IACUC REVIEW AND APPROVAL PRACTICES
(AMENDMENTS TO APPROVED PROTOCOLS)

PERFORMANCE STANDARD: All protocols are to be amended accurately, in a timely fashion, and in compliance with federal regulations, Public Health Service (PHS) policy, and accreditation expectations. No animal will be used, or numbers or procedural changes performed until approved by the Institutional Animal Care & Use Committee (IACUC) and a notice of the approval is received by the PI.

BACKGROUND: According to the 9th CFR (USDA regulations) and the Public Health Service Policy, the IACUC shall “review and approve, require modifications in (to secure approval), or withhold approval of proposed significant changes regarding the care and use of animals in ongoing activities.” According to PHS ‘NOT-OD-14-126,’ institutions may establish and IACUCs may approve policies for conduct of animal activities. The institution is charged with developing the approval mechanisms, within the context of USDA and PHS boundaries. An efficient procedure is necessary to facilitate research progress and outcome success. The goal of this policy is to establish a clear, appropriate review process that is within the context of the regulatory requirements, is responsive to the needs of the research community, and serves to efficiently utilize institutional resources and skills.

DEFINITIONS:

- **Amendment:** A proposed change to a currently approved animal use protocol. The proposed change must fit with the objectives, purpose, or aims stated in the original protocol to qualify for the status of ‘amendment.’ Proposals not qualifying as an ‘amendment’ will require submission of a new protocol.

- **Designated Member Review (DMR):** A process of ‘extra-IACUC approval’ that includes advisement of IACUC members prior to approval of the proposed activities to allow any member the opportunity to call for full-committee review, if desired. The DMR process immediately ceases if any member requests full committee review, at which time the proposal is placed on the agenda of the next full committee meeting. If no member calls for full committee review, then the IACUC Chairperson may appoint one or more appropriately qualified IACUC members to serve as the designated reviewer(s). Designated member review may result in approval, a requirement for modifications (to secure approval), or referral to the full committee for review. Designated review may not result in withholding of approval. If a protocol is assigned more than one designated reviewer, the reviewers must be unanimous in any decision. They must all review identical versions of the protocol and if modifications are
requested by any one of the reviewers then the other reviewers must be aware of and agree to the modifications. Generally, this process style is used for: a) review post-IACUC meeting; or b) the Significant Change Subcommittee (SCSC) activity.

- **IACUC Leadership Review (ILR):** A process of 'extra-IACUC approval' (an administrative review process) that applies to modifications of an approved activity that are not classified as significant (e.g. minor amendments), and that occurs in-between the regularly scheduled IACUC meetings. The IACUC Chair may appoint one or more appropriately qualified IACUC members to serve as the ILR. The ILR may result in approval, a requirement for modifications (to secure approval), or referral to the IACUC (either SCSC or full committee) for review. The ILR may not result in withholding of approval. If a proposed amendment is assigned more than one ILR, then the reviewers must be unanimous in any decision for approval (and difference in outcome position will result in an immediate forward to the full committee). The ILRs must review identical versions of the proposed amendment and if modifications are requested by any one of the reviewers then the other reviewers must be aware of and agree to the modifications. The IACUC has approved the use of this process. This process style is used for:
  - Proposed minor amendments;
  - Proposed minor amendments that require veterinary review prior to approval.

- **Significant Change:** Changes that have, or have the potential to have, a negative impact on animal welfare. Additional activities that may not have a direct impact on animal welfare may also be considered significant. Significant Change actions are described as Category III and IV changes. (NOT-OD-14-126)

- **Veterinary review:** Review by a veterinarian authorized by the IACUC to meet the intent of this policy as described and outlined in NOT-OD-14-126. For the purposes of the Policy, the veterinary reviewer is an OAWA veterinarian, DLAR veterinarian, or DLC veterinarian. (NOT-OD-14-126)

- **Administrative review:** For the purposes of the Policy, the administrative review is an OAWA staff review or ILR review. (NOT-OD-14-126)

- **Administrative handling:** Authority for approval of modifications of an approved activity that lies outside of the IACUC. Administrative review and action would fit this definition. (NOT-OD-14-126)
ROLES:
1. The Principal Investigator will submit an amendment request to iacuc@duke.edu, using a form available on the web site.
2. The OAWA Protocol Specialist will receive the amendment, process according to this policy, and coordinate review / approval of the request.
3. The IACUC shall periodically review this policy and re-affirm its position regarding categories, processing, and outcomes.

OUTLINE OF POLICY:
1. Amendments to approved animal care and use activities are classified into four categories. The categories are based upon the perception of risk to the welfare and wellbeing of the animal as pre-determined by the IACUC. Categories are processed according to IACUC-approved practices as defined below:

   a. **Category I: Significant Changes reviewed by the Full Committee Review process.** These proposals have been determined by the IACUC to be sufficiently serious to require documented deliberation of the full committee. While any style of proposed change may be reviewed by this process (e.g. if called by a member for FCR), the more common example includes:
      i. Request for ABSL-2 or greater PI-Managed Housing (housing for greater than 12 hours in a non-DLAR facility). A Section T of the protocol template must be submitted for review with the amendment.

   b. **Category II: Significant Changes reviewed by the SCSC or by Full Committee Review.** These categories of proposals have been determined by the IACUC to be less serious and generally not requiring of Full Committee Review. These proposals may be reviewed as a Category I proposal (if determined by the IACUC leadership or requested by an IACUC member). This method meets the criteria of Designated Member Review as described in NOT-OD-14-126. Examples of proposals that qualify for this Category II process include:
      i. Addition of a new species.
      ii. Increase in non-USDA species numbers > 20% of the approved animal numbers. Note: Any increase in animal numbers requires IACUC approval, by one of the four processes, prior to ordering or use.
iii. Any increase in numbers of USDA-regulated species. Note: Special species (i.e., primates, dogs, cats, and swine) will be approved by the FCR process.

iv. A procedure which results in greater pain, distress, or degree of invasiveness and might be evidenced as a:
   1. Change of a non-survival to survival surgery.
   2. Change in anesthetic drug regimens which increase the potential for pain or distress.
   3. Change in analgesic drug regimens which increase the potential for pain or distress.
   4. Change in humane endpoints which increase the potential for pain or distress.
   5. Increase in overall invasiveness of a procedure.
   6. Increase in proportion of expected animal deaths.
   7. Increase in the duration of pain, discomfort, or distress to an animal.

v. Addition of hazardous agents (as defined by OESO) being administered to animals.

vi. A change in the Principal Investigator (PI).

vii. Addition of neuromuscular blocking agents.

viii. A request for ABSL-1 PI-managed housing (Housing for greater than 12 hours in a non-DLAR facility). Complete Section T (PI-Managed Housing) of the protocol template for review with the amendment. Proposals destined for the SCSC process are provided to IACUC member prior to performing the SCSC activity (to allow IACUC members an opportunity to call for Full Committee Review). SCSC-approved activities are reported to the Full Committee as part of the business items report and may be called up for further review by member of the IACUC.
ix. Exemptions to The Guide or other regulatory guidance or institutional policy. A completed Section U (Exemption) of the protocol template is required for this style of amendment. Such requests are discussed by the SCSC but must be approved by the FCR process. (NOTE: Section U associated with an Annual Progress Report will stay with that processing activity.)

x. A change in the study objectives.

c. **Category III: Minor Amendments reviewed by the ILR process that incorporates a veterinary review.** These categories of proposals have been determined by the IACUC of having a potential welfare \ well-being impact, but generally the outcome is more favorable and in the best interest of the animal. These proposals may be reviewed as a Category II proposal, if determined by the IACUC leadership or veterinary review; or Category I if requested by an IACUC member. This method meets the criteria of administrative handling and veterinary review as described in NOT-OD-14-126. Examples of proposals which qualify for this Category III process include:

i. A change in anesthetic drug regimens which decreases the potential for pain or distress; or due to unavailability of protocol-approved medications; or change from pharmaceutical grade to non-pharmaceutical grade compounds.

ii. A change in analgesic drug regimens which decreases the potential for pain or distress; or due to unavailability of protocol-approved medications, a change from pharmaceutical grade to non-pharmaceutical grade compounds.

iii. A change in sedation drug regimens which decreases the potential for pain or distress; or due to unavailability of protocol-approved medications, a change from pharmaceutical grade to non-pharmaceutical grade compounds.

iv. A change in humane endpoints which decreases the potential for pain or distress.
v. Addition of a procedure which should decrease the proportion of adverse outcomes (e.g. post-procedure death, distress, or pain).

vi. A change in animal care and / or monitoring practices which increase the frequency or methodology of monitoring.

vii. Addition of sample collection (as long as sample collection volumes do not exceed IACUC-accepted standards for the period of collection, such as the 24 hour maximum for blood collection from mice).

viii. Repetition of an already approved experiment (where no additional animals are required) to re-affirm or replace questionable data.

ix. Addition of noninvasive sampling/analysis (e.g., MRI, motion sensor, etc.).

x. A change or addition of euthanasia procedures that is/are approved in the AVMA Guidelines for the Euthanasia of Animals and Duke’s species-appropriate policy on euthanasia.

xi. A request for delayed weaning (generally rodents) as described in the Cage Space Requirements for Mice Policy or the Policy for Enrichment for Species Other Than Non-Human Primates.

xii. A request for single housing for animal welfare purposes (e.g., aggressive male rodents) as described the Cage Space Requirements for Mice Policy or the Policy for Enrichment for Species Other Than Non-Human Primates.

xiii. Addition of a non-hazardous experimental substance.

d. Category IV: Minor Amendments reviewed by the ILR (not requiring a veterinary review). These categories of proposals have been determined by the IACUC as having no direct animal welfare \ well-being impact). These proposals may be reviewed as a Category III, II or I proposal, if determined by the IACUC leadership,
or Category I requested by an IACUC member. This method meets the criteria of administrative handling as described in NOT-OD-14-126. Examples of proposals which qualify for this Category IV process include:

i. A transfer of animals to another protocol where animals (same stock / strain) already approved on that study.

ii. Addition or deletion of personnel to an active approved protocol.

iii. Adding or changing the site of animal procedures (less than 12 hours)

iv. A change in or addition of euthanasia procedures to an AVMA ‘Approved Method’ (AVMA Guidelines).

v. An increase in non-USDA species numbers < 20% of the approved animal numbers of species.

vi. A change of controlled substance sourcing for the protocol activities.

   Note 1: Any increase in numbers of USDA-regulated species is considered Category II. Note: Special species (e.g., primates, dogs, cats, and swine) will be approved by the FCR process.

   Note 2: The ILR may bring to the IACUC any extraordinary numbers requested; even though the number requested may be less than 20%.

vii. Addition of another strain/stock of the same animal species.

viii. Addition of a location for PI-managed housing if an approved Section T is already in place in the protocol (Step 1: Scientific Justification has already been approved). The amendment will be processed according to Step 2 of the Policy on PI Managed Housing Facilities detailing facility inspection of the new area.
e. **Category V: Administrative Reviews by OAWA Staff.** The following changes can be administratively reviewed and handled by OAWA staff.

   i. Correction of typographical errors
   
   ii. Correction of grammar
   
   iii. Contact information updates
   
   iv. Addition of supporting protocol information (e.g., controlled substance source)
   
   v. Removal of personnel from protocol

2. Use of fewer animals than approved does not require IACUC approval, notification, consultation, or administrative handling.

3. Classification of proposed amendments that are not described herein will be determined as either significant or minor as defined by the IACUC Chair or designee.

4. Review processes:

   a. **Category I:** Significant Changes Requiring Full Committee review according to standing procedures of the monthly IACUC meeting. These amendments should first be reviewed through SCSC or be assigned to an OAWA veterinary pre-reviewer and IACUC primary reviewer prior to the monthly IACUC meeting.

   b. **Category II:** Significant Changes reviewed by the SCSC. These changes are covered by the Policy on IACUC Review and Approval Practices – Significant Changes.

   c. **Category III:** Minor Changes with Veterinary Review. This style of amendment requires a Duke Veterinarian (not necessarily an IACUC member) to review the requested change from a veterinary care/use perspective. This veterinary review is to assist the ILR with identifying concerns with veterinary-specific issues (e.g. anesthesia, analgesia, pain management, etc.). Generally, the IACUC Chair, IACUC Vice Chair, the Director, OAWA, or the Associate Director, OAWA will serve as the ILR. The veterinarian providing the veterinary review/clearance shall not also function as the ILR of the amendment. The approval of the amendment is immediate, with the
signature of the ILR. The PI will be notified of the approval and a copy of the approved amendment will be maintained in their IACUC master protocol file. All approvals via the ILR method will be reported to the IACUC at the next scheduled meeting. Any approved activity may be called for re-consideration by the IACUC if any member determines that such a review of an approved amendment is necessary.

d. **Category IV:** Minor Changes. This style of amendment may be approved by the IACUC Chairperson or IACUC member designee in an ILR procedure. The approval of the amendment is immediate, with the signature of the ILR. The PI will be notified of the approval and a copy of the approved amendment will be maintained in their IACUC master protocol file. All approvals will be reported to the IACUC at the next scheduled meeting. Any approved activity may be called for re-consideration by the IACUC if any member determines that such a review is necessary.

e. **Category V:** Administratively reviewed by OAWA.