Duke University & Duke University Medical Center
Animal Care & Use Program
Policy

PROTOCOL MANAGEMENT
(NEW PROTOCOLS, DE NOVO PROTOCOLS, AND ANNUAL PROGRESS REPORTS)

PERFORMANCE STANDARD: All animal use protocols are within federal guidelines and meet all institutional expectations.

BACKGROUND: The IACUC has the responsibility to assure that all animal use activity meets federal law mandates, Public Health Service policy, and accreditation expectations. The funding agencies will hold the institution and the researcher accountable that all animal procedures are performed in accordance with the rules and stipulations of the granting agency. This means that in some cases, the granting agency may require advisement and/or approval of proposed animal activities. This policy specifically addresses the requirements of the funding agencies in a manner that assures Duke researchers are fully compliant with granting agency stipulations.

ROLES:
1. Researcher: The investigator should work with the IACUC to assure that current protocols remain within the approved ‘life span.’
2. IACUC: The IACUC should provide sufficient time to allow for renewal applications and/or responses to clarifications of IACUC concerns required for approval.

PROTECTION POSTURES REQUIRED: None

POLICY:

1. New Protocols & De Novo Reviews (also called 3-year Re-Writes):
   a. Federal regulations do not permit protocols to extend beyond 3 years, more precisely 1095 days (which is 35 ½ months).
   b. Protocols must be reviewed and approved by a called meeting of the IACUC, which must fit within the approval window, or work must not be charged to federally funded grants. Animal experimentation cannot continue without an approved IACUC protocol.
   c. Therefore, the Duke IACUC has established a protocol life span of 1088 days to assure all protocols fall within the window for a regularly scheduled IACUC meeting by the 35th month of the lifespan. The one week difference between NIH authority and Duke policy is necessary to allow sufficient time to address any remaining outstanding issues of protocols that are approaching the NIH mandates termination date.
   d. The start of the protocol clock is the date of the IACUC meeting where the protocol was first considered.
e. At thirty-two (32) months into the life of the protocol, the OAWA will send a *Renewal Notice* to the Principal Investigator advising them of the need for a renewal protocol and requesting that the renewal be submitted, so that it can be reviewed during a regularly scheduled IACUC meeting in the 34th or 35th month of the protocol.

f. Immediately following the IACUC meeting on the 35th month, if the new protocol remains unapproved, the OAWA will advise the Principal Investigator that prior to the final date of the protocol (generally in 2 – 3 weeks after the 35th month meeting), one of the following actions must be performed:
   i. Use all of the remaining animals on this protocol; or
   ii. Initiate transfer of all remaining animals on this protocol to another of the PI’s currently approved protocols; or
   iii. Initiate DLAR transfer of all remaining animals on this protocol to the DLAR Holding Protocol. **NOTE:** During this period the PI remains responsible for the cost of per diem and all other animal care charges while animals on the DLAR Holding Protocol. *No experimentation or animal use activities are allowed* while animals are assigned to the DLAR holding protocol; or
   iv. Euthanize all remaining animals.

g. If none of these actions are selected prior to the final date of the protocol, the IACUC has standing instructions to DLAR to transfer of any remaining animals to the DLAR Holding Protocol. See the policy on the USE OF THE DLAR HOLDING PROTOCOL for additional information.

2. **Blanket Protocols:**

   a. In certain circumstances, the animal program will create a ‘Blanket Protocol’ to use as an instrument to gather specified items under a single umbrella. As example, training grants do not have animal procedures listed, but the grants management system requires an animal protocol number to clear the training grant. The blanket protocol will list the animal protocols which the trainees are anticipating work effort.

   b. Blanket protocols are approved with an expiration date of the last day of the 12th month from the approval date. For example: A Blanket Protocol approved on March 25, 2012 would expire on March 31, 2013.

   c. **Blanket Protocol Amendments:** Since blanket protocols are umbrella protocols for already approved protocols and have no direct implication on animal care, use, or welfare, any amendment to a blanket protocol would be considered a minor amendment, including PI change. For example, the addition of another approved protocol to the blanket protocol list of approved protocols; or change of one approved protocol for a second approved protocol.

3. **Pre-Approval (Clearance Signatures):**

   a. The IACUC will review animal use applications without consideration of the status of MOU, OESO or EOHW reviews, final approval of the Medical Center Transport Sub-
Committee, or signatures from DLAR, VAMC, DLC, CCIF, Principal Investigator, or Co-Investigator.

b. If the animal use concerns are resolved, the IACUC will ‘APPROVE’ the proposed application for animal use.

c. The ‘APPROVAL DATE’ will be the date of IACUC action without regard to the state of MOU, OESO or EOHW clearance. The 3-year life of the protocol will begin with the date of IACUC meeting at which the protocol was first reviewed.

d. The IACUC assigns to OAWA the administrative responsibility for assuring clearance of all applicable agencies.

4. Management of IACUC-Approved but not Cleared Protocols:

a. In the case where the protocol has received IACUC approval, but requires additional ‘clearances,’ the OAWA (under IACUC direction) will delay issuing the ‘IACUC Approval Letter’ to the Principal Investigator until receiving clearance from all of the aforementioned activities. The OAWA will not enter an ‘APPROVED’ status in the animal ordering software (GRANITE) until receiving ‘clearance’ from all of the aforementioned activities.

b. The OAWA may (if requested by the PI) provide a ‘Grant Certification Letter’ to the appropriate funding agency to facilitate the needs of the Principal Investigator and the funding agency regarding grant status activities or non-animal funds. However, animals may not be purchased nor may animal monies be expended in animal-based activities until the IACUC Approval Letter has been published by OAWA.

c. The date of approval will be the date the IACUC originally approved the protocol, not the date at which clearance was obtained.

d. Closing an IACUC-approved but not cleared protocol: In those few cases where the PI either hasn’t or can’t clear the protocol with one of the ancillary activities (OESO, EOHW, MOU, etc.), the OAWA shall wait for 60 days from the initial review date, and at that time may return the protocol to the IACUC for reconsideration of its prior decision. The IACUC can close the protocol without engaging the federally required reporting for a suspended protocol (Note: This action is not suspending an approved activity, but rather closing an approved activity due to an inability to obtain necessary clearances to permit performance of the activity which had never began). Exceptions can be granted by OAWA or ILR based on communication with the PI on the circumstances of delay.

5. Administrative Termination of a Proposed Animal Activity (before protocol is approved): The process for PI notification of administrative applications for animal use is as follows, counting from the day the IACUC [either full Committee or Sub Committee] meets as day 0:

a. Day 0 - 7: OAWA staff will provide IACUC communication to Principal Investigator detailing the requirements for approval, including specific IACUC clarifications, required training, and requirement for OESO / EOHW clearance. Email is preferred and should
have a Return Receipt to assure receipt by the PI. If there is no Email address, then a FAX or hard copy mailed letter may be used.

b. Day 25-50: If no response from the PI is received by this milestone, then the OAWA staff will send correspondence to the PI requesting a response to the IACUC’s previous correspondence. Email will be used.

c. Day 50-55: If no response from the PI is received by this milestone, then the:
   i. OAWA Protocol Specialist will send correspondence to the PI requesting a response to the IACUC’s previous correspondence. Email will be used.
   ii. OAWA Protocol Specialist will also place a phone call to the PI, and if the PI is not available, a message will be left on the voice messaging system.

d. Day 60: If no response by the PI is received by this milestone, then the OAWA staff member is authorized to administratively terminate the application. Exceptions can be granted by OAWA or IACUC leadership based on communication with the PI regarding the circumstances for the delayed response.

e. Day 60+: OAWA will send an Email to the PI advising them of the action and advising them that a new protocol / amendment must be submitted to the IACUC if they wish to pursue this proposed activity.

6. Annual Progress Reviews:

a. Duke uses the Annual Progress Report as one means to provide ‘on-going oversight’ of all IACUC approved activities. USDA regulations require an annual review of on-going activities of all USDA-covered species. Duke’s Assurance Statement on file with the NIH confirms that Duke will apply these standards to all animals covered under the Duke Animal Care & Use Program. The review and approval of the Annual Progress Report is a DMR-styled approval process for continuation approval of the previously approved work, for another year.

b. The Annual Protocol Period: The annual period on which Annual Progress Reports are based is from the month of IACUC approval, with annual approval required on or before the IACUC meeting of the same month. For example, the IACUC reviewed and approved the protocol on 23 June. The annual approval period ends after the June IACUC meeting of the following June (which may or may not be exactly the 23rd of June).

c. Process for review and approval: At ten (10) months into each year of the approved protocol, the OAWA will send a notice to the Principal Investigator advising them to submit the Annual Progress Report (APR) within the next 30 days. The notice will include the web link for the Annual Progress Report (http://vetmed.duhs.duke.edu/PDF/Forms%20&%20Reports/Protocol/annual_progress_report.pdf)

d. Receipt and initial review actions: The OAWA Staff will process the received Annual Progress Reports upon arrival and place a copy in the Chair’s document processing folder. See the attached processing flow chart for details.
e. **ILR Clearance and Approval**: The IACUC Chair (or designee) will review the *Annual Progress Report*. When all issues have been resolved, the IACUC Chair (or designee) will ‘clear’ the *Annual Progress Report*, in preparation of an ILR approval in the 12th month. The review and clearance may occur at any time up to and during the 12th month, may be separate, or may be congruent events; but the ILR approval date will be the IACUC meeting date in the 12th month. The approved *Annual Progress Report* shall be dated the same month in which the Annual Progress Report is placed on the agenda for advisement of the Committee (It is preferred and planned that this is the 12th month). The goal is to maintain *Annual Progress Reports* on the same 12 month cycle. The approved APR grants authority to continue the approved work for one more year.

f. **Disposition of Annual Progress Reports**:
   
i. **For Annual Progress Reports which are cleared prior to the 12th month IACUC meeting**: While the APR may be ‘cleared’ prior to the 12th month, the actual ILR approval will occur as of the date of the 12th month IACUC meeting, unless objections are raised by IACUC members and alternative actions are taken at the meeting. IACUC members are notified in the monthly ‘Whalemail’ of APRs posted for consideration.
   
   ii. **For Annual Progress Reports which could be cleared prior to the 12th month IACUC meeting, but have outstanding items Administrative in nature**: APRs may be cleared and ILR approved with non-welfare/well-being items, such as select outstanding administrative items (e.g. Adverse Event Reports, MOUs, select recurrent OESO training). The ILR will notify the OAWA of delays or incompletions. The OAWA will monitor / provide assistance to the PI in hopes of resolving the concern. Outstanding items (e.g. Administrative items not cleared) remaining at 60 days post-approval shall be returned to the IACUC for deliberation and disposition.
   
   iii. **For Annual Progress Reports which are not cleared prior to the 12th month IACUC meeting, and have outstanding Animal Welfare / Well-being items**: If an Annual Progress Reports contains animal welfare/well-being items (e.g. absence of animal numbers, adverse event reports, critical safety training/audits, skills/husbandry training) which are not resolved by the date of the IACUC meeting, the protocol is not renewed and is considered closed (the APR process is an annual approval process).
      
      a. A new protocol must be submitted prior to continuing any animal related activities.
      
      b. Animals remaining on the closed protocol will be transferred to another active protocol or moved to the DLAR Holding protocol.
   
   iv. **For Annual Progress Reports not cleared due to PI non-responsiveness by the 12th month**: When the PI has been non-responsive by the 12th month IACUC meeting date (e.g. the PI failed to provide the APR, the APR was insufficiently completed, or there was insufficient responsiveness regarding requested clarifications), the protocol is not renewed and is considered closed (the APR process is an annual approval process).
      
      a. A new protocol must be submitted prior to continuing any animal related activities.
b. Animals remaining on the closed protocol will be transferred to another active protocol or moved to the DLAR Holding protocol.

The OAWA will notify the principal investigator of the anticipated action prior to the IACUC meeting on the 12th month and as soon as practical after the 12th month IACUC meeting noting that the protocol is closed and no further work can be performed.

The OAWA memorandum will cover the following:

a. Animal Welfare Act and Animal Welfare Regulations state that animal use activities must be reviewed annually (Duke uses an annual re-approval process). Any Annual Progress Reports that are not cleared on or prior to the meeting on the 12th month are considered closed (e.g. failure to obtain a re-approval). A new protocol will need to be submitted to perform animal activities described on the closed protocol.

b. All protocol activity must cease the day after the 12th month IACUC meeting, and:
   1. Animals will be transferred to the DLAR holding protocol.
   2. Only DLAR personnel may handle animals for routine husbandry. Feeding and sanitation will be performed only by DLAR.
   3. No experimental procedures or additional breeding are authorized.
   4. Environmental enrichment will be provided to all animals.
   5. No federal funding can be used to support animal activities.

Note: See the Policy on Use of DLAR Holding Protocol for additional details. DLAR will monitor use of such animals and report violations to the IACUC.

g. The start of the Annual Progress Report clock is the date of the IACUC Meeting where the Protocol was first considered. The review of the Annual Progress Report for subsequent years will occur during months 12, 24, and 35.

h. Collaborating institutions: Duke preferentially collaborates with AAALAC accredited, PHS Assured and/or USDA registered institutions that have completed a MOU stipulating reporting of adverse events to the Duke animal program within 90 days of occurrence of the adverse event. Thus, adverse events have been (or will be) communicated. However, the Duke animal program may request a specific report of adverse events at collaborating institutions. The request is generally an expectation if the institution is not accredited, assured, and/or registered; and may be performed as an auditing function at a sub-set of accredited, assured, and/or registered institutions.

i. Final Report: The Annual Progress Report for month 35 may be submitted as a final report. If a de novo protocol is being submitted, the report is expected along with the de novo report. If no continuation studies are anticipated, then the final report is submitted in a reasonable time frame.

7. Accelerated Reviews: While proper planning will accomplish most review requirements and while the Duke IACUC has several efficient processes for review of proposed activities; there may be the rare occasion where a PI needs a review/approval more rapidly than can be
accommodated by the standard Duke IACUC processes. The process for an accelerated review consists of:

a. The Principal Investigator apprises the IACUC Chairperson (or designee) of the need for an accelerated review. Such proper uses could include “sudden” experiment to prevent the loss of data or wastage of an animal or a human clinically relevant proposal involving skills training.

b. Assuming the petition to the Chair is accepted, a routine OAWA pre-review is performed.

c. With pre-review clarifications (& responses), OAWA will submit an email to all IACUC members (primary & alternate) which will include the requested change. Members will be provided at least 24 hours from the message date/time for response, prior to proceeding. Note: Only the primary member should respond unless the primary member is unavailable, then the alternate member will respond.

d. After at least 24 hours has passed, and assuming no members have called for Full Committee Review, the Designated Member Review (DMR) process will proceed.

e. If any member calls for Full Committee, then the proposal is placed on the agenda for the next schedule IACUC meeting (or Subcommittee Meeting if the criteria fits the SC guidelines)

f. All such actions are reported to the next regularly scheduled IACUC meeting.

g. Note: any clearance items (OESO / EOHW) must be addressed prior to release of the approval letter.