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Written by:	*April 2024*	*C. Moats*
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Distribution	All	

VC-10: Guidelines on Handling, Use, Storage, and Disposal of Drugs for Animal Use

Purpose: This guideline describes proper handling, use, and storage of drugs used in animal studies at the Johns Hopkins University.

Scope: This guideline is applicable to all Research Animal Resources and research staff using drugs for experimental and clinical purposes in animals at the Johns Hopkins University. Drugs refer to any substance or biological product, other than unmedicated food, that is administered to animals for clinical or experimental purposes.

Personnel Responsibilities:

Investigative staff: Use drugs consistent with manufacturer labelling per veterinary instruction, per this guideline, and/or per the IACUC approved protocol.

Clinical Veterinarians and Veterinary Technicians: use drugs consistent with manufacturer labelling per veterinary instruction, per this guideline.

Attending Veterinarian: Will review all deviations in this process and implement corrective actions or document revisions accordingly.

Procedures:

Handling and Use of Drugs

General principles:

- All drugs should be clearly labeled with full drug name, concentration, date of transfer (if applicable), and the expiration date. If the primary container is too small to fit all labeling information (ex. Eppendorf tube), the primary container must be labeled with at minimum the drug name and expiration date, and must be stored in a secondary container (ex. freezer box) which is labeled with full drug name, concentration, date of transfer, and the expiration date of all aliquots stored within the secondary container.
    - *HSE703 Management of Hazardous Chemicals* details storage and labeling of potentially hazardous chemicals and must be followed for all potentially hazardous drugs.

- Regardless of the route of administration, do not use any compound that has altered physical appearance (e.g., discoloration).
- Liquid compounds given parenterally (via subcutaneous, intraperitoneal, intramuscular, or intravenous routes) must be kept under antiseptic conditions. When drawing up medications, use only sterile needles and syringes. Never replace a drawn-up drug back into its original vial. The stopper should also be cleaned with an alcohol wipe prior to puncture. If precipitates, discoloration, leaks, or know breaks in sterility are noted for the fluid/container, do not use.

Aliquoting, diluting, or mixing of drugs for parenteral use:

- The following applies to drugs or compounds intended for parenteral use in animals, which have been transferred or adulterated from their original form or container (aliquoted, diluted, or mixed) in a manner not specified by the manufacturer. When available, manufacturer instructions should always be followed for reconstitution, dilution, storage, and expiration of drugs.
- Strict antisepsis should be followed when transferring drugs intended for parenteral use from the original vial to a new vial. This includes use of sterile empty vials, sterile diluent (if diluent is utilized), and sterile/single use needles and syringes. Additionally, when transferring drugs, clean gloves should be worn and vial stoppers should be wiped with alcohol before withdrawing medications or injecting medications into new vials.
- Suitable commercial diluents include bacteriostatic water, PBS, or sterile saline for injection. If diluents are made in the laboratory, they must be processed through a sterile 0.2 micron filter into a sterile container, in a biosafety cabinet or clean air bench when available.
- To minimize drug wastage, only mix/aliquot/dilute as small of a volume as needed.
- The vial containing the transferred drug should be clearly labeled with drug name, concentration, date of transfer, and the expiration date.
- The expiration date for transferred drugs should be 30 days after drug transfer, or on the expiration date of the stock vial, whichever occurs sooner.
- For drugs that do not list expiration dates:
    - Powdered forms of drugs or compounds: the PI should determine stability of the drug to identify a reasonable shelf-life. This is commonly obtained from the manufacturer. The drug should be stored in a light proof airtight container and labeled as described in this document. If any visible alteration (e.g. discoloration, consistency, etc.) of the drug has occurred during storage, the drug should be discarded.
    - For drugs or solutions which have been reconstituted for use: Once reconstituted, they must be labeled as described in this document and expire 30 days following reconstitution, unless the manufacturer specifies a longer shelf-life for dilutions and the manufacturer specifications are followed for preparation and storage. Note that when combining drugs into a new vial (ex. ketamine/xylazine cocktail, "TKX," etc.), the drugs should be compatible (ex. not result in precipitation or inactivation of mixed drugs), must be prepared antiseptically, and labeled as described above.

Use of sterile fluid bags/vials:

- Single-use sterile fluids or fluid diluent vials (e.g. saline) may be accessed multiple times, as long as the fluid is accessed antiseptically and stored per recommendations of the manufacturer.

- Sterile fluids expire on whichever date or condition occurs first:
    - The manufacturer expiration date, or
    - 30 days after opening/puncture

Expired drugs:

- Always consult the drug packaging for expiration dates. Dispose of expired drugs once expired. If there is a delay in the disposal of expired drugs, they should be segregated from other drugs in the storage location to ensure that expired drugs are not used by accident until they are disposed of.
- The use of expired drugs, medical supplies and/or devices is not acceptable veterinary practice and does not constitute adequate veterinary care. Thus, **the use of expired medical materials for survival procedures in animal research studies is prohibited.**
- However, the use of expired medical materials and drugs may be permissible for acute terminal procedures, under the following conditions:
    - **It is never acceptable to use expired anesthetics, sedatives, analgesics, and euthanasia agents, even for acute terminal (non-survival) procedures.**
    - However, use of expired medical supplies or other drugs (with the exception of anesthetics, sedatives, analgesics, and euthanasia solutions) is permissible if the animal is anesthetized and utilized for an acute terminal procedure. The expired supplies or drugs must not compromise the animal's welfare in any way or have a negative impact on the research outcomes. The drugs/materials must be clearly labeled as being expired, must state "for terminal use only," and must be physically segregated from in-date items.

Storage:

- Refer to the drug packaging and packaging inserts for special considerations with regards to storage. Generally speaking, drugs should be kept in a designated area or "pharmacy" at room temperature. For drugs requiring lower storage temperatures, they should be stored in a refrigerator or freezer (per manufacturer instructions) which is regularly monitored for appropriate temperatures.
- If a drug is light sensitive (ex. tribromoethanol, MS-222), it will often be provided in an amber vial. If drawing up a light sensitive medication to be stored in a different sterile vial, or a syringe, wrap the vessel in aluminum foil to prevent the drug's exposure to light.

Disposal:

- All drug disposal must comply with JHU policies.
    - For potentially hazardous drugs, HSE MDUP002 Hazardous Drugs: Safe Handling and Waste Disposal.
    - For controlled substances, *ACUC Guidelines for Storage and Record Keeping of Controlled Drugs* and *HSE GEN005 Use of Controlled Substances in Laboratory Research.*

Special Considerations:

Controlled substances:

- Handling, storage, use, and disposal of controlled substances is detailed further in the *ACUC Guidelines for Storage and Record Keeping of Controlled Drugs* and *HSE GEN005 Use of Controlled Substances in Laboratory Research*. However, general principles described in this protocol (e.g. maintenance of sterility, aliquoting from original container, expiration) should also be followed.

Non-pharmaceutical grade drugs:

- Investigators must follow the *ACUC Guidelines for Use of Non-Pharmaceutical Grade Substances in Laboratory Animals*.
- The JHU ACUC expects that the duration of storage and use of a non-pharmaceutical grade formulation will be compatible with the duration for which the formulation will remain potent, as per technical information available. Methods for preparing and storing formulations must prevent contamination that could adversely affect animal welfare or the interpretation of data. Formulations must be labeled with the name of the compound and the concentration as well as the date of preparation and planned date of disposal.
- General principles described in this protocol (e.g. maintenance of sterility, appropriate labeling, etc.) should also be followed.

Related Documents:

- *ACUC Guidelines for Storage and Record Keeping of Controlled Drugs* https://animalcare.jhu.edu/guidelines/
- *ACUC Guidelines for Use of Non-Pharmaceutical Grade Substances in Laboratory Animals* https://animalcare.jhu.edu/guidelines/
- *HSE GEN005 Use of Controlled Substances in Laboratory Research* https://policies.jhu.edu/doc/fetch.cfm/UTREDbbG
- *HSE MDUP002 Hazardous Drugs: Safe Handling and Waste Disposal* https://hpo.johnshopkins.edu/doc/fetch.cfm/EriQ7i51
- *HSE703 Management of Hazardous Chemicals chrome-extension://efaidnbmnnnibpcajpcglclefindmkaj/https://hpo.johnshopkins.edu/doc/fetch.cfm/qEhFm4oK*

References:

National Research Council (US) Committee for the Update of the Guide for the Care and Use of Laboratory Animals. (2011). Guide for the Care and Use of Laboratory Animals (8th ed.). Washington, D.C.: National Academies Press (US).

Matthews KA and Taylor DK. Assessment of sterility in fluid bags maintained for chronic use. J Am Assoc Lab Anim Sci. 2011 Sep;50(5):708-12. PMID: 22330719; PMCID: PMC3189676.

I acknowledge that I have read and understand the JHU Animal Care and Use Program document "**Guidelines on Handling, Use, and Storage of Drugs for Animal Use**" and I will follow this procedure. I agree to bring any deviations in this procedure to the attention of my supervisor/GPS Working Group.

Name (Print) Date

Signature