Significant Changes to Animal Study Protocols

**Background/Purpose:** As described in the PHS Policy (IV.C.1) and the Animal Welfare Regulations [9 CFR 2.31 (d) (1) (i)- (iv)], the IACUC is responsible for reviewing and approving proposed significant changes to Animal Study Protocols (ASPs). Changes must be conducted in accordance with the University’s Animal Welfare Assurance and be consistent with the Guide for the Care and Use of Laboratory Animals (the Guide) and requirements in the PHS Policy. Recent guidance from the Office of Laboratory Animal Welfare (OLAW) describes types of significant changes that may be administratively handled if an IACUC-reviewed and –approved policy is in place to describe the conduct of animal activities consistent with the references above. **The purpose of this policy is to define significant changes to ASPs, to describe the procedures by which significant changes may be handled, and to communicate these procedures to investigators.**

**Definition(s):**

1. A *significant change* to an ASP is one that negatively impacts (or has the potential to negatively impact) animal welfare, substantively alters animal use from that originally approved in the protocol, or impacts personnel safety. (NIH NOT-OD-14-126; Examples are listed below.)

2. An *IACUC-reviewed and -approved policy* for the conduct of animal activities includes guidance documents, standard operating procedures (SOPs), drug formularies, etc., that have been periodically (at least once every three years) reviewed by the IACUC and have been approved as resources to describe appropriate animal use procedures or activities (NIH NOT-OD-14-126). These approved policies will be used when determining administrative processing for proposed significant changes.

**UMD Policy:**
The UMD IACUC will generally review proposed significant changes to ASPs using Designated Member Review unless a committee member calls for Full Committee Review or unless an IACUC-reviewed and -approved policy or guidance document is in place to address the proposed change. In the latter case, the IACUC staff may administratively process the proposed significant change, with or without veterinarian consultation and verification, as described below.

1. Significant changes that **must be approved by either DMR or FCR** include changes:
   a. from nonsurvival to survival surgery;
   b. resulting in greater pain, distress, or degree of invasiveness;
   c. that add new experiments;
   d. in housing and/or use of animals in a location not overseen by the IACUC;
   e. in species;
   f. in study objectives;
   g. in Principal Investigator (PI), and
   h. that impact personnel safety.

2. Significant changes that **may be handled administratively** according to UMD IACUC-reviewed and –approved policies subsequent to Attending Veterinarian (AV) consultation...
and verification (VVC) that the change is consistent with the approved resource documents include:

**a. changes in anesthesia, analgesia, tranquilizers and sedatives, or other pain-relieving or post-operative measures.** Changes must be consistent with the information found in the guidance below and must be consistent with UMD guidelines and SOPs.

i. Hawk and Leary’s *Formulary for Laboratory Animals*
ii. Plumb’s *Veterinary Drug Handbook*
iii. Hawk’s *Formulary for Laboratory Animals*
iv. Carpenter’s *Exotic Animal Formulary* (or peer-reviewed scientific journal articles)

**b. changes in euthanasia** to any method approved in the most current version of The *AVMA Guidelines for the Euthanasia of Animals*.

**c. increases in animal numbers up to 100%** of the total previously approved animal numbers. This increase may include changes in genotype/strain/stock of animal of the same species provided:

i. there is no anticipated adverse phenotype/phenotype unknown (newly developed GMOs)
ii. the GMO has been or does not require review by the IBC ( Institutional Biosafety Committee)
iii. a detailed rationale for the increase is provided. The AV or IACUC Chair will alert the IACUC if the increase is the result of animal mortality or unexpected and/or adverse events.

**d. change in duration, frequency, type or number of procedures** performed on an animal that are not expected to increase pain or distress, impact the approved endpoint criteria, or impact the approved personnel safety considerations. Changes/additions to procedures listed below maybe handled via VVC provided they are performed within the conditions stipulated in the approved protocol DLAR guidelines or SOPs, as indicated:

i. change in substances that are the same class of compounds currently approved in the ASP and which are not expected to increase pain or distress, impact the approved endpoint criteria, or impact the approved personnel safety considerations
ii. change of compounds to control gene expression, consistent with compounds currently approved in the ASP,
iii. change in injection/administration/procedural frequency consistent with those currently approved in the ASP, and which are not expected to increase pain or distress (changes in food/water restriction must be consistent with DLAR guideline D.17.a)
iv. change in genotyping methods consistent with DLAR guideline D.6.a.

v. change in injection method consistent with DLAR SOP 1402 including:

- Intradermal (ID)
- Intravenous (IV)
- Intramuscular (IM)
- Subcutaneous (SQ)
- Intraperitoneal (IP)
• Intracardiac (IC)
• Intraorbital (IO)
• Intranasal (IN)

vi. change in blood collection method consistent with DLAR guideline D.19.a including:
• Lateral Tail Vein or Ventral/Dorsal Artery or Tail Clip
• Jugular (limited to the rat)
• Saphenous (medial or lateral approach)
• Retrorbital Sinus

**Method of Amendment Submission:**
Amendments handled via VVC methodology will be processed as described below.

1. Submission of changes to an existing, approved protocol must be submitted via our online protocol submission system (IRBnet) using the amendment form, and including an updated Animal Study Protocol form (ASP) and updated Personnel Qualifications Forms for all personnel performing any new procedure. A full description of the reason for the change must be provided so that the IACUC office staff may perform a pre-screened to determine whether the requested changes are covered under this policy, as described above (2a-d). Qualifying amendments will be referred to the AV for verification that the requested changes are: consistent with the IACUC-reviewed and -approved policies, appropriate for the circumstances, and that no IBC concerns are present.

2. The AV, IACUC Chair, and/or any IACUC members may, for any reason, refer the proposed change back to the committee for review and approval. If the proposed significant changes do NOT meet the parameters in the IACUC-reviewed and -approved policy, the AV or IACUC Chair MUST refer the request back to the IACUC. If applicable policy or resource documents do not exist, the significant change request must be reviewed by DMR or FCR.

3. VVC handling of changes to protocols must be documented by the AV in the online protocol submission system. Following review and signoff by the AV, the IACUC will issue an approval letter. Changes may not be implemented until the approval letter is issued.