



Johns Hopkins University

Animal Care and Use Committee

Veterinary Verification and Consultation (VVC)

BACKGROUND:

The PHS Policy on Humane Care and Use of Laboratory Animals (Policy) (IV.C.1.) and Animal Welfare Regulations (9 CFR 2.31 (d) (1) (i)-(iv)) define the responsibilities of the Institutional Animal Care and Use Committee (IACUC) regarding review and approval of proposed significant changes to animal activities. Changes to approved research projects must be conducted in accordance with the institution's Assurance, the United States Department of Agriculture (USDA) Animal Welfare Act and Animal Welfare Regulations and must be consistent with the Guide unless an acceptable justification for a departure is presented. Additionally, IACUCs are responsible for assuring that the changes to approved animal activities meet the requirements described in the PHS Policy IV.C.1.a-g.

PURPOSE:

This policy outlines situations and circumstances where specific significant changes to an IACUC protocol may be handled administratively, without Full Committee Review (FCR) or Designated Member Review (DMR), in compliance with NIH and USDA guidance. The Johns Hopkins University (JHU) IACUC developed this policy to allow certain significant changes to be pre-approved by the IACUC and verified by a JHU laboratory animal veterinarian with a faculty appointment, in accordance with the Office of Laboratory Animal Welfare (OLAW) guidance on Significant Changes to Animal Activities NOT-OD-14-126. The goal of this policy is to support the use of performance standards and professional judgment to reduce regulatory burden. The veterinarian is not conducting DMR, but is serving as a subject matter expert to verify that the proposed changes are appropriate for the animals in the circumstance, and are consistent with relevant IACUC-approved guidance.

GUIDELINES:

The JHU laboratory animal veterinarian (with a faculty appointment) has the authority to request IACUC review of proposed changes for any reason, and must request IACUC review for any changes that do not meet the parameters of this policy. The veterinarian is the subject matter expert who determines that the change meets IACUC policies and does not require committee review.

1. Changes not authorized by VVC

Changes that would otherwise fit under the categories listed above in accordance with IACUC policies, procedures, or guidelines may still require IACUC committee review. A proposed change requires IACUC review by either DMR or FCR if it:

- Is expected to result in greater pain, distress, degree of invasiveness, or mortality;
- Changes the study objectives;
- Addition of animal numbers;
- Impacts personnel safety or requires JHU Health, Safety, and Environment (HSE) review;
- Changes the Principal Investigator (PI);
- Changes a surgery from non-survival to survival surgery;
- Changes study species;
- Changes duration or adds new location of satellite housing area;
- Changes location of surgical area;
- Adds new type of procedure(s) to the protocol: or
- Adds injection with new human cell lines or transgenic mouse lines.

2. Changes authorized by VVC

Specific significant changes may be approved via Veterinary Verification and Consultation (VVC) without Full Committee or Designated Member review in the following areas:

a. Changes to compounds or dosage of anesthesia, analgesia, sedation, veterinary therapeutics, or experimental substances not impacting personnel safety. Examples of changes that may be approved under this category using agents listed in the Reference section below are:

i. A change in dosage, route, frequency, or duration within acceptable and known veterinary parameters;

ii. Addition of or change in analgesic, anesthetic, sedative agent, or veterinary therapeutic agent, or experimental substances; (See ACUC Guidelines on Analgesia for Rodents and Anesthesia-Gas)

iii. Changes in substances that are the same class of compounds (ex. novel peptides, chemotherapeutic drugs) currently approved in the protocol

iv. Changes in substances that are different types of compounds than those currently approved in the protocol - examples of the types of compounds include: antibiotics, colloidal fluids, diluents/ vehicles (DMSO, diluted ethanol, carrier oil, commonly formulated physiologic saline and buffer solutions, distilled water, heparin flush), imaging contrast agents, gene expression modulators, etc. with published doses referenced in materials listed in References section, below, for "Anesthesia, analgesia, or sedation;"

v. Injection with new tumor non-human cell lines, provided the tumor size and condition endpoints are consistent with the originally approved protocol (See ACUC Tumor Study Guidelines)

b. Use of non-pharmaceutical-grade substances, when pharmaceutical-grade alternatives are not available, for the following reasons (See ACUC Non-pharmaceutical Grade Drug Policy):

i. An equivalent veterinary or human pharmaceutical-grade compound does not exist, it is unavailable, or it is in short supply;

ii. The equivalent veterinary or human pharmaceutical-grade compound is not available in the appropriate formulation or concentration required;

iii. Although there is an equivalent veterinary or human drug available, the chemical grade is required to replicate methods from previous studies;

iv. The equivalent veterinary or human pharmaceutical-grade compound contains preservatives or inactive ingredients which may confound the research goals of the study.

c. Changing euthanasia method to a method approved in the current AVMA guidelines.

d. Changes in duration, frequency, number, and type of previously approved procedures performed.

Typical examples under this category may include:

i. Changing an already approved procedure on the protocol in terms of its duration, frequency, number, or type consistent with IACUC and RAR policies, guidelines, and standard procedures;

1) Change in the amount, route, and/ or frequency of blood collection, while adhering to the ACUC Multiple Blood Draws Guideline.

2) Method of animal identification (See ACUC Guidelines for Ear Tagging and Toe Clipping)

3) Biopsy procedure for genotyping. (See ACUC Tail Biopsy Guideline)

4) Frequency/interval/number of non-invasive procedures such as imaging.

5) Increases or enhancements in enrichments. See JHU Environmental Enrichment Program.

6) Method of restraint (does not include “prolonged restraint”). (See ACUC Restraining Animals Guideline)

7) Care during recovery from anesthesia. (See ACUC Survival Surgery Guidelines)

8) Use of Elizabethan collar (e-collar). (See RAR GP-8 Use of E-Collar Check List)

9) Wound Closure

10) Method of hair removal (See ACUC Hair Removal Guideline)

11) Adding or altering behavioral testing methods providing they do not involve unrelieved pain or distress.

ii. Changes in experimental timeline that do not negatively impact animal welfare and health. Approved monitoring, humane endpoints and associated documentation are required, when applicable, during periods of delay;

iii. Changing a surgery from survival to non-survival, or changing a surgery from survival to euthanasia and tissue harvest.

e. Change to animals of a different sex (excluding transgenics) with no increase of animal numbers.

3. Process

The VVC Request Form is available from ACUC staff via acuc@jhmi.edu.

a. Ways to initiate the VVC process:

i. Any amendment submitted to the IACUC through the normal submission process, in which the changes described qualify for VVC, may be assigned administratively to an IACUC-approved veterinarian for VVC.

ii. An IACUC-approved veterinarian can initiate a VVC by sending the completed VVC form to ACUC and the PI with or without the PI signature. If there is no PI signature, the PI must respond by email that they are aware of the change.

iii. A PI may request the form from ACUC staff, fill it out, sign it, and consult with an approved veterinarian.

b. Upon review from the PI, the veterinarian will sign and send the approved document to the IACUC office directly via e-mail; the subject line will contain the letters "VVC." The IACUC will add the VVC document to the file of the protocol for which the change is authorized.

c. The Principal Investigator will retain a copy of the approved VVC document with the protocol for which the change is authorized.

d. The PI will be required to include the amended procedure(s) in subsequent renewal submissions of the affected protocol, if it is to be performed in the future.

4. References

- a. NIH Guidance on Significant Changes to Animal Activities, NOT-OD-14-126
<https://grants.nih.gov/grants/guide/notice-files/not-od-14-126.html>
- b. AVMA Guidelines for the Euthanasia of Animals-2020 Edition
<https://www.avma.org/sites/default/files/2020-02/Guidelines-on-Euthanasia-2020.pdf>
- c. RAR Veterinarians' Anesthesia and Analgesia Recommendations for JHU Rodents
- d. Paul Flecknell. Laboratory Animal Anaesthesia. Elsevier/Academic Press, 2016.
- e. Richard E. Fish, Peggy J. Danneman, Marilyn Brown, and Alicia Z. Karas, eds. Anesthesia and Analgesia in Laboratory Animals (Second Edition), Academic Press, 2008.
- f. Donald C. Plumb. Plumb's Veterinary Drug Handbook (Ninth Edition), Wiley-Blackwell, 2018.
- g. James W. Carpenter and Christopher J. Marion, eds.: Exotic Animal Formulary (Fifth Edition), W.B. Saunders, 2018. h. "Nonhuman Primate Formulary", Association of Primate Veterinarians.
- h. C. Terrance Hawk, Steven Leary, Timothy Morris, eds. Formulary for Laboratory Animals (3rd Edition), Wiley-Blackwell, 2005.
- i. Harkness and Wagner's Biology and Medicine of Rabbits and Rodents, (Fifth Edition), Wiley-Blackwell, 2009.
- j. Lumb and Jones Veterinary Anesthesia and Analgesia, (Fifth Edition), Wiley, 2015.
- k. Quesenberry and Carpenter's Ferrets, Rabbits and Rodents Clinical Medicine and Surgery, (Fourth Edition), Elsevier, 2020.