



Standard Operating Procedure for the Use of Particularly Hazardous Drugs/Chemicals in Animals

1. Purpose

The purpose of this Standard Operating Procedure (SOP) is to describe the best practices for the identification, risk communication, and disposal of waste when using Particularly Hazardous Drugs/Chemicals in animals. Compliance with this SOP will protect workers and the environment from potential exposure to these chemical hazards. Exposure to hazardous and Particularly Hazardous Drugs/Chemicals (i.e. carcinogens, developmental & reproductive toxins, and highly/acutely toxic chemicals) may occur when substances are compounded, administered (e.g. administered in the animal's drinking water or food), and/or when they or their toxic metabolites are released from the animal (e.g. in the urine, feces, exhalation, etc.). Therefore, hazardous and particularly hazardous drug/chemicals administration to live animals not only impacts the animal but also has the potential to affect researchers and University's Animal Care (UAC) staff handling these animals and their waste. Researchers must inform UAC before using any new hazardous chemicals (to include and Particularly Hazardous Drugs/Chemicals) in animals.

2. Scope

The use of any of the drugs/chemicals listed within the National Institute for Occupational Safety and Health (NIOSH) "[List of Antineoplastic and Other Hazardous Drugs](#) (2016)" in animals falls under the purview of this SOP. RLSS performs a protocol-specific assessment for all submitted IACUC protocols to classify any Particularly Hazardous Drugs/Chemicals not identified on the NIOSH list. Similar assessments will also be performed to determine requirements for particularly hazardous drugs/chemicals administered to large animals. Updated or amended protocols must be re-assessed by RLSS prior to the implementation of any changes.

This SOP addresses the hazards of these drugs/chemicals during and after administration only. Refer to the [University Chemical Hygiene Plan](#) on the [RLSS website](#) for information on how to safely handle particularly hazardous chemicals in their pure form.

3. Hazard Classification

Particularly Hazardous Drugs/Chemicals can pose the following hazards either during administration to animals or after they have been administered to the animal:

3.1 Injection Hazard: Accidental needle sticks when administering compounds to animals can allow particularly hazardous drugs/chemicals to directly enter the bloodstream.

3.2 Dermal Hazard: Handling animals that have been administered creams/ointments and/or handling contaminated bedding can allow Particularly Hazardous Drugs /Chemicals to be absorbed through the skin when personal protective equipment is not used and/or not properly used.



3.3 Inhalation Hazard: Particularly hazardous drugs/chemicals or their toxic metabolites that are excreted and/or exhaled from the animal pose an **inhalation hazard**.

3.3.1 Bedding Dust Hazard: These are particularly hazardous drugs/chemicals and/or their toxic metabolites that are excreted via the animal's urine, released into the bedding from contaminated drinking water, or otherwise adsorbed onto bedding particles and which pose a particulate inhalation exposure risk. Dumping contaminated cage bedding can generate particulates with adsorbed toxic compounds.

3.3.2 Animal Exhalation Hazard: Particularly hazardous drugs/chemicals or their toxic metabolites that are exhaled from the animal and pose an inhalation hazard to the workers when opening cages, changing bedding, or otherwise working with animals post-administration. Please contact RLSS for calculated exposure estimates for animals administered with drugs/chemicals that can post exhalation hazards.

3.4 Resource Conservation and Recovery Act ([RCRA](#)) Chemicals : The waste from animals that have been administered heavy metal-containing particularly hazardous drugs/chemicals require special disposal procedures detailed below. Compounds containing any of the following metals fall directly under RCRA and must follow the special disposal requirements:

- **Mercury**
- **Arsenic**
- **Lead**
- **Silver**
- **Barium**
- **Selenium**
- **Cadmium**
- **Chromium**

Table 1: RCRA Waste Determinations shows common concentration limits for RCRA Waste Determination. Concentrations in or above these values are considered part of the RCRA regulatory requirement and therefore need special disposal requirements.



Table 1: Common RCRA Waste Determinations

RCRA Waste
Mercury (≥ 0.2 mg/L)
Cadmium (≥ 1 mg/L)
Selenium (≥ 1 mg/L)
Arsenic (≥ 5 mg/L)
Chromium (≥ 5 mg/L)
Lead (≥ 5 mg/L)
Silver (≥ 5 mg/L)
Barium (≥ 100 mg/L)

All RCRA waste must be tracked using a log. More information about this log can be found in the *Exposure control* section and the *Appendix B* section of this document.

4. Exposure Control

All researchers using hazardous chemicals in animals must follow the steps below to prevent exposure to particularly hazardous drugs/chemicals.

4.1 Program Registration: The use of any hazardous chemicals in a laboratory setting requires registration into the Laboratory Chemical Safety Program (LCSP). Principal investigators who are new or have not previously registered can register by contacting RLSS at rlss-chemsupport@email.arizona.edu.

4.2 Hazard Identification: Inform RLSS of any planned use of hazardous chemicals in research animals. This is typically accomplished through the submission of an IACUC application. RLSS will inform researchers and UAC of any proposed drugs/chemicals that are classified as particularly hazardous. RLSS will work with researchers to ensure appropriate protective measures are in place during animal protocols, including choosing the appropriate housing to protect against inhalation hazards.

4.3 Informing UAC: Inform UAC of your use of particularly hazardous drugs/chemicals in animals; this must be completed by utilizing the Hazard Cage Card. RLSS will work with researchers and UAC staff to ensure appropriate protective measures are in place during animal protocols, including choosing the appropriate housing to protect against inhalation hazards.

4.4 Hazard Cage Card: Researchers must complete the Hazard Cage Card (example included as Appendix A) for each cage housing animals that will be administered particularly hazardous drugs/chemicals according to the hazard identification performed by RLSS and the training provided by UAC. This is required, at minimum, from the time of first dose to 72-hours after the last dose was administered to the animal(s). If animals



(e.g. mice and rodents) are caged outside of UAC facilities, Hazard Cage Cards must be used in all situations and at all times to properly communicate potential hazards. It is the researcher's responsibility to remove the card 72-hours after the last drug administration.

4.5 Personal Protective Equipment: The researcher must wear appropriate Personal Protective Equipment (PPE) when handling particularly hazardous drugs/chemicals and/or when administering drugs/chemicals to animals:

- **Double disposable nitrile gloves**
- **Lab coats and/or disposable gowns**
- **Splash goggles (preferred) or safety glasses (minimum)**
- **Long pants**
- **Close-toed shoes**

Additional PPE may be required and could include puncture-resistant gloves, face shields, and/or respirators. RLSS should be contacted and consulted prior to the implementation of additional/elevated PPE, as there may be additional training and/or requirements (e.g. participation in the UA Respiratory Protection Program).

4.6 Particularly Hazardous Drug/Chemical Administration: The administration of particularly hazardous drugs/chemicals via inhalation (or in any manner that creates a potential inhalation hazard) must be performed in a chemical fume hood or other approved ventilated enclosure (e.g. fully exhausted, interlocked biosafety cabinets) that are labeled with the "[Designated Area](#)" label available on the RLSS website. Contact RLSS prior to administration to ensure appropriate ventilation is being utilized.

When particularly hazardous drugs and chemicals are administered by injection, syringes and IV sets must include Luer (lock preferred over slip-type) fittings to avoid potential injection hazards.

4.7 Waste Disposal: After most particularly hazardous drugs/chemicals have been administered to an animal, the resulting waste (i.e. used bedding, disposable cages, etc.) may be disposed of as general non-hazardous waste for landfill disposal. Some exceptions exist to this rule. For example, any particularly hazardous drug/chemical waste containing biohazardous material or unfixed animal tissue/blood must be disposed as biohazardous waste. In addition, particularly hazardous drugs/chemicals containing heavy metals fall under RCRA requirements. Researchers generating RCRA waste must use the Waste Container Content Log (seen Appendix B) to track the amount of heavy metals being added within the specific container from each protocol. This log will be used to complete [Risk Management Services](#) waste tags before requesting waste collection.

4.7.1 Dumping Animal Bedding: Dumping or otherwise manipulating the bedding (such as taking empty caging to dirty-side cage wash) that housed animals (e.g. mice and rodents) administered a particularly hazardous drug/chemical must be performed in a chemical fume hood or another approved ventilated enclosure such as a biosafety cabinet or HEPA-filtered change station. To allow for full



excretion of the drugs/chemicals, these special procedures must be followed for any bedding dumping between the administration “Start Date” and 72 hours after the “End Date” noted on the Hazardous Materials Cage Card. Approved ventilated enclosures vary dependent upon the chemical the animal has been dosed with prior to excretion; please work with RLSS to determine the appropriate ventilated enclosure.

Chemicals classified as “**Bedding Dust Hazards**” should be dumped in a non-recirculating ventilated enclosure such as a chemical fume hood. If a fume hood or other non-recirculating ventilated enclosure is unavailable, however, they are permitted to be dumped in ventilated enclosures that have high efficiency filters such as an A2 BSC, HEPA-filtered change station, or other RLSS approved enclosure.

Chemicals classified as “**Animal Exhalation Hazards**” require the use of a non-recirculating ventilated enclosure, such as hard-ducted Type II/B2 Biosafety Cabinet (BSC), chemical fume hood, or other RLSS approved enclosure. These chemicals include azoxymethane (AOM), carbon tetrachloride, and others as communicated by RLSS.

Exceptions to these rules, such as for large animals like pigs, sheep, and more. Please work directly with RLSS to assess these situations on a case by case basis and ensure the continued safety of research and UAC staff members.

RLSS will inform the researcher and UAC when specific compound waste cannot be disposed of in a landfill. Consult with the Hazardous Waste Supervisor from [hazmat@arizona.edu](http://Risk_Management_Services_(RMS)_(Risk Management Services (RMS) (hazmat@arizona.edu) if you have any questions or concerns regarding the disposal of RCRA classified materials.



Appendix A – UAC Hazardous Material Cage Card

HAZARDOUS MATERIAL

Product _____

Drug/Chemical

Dermal

Bedding Dust

Exhalation

RCRA(heavy metal)

Biological

Human Cell Line

Non-Replicating Viral Vector

Date(s) Administered:

Start Date _____

End Date _____

Contact Information:

Name _____

Phone _____

Order (V)/CC # _____

Instructions:

Obtain a Hazardous Materials Cage Cards from UAC husbandry staff. Follow their instructions on how to complete each section and how to post them on the appropriate animal cages.



Appendix B- Example RCRA Drug/Chemical Waste Container Content Log

RCRA Drug / Chemical Sharps / Solid / Liquid Waste Container Log <i>Circle waste form</i>				
Date	P.I. Name	Drug/ Chemical Name	Waste Description (e.g. bedding, food, etc.)	Estimated Volume of Waste
1/7/2020	Dr. Wilbur Wildcat	Sodium Arsenite	Bedding	1 kg

Instructions: Download the “[RCRA Particularly Hazardous Drug-Compound Waste Container Content Log](#)” from the [RLSS website](#). Circle the physical form of the waste at the top of the page and attach one of these Content Logs to each waste container containing RCRA waste compounds/drugs. Complete the log as shown in the example above every time the RCRA drug/chemical is added to the waste container, following the information in Section 4.8. This information is vital to the proper labeling of an RMS tag for collection of the RCRA waste.