Guideline for the Use of Novel Compound in Animals

University of Mississippi Institutional Animal Care and Use Committee

Purpose: A novel substance is any chemical entity that has never been tested, is in the early stages of animal testing, or is a previously characterized substance administered in a novel way. This guideline provides guidance to UM PIs and IACUC on the information that should be included in the Animal Use Protocol Form to protect animal health and welfare and promote scientific rigor.

Background: Unlike traditional hypothesis testing, drug discovery research on novel compounds and extracts 1) cannot always predict precisely how many compounds and extracts will be tested in a protocol and, therefore, cannot always predict the numbers of animals required, and 2) cannot always predict adverse effects that could produce pain or distress in animals.

Guideline

If an investigator proposes to administer a novel substance to a particular species, the following information should be provided to the IACUC in the protocol application:

- By default, novel substances would be classified as non-pharmaceutical grade. Please refer to UM Guideline for the Use of Non-Pharmaceutical Grade Compounds in Laboratory Animals for the definitions and preparation requirements.
- A synopsis of any available *in vitro* or *in vivo* data including pharmacological and toxicological actions of this or related compounds
- A brief description of the class of compound, including mechanism of action (if known)
- Information on the source of the novel substance (e.g., will it be created in the PI's laboratory, provided by a company, etc.?)
- A description of the grade/purity being proposed, the formulation of the final product, compatibility of components, and issues such as sterility, pyrogenicity, stability, pH, osmolality, storage, [*]shelf life, toxicity, pharmacokinetics, physiological compatibility, and quality control, if available.

  [*]*If the shelf life is unknown, the final product should be prepared no less frequently than weekly.*

- A complete description of dosage, site and route of administration, how long compound will be administered, the intervals by which dosages will be increased/decreased (if applicable), and the rationale for increasing/decreasing dosages.
- The plan for monitoring of animals for side effects and adverse events after compound administration, including:
  - Frequency of monitoring should be:
    - more frequent if there is a potential for acute toxicity or unknown adverse effects
    - less frequent if there is previous data after administration to animals and no adverse effects were identified at the maximal dose
  - Identification of staff performing the monitoring
  - How monitoring will be documented
  - Behavioral signs of pain and distress that will be monitored

    - Objective monitoring parameters (e.g., biochemical, or metabolic changes)
    - Plans for treating animals for toxicity, if indicated
    - Notification of Attending Veterinarian of any adverse effects
- Specific humane endpoints, such as (but not limited to):
    - Impaired ambulation
    - Seizures
    - Rapid weight loss (usually due to dehydration)
    - Labored breathing
    - Impaired mentation
    - Anaphylaxis
- Study endpoints
- Records to be kept
    - Compound dose
    - Animal weights
    - Number of animals euthanized to achieve humane endpoints.
- Potential occupational health and safety concerns for laboratory staff, animal caretakers, veterinarians, etc., during and after administration to animals, including handling of carcasses, bedding, and caging. Some compounds may require an IACUC approved SOP and/or IBC review before work can begin.

If you have any questions or concerns regarding this guideline, please contact the IACUC office at 662-915-5062 or email at iacuc@olemiss.edu.

References

1. NIH Guidelines for the Use of Non-Pharmaceutical Grade Compounds in Laboratory Animals
2. OLAW FAQs (F4)