Guidelines Regarding Significant Changes to Animal Study Proposals

The Animal Welfare Act Regulations and the Public Health Service Policy on Humane Care and Use of Laboratory Animals (PHS Policy) require that Animal Care and Use Committees (ACUCs) review and approve significant changes regarding the use of animals in on-going activities described in an ACUC-approved Animal Study Proposal (ASP).

In accord with Office of Laboratory Animal Welfare (OLAW) Guidance on Significant Changes to Animal Activities[1], the NIH intramural research program Animal Research Advisory Committee (ARAC) recognizes that the individual Institute/Center (IC) ACUCs have the authority to establish and approve internal policies for the review and approval of proposed changes to ASPs.

Several categories of proposed change review and approval are outlined in OLAW guidance, including Mandatory, Conditional administrative, and Unconditional administrative handling of significant change proposals. These categories allow IC-ACUCs some discretion to use internal policies to define what it considers a significant change or to establish a mechanism for determining significance on a case-by-case basis in accordance with the PHS Policy.

Category 1: *Mandatory non-administrative* IC-ACUC review by one of the valid methods described in the PHS Policy, i.e., full committee review (FCR) or designated member review (DMR):

a. Changes from non-survival to survival surgery;
b. Changes resulting in greater pain, distress, or degree of invasiveness;
c. Changes in housing and or use of animals in a location that is not currently part of the animal program overseen by the IC-ACUC;
d. Changes in species;
e. Changes in study objectives;
f. Changes in Principal Investigator (PI); and
g. Changes that could impact personnel safety.

Notes: The IC-ACUC internal policies may establish procedures that define the scope of changes in overall aims and study objectives that require non-administrative IC-ACUC review, and procedures for Division of Occupational Health and Safety review to determine the potential for personnel safety impact of the proposed changes.

Category 2: *Conditional administrative* handling of significant change proposals may be performed under particular specified conditions. Use of these administrative options is not required; however, if not used, then these significant changes must be reviewed and approved in the same manner as Category 1 items:

Category 2.1: *Veterinary review and consultation:* Conditional upon having applicable IC-ACUC-reviewed and -approved policies (i.e. guidance documents, standard operating procedures, and drug formularies, etc.), and upon consultation with a veterinarian authorized by the IC-ACUC:

a. Changes in anesthesia, analgesia, sedation, or experimental substances;
b. Change in method of euthanasia (as long as the new method is approved in the AVMA Guidelines for the Euthanasia of Animals); and
c. Change in duration, frequency, type, or number of procedures performed on an animal. (A list of IC-ACUC accepted specific procedures and scope of changes may be incorporated here).
d. Transportation of animals along acceptable traffic routes by acceptable means or movement of animal source materials between facilities following NIH approved containment.

Notes: The veterinarian is not conducting DMR on behalf of the IC-ACUC, but is serving as a subject-matter expert to verify that compliance with the IC-ACUC-reviewed and approved policies are appropriate for the animals in those particular circumstances. The IC-ACUC policies are expected to allow the veterinarian to refer any request to the IC-ACUC for FCR or DMR review for any reason and specify that the veterinarian must refer any request that he or she determines do not meet the parameters of the IC-ACUC-reviewed and approved policies. The IC-ACUC internal policies may also define experimental substances and delimit the scope of changes in duration, frequency, type, or number of procedures permitted or that require this conditional administrative handling. For example, a reduction in the number of procedures performed may be handled as per Category 3.

The consultation with the veterinarian must be documented. The approved change must be documented in the ASP; must be sent to the appropriate animal facility staff; and the IC-ACUC should be kept informed of changes made through this process. This process does not preclude routine veterinary intervention for individual animals but would apply if an intervention results in a change that is applied to animals going forward.

Category 2.2: *IC policy permitted:* Conditional upon having applicable IC-ACUC-reviewed and approved policy:

a. Change increasing previously approved animal number(s) as per IC policy.

Notes: The IC-ACUC policies may establish guidance documents that define the scope of changes in the number of animals permitted or that require this conditional administrative handling. No additional consultation or notification is required. However, the approved change must be documented in the ASP, must be sent to the appropriate animal facility staff, and the IC-ACUC should be kept informed of changes made through this process.

Category 3: *Unconditional administrative handling* (i.e., without IC-ACUC-approved policies, consultations, or notifications):

a. Correction of typographical errors;
b. Correction of grammar;
c. Contact information updates; and
d. Change in personnel other than the PI.

Notes:

1) There must be an administrative review to ensure that all personnel are appropriately identified; adequately trained and qualified; enrolled in occupational health and safety programs; and meet other criteria as required by the IC-ACUC. The approved change must be incorporated into the ASP, must be sent to the appropriate animal facility staff, and should be reviewed by the IC-ACUC for concurrence.

The IC-ACUC policies (guidance documents, standard operating procedures, and drug formularies) must be reviewed by the IC-ACUC at appropriate intervals of no less than once every three years to ensure they are appropriate and accurate. A method must be developed for informing the PI of the policies and how they will be applied.

It should be understood that changes covering details beyond what is required in the original ASP are not to be considered significant, and do *not* need IC-ACUC review and approval. In this regard each IC-ACUC should specify in their policies the level of detail it requires for the evaluation of procedures involving animals. Inclusion of trivial details, especially those that cannot be reliably anticipated, or may need to be altered without significant consequence, should be discouraged. Investigators are encouraged to write their protocols broadly with parameter ranges where appropriate to help avoid the need for unnecessary post-approval modifications.

To fulfill their responsibilities regarding review of changes in previously approved ASPs, and to perform that review expeditiously, IC-ACUCs may find it useful to delegate to one member, (e.g. the Chair or the Animal Program Director), to determine the significance or other intended changes within the context of that ASP. Minor changes not deemed significant, such as changes in trained personnel performing animal activities, which are then reviewed and approved by the delegated reviewer(s), should be reported to the IC-ACUC at its next regular meeting. IC-ACUCs may further require principal investigators to report minor changes to update an ongoing ASP.

Note: Investigators may use fewer animals than approved. This does not require IACUC approval, notification, consultation, or administrative handling.

Reference:

NIH Guide Notice OD-14-126, August 26th, 2014 – OLAW Revised Guidance on Significant Changes to Animal Activities: http://grants.nih.gov/grants/guide/notice-files/NOT-OD-14-126.html

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