Guiding Principle

The IACUC shall review and approve, require modifications in (to secure approval), or withhold approval of activities related to the care and use of animals. This Guiding Principle pertains to all protocols, proposed significant changes, annual updates, and re-reviews of approved protocols related to the care and use of animals.

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

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

Protocol Review

The investigator should carefully examine all procedures to be applied to animals and determine his or her best estimation of the level of pain, discomfort, and distress and designate the appropriate pain category. 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 following review.

All personnel proposing to use a live animal in research, teaching, testing or for related purposes must submit a completed IACUC Application form to the IACUC Office. Submissions are reviewed by either FCR or DMR as described previously.

Change in Protocol Requests
Significant changes include changes that have, or may have, a negative impact on animal welfare. In addition some activities that may not have a direct impact on animal welfare are also considered to be significant.

Significant changes listed below must be approved by DMR (Category B or C) or FCR (Category D or E).

- From non-survival to survival surgery;
- Resulting in greater pain, distress, or degree of invasiveness;
- In housing and or use of animals in a location that is not part of the animal program overseen by the IACUC;
- In species;
- In study objectives;
- In Principal Investigator (PI); and
- That impact 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 that compliance with the IACUC–reviewed and –approved policy 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–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
• In housing 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 and submitting the Request for Change Form.

The approval of significant changes are communicated to the IACUC at the IACUC meetings.

Annual Update Requirement

The IACUC will conduct continuing reviews of protocols which are USDA regulated on an annual basis. USDA regulated protocols involve animals such as dog, cat, monkey (nonhuman primate mammal), guinea pig, hamster, rabbit, or such other warm-blooded animal (including wild or exotic species) being used for research, teaching, or testing.

USDA excludes (1) birds, fish, reptiles, rats of the genus Rattus, and mice of the genus Mus, bred for use in research, (2) horses not used for research purposes, and (3) other farm animals, such as but not limited to livestock or poultry, used or intended for use as food or fiber, or livestock or poultry, used or intended for use for improving animal nutrition, breeding, management or production efficiency, or for improving the quality of food or fiber.

USDA also excludes animals used in clinical trials in the context of a veterinary client relationship and animals used in a field study. USDA defines a field study as a study conducted on free-living wild animals in their natural habitat. However, this term excludes any study that involves an invasive procedure, harms, or materially alters the behavior of an animal under study.

Annual updates are reviewed administratively by the IACUC Chair and Attending Veterinarian. A list of annual updates is provided to the IACUC on a monthly basis.
The IACUC will conduct 3 year de novo reviews of non-USDA regulated protocols.

Three-year de novo reviews will be reviewed via the DMR or FCR based on the pain category.

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 that the proposed research projects are in accordance with this policy. In making this determination, the IACUC shall confirm that 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 that the research project conforms to the institutions Animal Welfare Assurance and meets the requirements contained in these regulations.

**USDA Animal Care Animal Welfare Act and Animal Welfare Regulations, 2017 2.31 (d)(5)** The IACUC shall conduct continuing reviews of activities covered by this subchapter at appropriate intervals as determined by the IACUC, but not less than annually.

**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:**

1.0 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 FCR which is 5 business days. Affirmation from all IACUC members is not required.

1.2 Under extenuating circumstances, the deadline can be reduced by the 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 At least two members of the IACUC are assigned by the chair as the designated reviewers (DR) who are qualified to conduct the review. The DR decisions must be unanimous; if not, the protocol will be referred for FCR.
1.4 Any member of the IACUC can make the decision to send the protocol for FCR at any time during the set deadline period. If no member of the IACUC refers the protocol to full committee review at a convened meeting, at the end of the set deadline period the assigned IACUC DRs have the authority to approve, require modifications in (to secure approval) or request full committee review.

1.5 The DRs do not have the power to withhold approval.

1.6 The IACUC minutes contain notification of all actions approved by DMR.

2.0 Veterinary Verification and Consultation (VVC)

2.1 The Request for Change form will be forwarded to the Attending Veterinarian and/or Designee.

2.2 The AV or Designee will make a determination on the change request or refer the change request to DMR or FCR.

3.0 Administrative Review

3.1 The Request for Change form will be reviewed by IACUC Office personnel.

3.2 IACUC Office personnel will make a determination or refer the change request to DMR or FCR.

4.0 Full Committee Review (FCR)

4.1 Full committee review of protocols requires a convened meeting of a quorum of the IACUC members. For a protocol to be approved, it must receive the approval of the majority of those members present at the convened meeting.

4.2 Protocols scheduled for full IACUC review are distributed to all members of the IACUC at least one week prior to the meeting. The IACUC meets once per month with additional meetings to address extenuating circumstances convened when necessary.

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 member of the committee at a properly convened IACUC meeting for discussion.

4.4 When it is determined that consultants or experts will be 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 in which the member has a conflicting interest (e.g. is personally involved in the project) except to provide information requested by the IACUC; nor may a member who has a conflicting interest contribute to the constitution of a quorum. At the beginning of each meeting the Chair of the IACUC reminds investigators to declare any conflicting interest not previously disclosed.
5.0 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 modification to secure approval, or 3) withhold approval.

5.2 If the motion is to require modifications (to secure approval), 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 will be provided with an electronic copy of the revised protocol and may request FCR of the revised protocol at that time. Providing no one requests FCR, the assigned designated reviewers are authorized to approve or require further modification to secure approval and their decision must be unanimous.

6.0 Notification Following Review

6.1 The IACUC Office will notify investigators in writing of its decision to approve or withhold approval of those activities related to the care and use of animals, or of modifications required to secure IACUC approval 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 The IACUC Chair or his/her designee shall notify the investigator in writing of the IACUC’s decision to approve the protocol, require modification in (to secure approval), or withhold approval (disapproval). In order to secure approval the investigator must revise the IACUC application and/or respond to other conditions set by the IACUC.

6.1.2 The IACUC Chair and/or designee shall provide the investigator with reasons, in writing, 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 All appeals are required to be in writing and must be submitted within 2 weeks.

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 that have been 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.