Guiding Principle

The IACUC shall complete a review process which approves, requires modifications or withholds approval of all proposed activity involving animals. This Guiding Principle pertains to all proposed protocols and proposed significant changes related to the care and use of animals.

PHS Policy and animal welfare regulations recognize two methods of protocol review: Full Committee Review (FCR) and Designated Member Review (DMR). However, any IACUC member, at any time, for any reason can request FCR of any protocol. Protocols classified as pain category B, C or D qualify for DMR. Category E protocol requires FCR at a convened meeting.

Protocols will be posted for review via the DMR process unless one the following criteria are met:

- Death as an endpoint
- Pain Category E
- Multiple Survival Surgeries
- Involves an investigational device/medication/biologic
- Other i.e., exceptions to The Guide, protocol that any committee member marks for FCR, etc.

Significant change in protocol requests will be reviewed according to OLAW *Guidance NOT- OD-14-126*

Protocol Review

The investigator should designate the appropriate pain category to the best of their estimation by carefully examining all proposed procedures. The pain category will be assessed by the IACUC Chair or IACUC Administrator to determine the type of review, but final determination will be made by the IACUC.

All personnel proposing to use a live animal in research, teaching, testing or for related purposes must submit an IACUC protocol via the Novelution system. Submissions are reviewed by either FCR or DMR as described previously.

All protocols will be terminated at the end of their three-year approval period. If the PI intends to carry on with the project beyond this approval period, a new protocol must be submitted and approved prior to the previously approved protocol's end date.

Change in Protocol Requests

Significant changes include changes that have, or may have, a negative impact on animal welfare. In addition, some activities not having a direct impact on animal welfare are also considered significant.

Significant changes listed below will be approved by DMR unless one of the criteria for FCR are met.

- Non-survival to survival surgery;
- Resulting in greater pain, distress, or degree of invasiveness;
- Housing and / or use of animals in a location that is not part of the animal program overseen by the IACUC;
- Species change;
- Changes in study objectives;
- Principal Investigator (PI) change; and
- Any changes impacting personnel safety (e.g. change in biosafety level).

Some specific significant changes may be reviewed and approved through the Veterinary Verification and Consultation (VVC) process. These changes may be handled administratively in consultation with the AV and/or a veterinarian serving on the IACUC. The veterinarian is not conducting DMR, but is serving as a subject matter expert to verify compliance with the IACUC's reviewed and approved policies is appropriate for the animals in this circumstance. Consultation with the veterinarian must be documented. The veterinarian may refer any request to the IACUC for review for any reason and must refer any request that does not meet the parameter of the IACUC's reviewed and approved policies.

Examples of significant changes below that may be reviewed via the VVC process include:

- Anesthesia, analgesia, sedation or experimental substances may be changed in accordance with the following formularies;
    - Veterinary Drug Handbook/Plumb's Veterinary Drugs by Donald C. Plumb
    - Laboratory Animal Anesthesia by Paul Flecknell
- Euthanasia to any method approved in the AVMA Guidelines for the Euthanasia of Animals and the NDSU Euthanasia Guiding Principle;

- Duration, frequency, type, (e.g. blood collection site or volumes, route of administration, volumes, and dosages) of procedures performed on an animal;
    - Blood Collection site or volume
    - Route of administration, volumes, and dosages
- Number of procedures performed on an animal, excluding surgical procedures contingent upon them not exceeding IACUC guidelines;
- Additional strains or sources of animals; and
- An increase in the previously approved animal numbers; of less than 25% of the originally approved number of animals.

The changes below will be reviewed and approved administratively without consultations or notifications.

- Correction of typographical errors;
- Correction of grammar;
- Contact information updates;
- Change in personnel, other than the PI. (Administrative review will ensure that all such personnel are appropriately identified, adequately trained and qualified, enrolled in the Occupational Health and Safety (OHS) Program and meet any other criteria required by the IACUC.); and
- Housing changes and / or use of animals in a location that is part of the animal program overseen by the IACUC.

All proposed significant changes must be submitted to the IACUC by completing an amendment via the Novelution system. The approval of significant changes is communicated to the IACUC at the committee meetings.

Requirements

The Public Health Service (PHS) Policy in accordance with IV.C. 1-8 and the **United States Department of Agriculture AWA USDA 2.31 (d):** in order to approve proposed research projects or proposed significant changes in ongoing research projects, the IACUC shall conduct a review of those components related to the care and use of animals and determine the proposed research projects are in accordance with this policy. In making this determination, the IACUC shall confirm the research project will be conducted in accordance with the Animal Welfare Act insofar as it applied to the research project and that the research project is consistent with the Guide unless acceptable justification for a departure is presented. Further, the IACUC shall determine research projects conform to the institution's Animal Welfare Assurance and meets the requirements contained in these regulations.

Office of Laboratory Animal Welfare (OLAW) *Guidance NOT-OD-09-035 IACUC*

Actions Following Full Committee Review.

Office of Laboratory Animal Welfare (OLAW) *Guidance NOT-OD-14-126*
Significant Changes to Animal Activities.

PROCEDURE:

1. Designated Member Review (DMR)
   1.1. Each eligible protocol is distributed to the entire IACUC with specific instructions regarding the designated member review process and a deadline to call for Full Committee Review (FCR): five (5) business days. Affirmation from all IACUC members is not required.
   1.2. Under extenuation circumstances, the deadline can be reduced by the A IACUC Chair / designee to a minimum of one day with affirmation required from all members regarding their decision whether or not to call for FCR.
   1.3. Designated Member Review Assignment
      1.3.1. Category B, C and D protocols: at least two members of the IACUC are assigned by the chair.
      1.3.2. Category E protocols: at least four members, which include a veterinarian and a subject matter expert, are assigned by the chair.
   1.4. Any member of the IACUC can make the decision to send the protocol for FCR at any time during the review period. If no member refers the protocol to full committee review during the review period, the assigned DRs have the authority to approve, require modifications in to secure approval, or request full committee review.
   1.5. The DR decisions must be unanimous; if not, the protocol will be referred for FCR. The DRs to not have the power to withhold approval.
   1.6. The IACUC consent agenda contains notification of all actions approved by DMR.
2. Veterinary Verification and Consultation (VVC)
   2.1. The amendment is routed to the Attending Veterinarian and / or designee.
   2.2. The AV or designee makes a determination on the change request of refers it to DMR or FCR.
3. Administrative Review
   3.1. The amendment is reviewed by IACUC Office personnel.
   3.2. IACUC office personnel makes a determination or refers the change request to DMR or FCR.
4. Full Committee Review (FCR)
   4.1. Full committee review of protocols requires a quorum be present at a convened meeting. To receive approval, the protocol must receive the approval of the majority of members present.
   4.2. Protocols scheduled for full IACUC review are distributed to all committee members at least one week prior to the meeting. The IACUC meets once per month with additional meetings convened when necessary to address extenuating circumstances.

4.3. The IACUC chair, or his / her designee, assigns at least two members to serve as technical reviewers. The technical reviewers present their findings to other committee members at a properly convened IACUC meeting for discussion.
4.4. When it is determined consultants or experts are required to advise the IACUC in its review of a protocol, the protocol shall also be distributed to the consultants or experts prior to the meeting, and if necessary, the consultant or expert may be invited to the full committee meeting. Consultants may not approve or withhold approval of any activity or vote with the IACUC.
4.5. No member may participate in the IACUC review or approval of a protocol I which they have a conflicting interest (e.g. is personally involved in the project), except to provide information requested by the IACUC. Nor may a member with conflicting interest contribute to the constitution of a quorum. AT the beginning of each meeting the IACUC Chair reminds members and investigators to declare any conflicting interest not previously disclosed.

5. IACUC Actions Following Full Committee Review
5.1. Following review of the protocol, a motion is made and vote taken to either: 1) approve, 2) require modifications or 3) withhold approval
5.2. If the motion is to require modifications, the motion must include how those modifications will be reviewed: 1) designated member reviewers assigned or 2) FCR. When the motion is to review the modifications by DMR, the vote must be unanimous. Reviewers are then assigned by the IACUC Chair. All members of the IACUC have access to amendment protocols via the Novelution system and may request FCR at that time. Providing there are no requests for FCR, the assigned designated reviewers are authorized to approve or require further modification to secure approval. Their decision must be unanimous.

6. Notification Following Review
6.1. Investigators are notified via the Novelution system of the committee's decision to approve, require modifications, or withhold approval of proposed activities as set forth in the PHS Policy IV.C.4. The IACUC procedures to notify investigators and the institution of its decisions regarding the protocol review are as follows:
6.1.1. Investigators shall be notified via notification by the Novelution system of the IACUC's determination of the protocol (approval, require modification(s), or withhold approval). When modifications are required, the investigator must revise the protocol and / or respond to conditions set by the IACUC.
6.1.1.1. Investigators have 60 days after notification to address the required modifications. After 60 days, the protocol or amendment will be withdrawn from the review process.
6.1.1.1.1. Protocols or amendments withdrawn from the review process will need to be resubmitted. The review timeline starts over.
6.1.2. The IACUC Chair and / or designee shall provide the investigator with reasons through the Novelution system for the IACUC's decision to withhold approval of a protocol and shall provide an opportunity for the investigator to respond and appeal.
6.1.2.1. The investigator may appeal a determination of the IACUC only if new information becomes available, or evidence is provided the IACUC has failed to

follow their own procedures, or incorrectly applied federal regulations, state law, or NDSU's policy. A written appeal citing specific regulations, NDSU policy or procedure may be made to the IACUC office or the Institutional Official (IO) within ten (10) business days after receipt of communication from the IACUC. The IACUC chair or chair's designee makes an initial assessment and forwards the appeal to the IACUC for consideration at the next convened meeting. The board's determination is considered final, and communicated in writing to the investigator.

6.1.2.2. In addition to the written appeal, investigators are provided an opportunity to appear, in person, before a full convened quorum of the IACUC.

6.2. Applications and proposals approved by the IACUC may be subject to further review by officials of the institution who can overturn an IACUC approval. However, those officials may not approve those sections of an application or proposal related to the care and use of animals if they have not been approved by the IACUC.

6.3. A copy of IACUC meeting minutes, which record all decisions regarding protocol review and activities, is available to the IO.