - DLAR Animal Health & Veterinary Information
  - DLAR Guidelines for Blood Collection in Laboratory Animals
  - Tumor Models in Rodents
  - DLAR Guidelines for Acclimation Periods for Newly Received Laboratory Animals
- Implantation of Osmotic Pumps in Rodents
- Tissue Collection (Biopsy) for Genetic Identification of Rodents (Care of Weanling Mice and Rat Pups, etc.)
- DLAR Investigator Handbook
- https://www.nc3rs.org.uk/general-principles, and other accepted published sources.

Examples include but are not limited to: sample collection intervals, peri-mortem collection of additional tissue samples while under terminal anesthesia, behavioral tests, food/water restriction, etc.

- Change of a strain generally accepted for the modeling/study of the disease/condition of interest as listed below or change of sex of the same species:
  - Rat Genome Database
  - Charles River Laboratories
  - Envigo
  - Jax Labs
  - other accepted published rodent databases

- Change (<10% increase) in animal number approved on the initial protocol and any subsequent committee reviewed amendments (see UK IACUC Policy 101 for definition of animal numbers).
- Change (reducing or eliminating) previously approved water or feed restrictions.

112.8 Administrative Cancellation of Protocols/Amendments Pending Approval:

This policy section establishes a time frame at which the IACUC will administratively inactivate a protocol or amendment application (pending approval) for failure to respond to IACUC requests for further clarification or additional information.

If the IACUC does not receive the pending items within a period of 6 months from the first IACUC communication, the protocol/amendment may be administratively cancelled.