Reviewed: July 19, 2022
Approved: July 19, 2022

Center for Biomedical Research / IACUC
Standard Operating Procedure - Guidelines

Use of High Hazard Chemicals in Animals

Purpose:
This document provides standard procedures for managing animals, animal bedding, and other objects potentially contaminated after animals have been dosed with hazardous chemicals or drugs.

Scope:
This SOP covers hazardous chemicals used in animal research which require hazard communication to employees involved in animal handling or husbandry on dosed animals

Hazards:
For the purposes of this document, high hazard chemicals are classified as having one or more properties described as acutely toxic, carcinogen, mutagen, or teratogen. Hazardous chemicals determined to have a considerable high risk/toxicity may have the following health hazards as defined by the Globally Harmonized System for the Classification of Chemicals (GHS):

- Fatal if inhaled, in contact with skin, if swallowed
- May cause cancer; suspected of causing cancer
- May damage fertility or the unborn child; suspected of damaging fertility or the unborn child
- May cause genetic defects; suspected of causing genetic defects
- May cause an allergic skin reaction
- May cause allergy or asthma symptoms or breathing difficulties if inhaled

And the following carcinogens:

- National Toxicology Program (NTP) known or reasonably anticipated
- International Agency for Research on Cancer (IARC) Group 1; 2A or 2B
- Occupational Safety and Health Agency (OSHA) regulated carcinogens

And:

- Investigational drugs with little or no toxicological data

Examples of chemicals considered to be a high hazard may include but are not limited to:

- Azoxymethane
- BrdU
- Heavy Metals
- Chemotherapeutics
- TNBS – 2,4,6-trinitro benzene sulfonic acid

Routes of Exposure:
Animals that have been dosed with a hazardous chemical may excrete the chemical or toxic metabolites, particularly during the first 48 – 72 hours after dosing. **The primary hazard is potential exposure to contaminated bedding.** To protect employees, precautionary steps are outlined below (see Procedures).

1. Injection – Accidental needle sticks allows direct access to bloodstream
2. Dermal – Handling animals and/or bedding contaminated with hazardous chemicals may allow for chemical to be absorbed through the skin when PPE is not used or properly used
3. Inhalation – Hazardous chemicals or their toxic metabolites excreted/exhaled from the animal are considered an airborne hazard
    a. Bedding dust hazard – Dumping contaminated cage bedding can generate particulates having adsorbed toxic compounds. Hazardous chemicals may be excreted via urine, released into bedding from contaminated drinking water, or otherwise adsorbed onto bedding
    b. Animal exhalation hazard – Hazardous chemicals exhaled from the animal are an inhalation hazard to workers opening cages, changing bedding, or otherwise handling animals post- administration

Procedures:
Except for the exemptions listed, the following procedures are required for the first 72 hours after dosing **AND** until contaminated bedding is changed. Procedures may need to be altered based on animal species.

Exemptions:

- Animals are sacrificed immediately after dosing
- Hazardous chemical metabolites in bedding or drinking water will be at a concentration considered to be low- minimal risk. **This determination must have supporting documentation.**

1. **Notification/Signa**ge – Cages occupied within the first 72 hours after dosing must be labeled with the hazardous chemical until the contents have been discarded.
    a. For animal housing sites, researchers will:
        i. Provide advanced notification to those who will care for the animals. This includes notifying Randy Luehring and/or Dr. Darin Meulebroeck of the dosing schedule at least 5 business days prior to dosing and wait for confirmation to proceed.
        ii. Write a chemical-specific SOP to include: hazard identification, risk, use/preparation, engineering controls, work practice controls, PPE, disposal method.
        iii. Send the Safety Data Sheet (SDS), completed door sign, AND chemical-specific SOP to Randy Luehring, IACUC, AND the Office of Safety.

iv. Label the animal cages with a hazardous chemical cage card containing the following information: PI name, start/end date, chemical identification.
v. Post chemical hazard door sign.
vi. Remove door sign and hazardous chemical cage card when the hazard is no longer present.

2. Engineering Controls

a. Cages will be covered with micro-isolator lids and/or be maintained on a ventilated rack.
b. Cages will be opened in a B2 biological safety cabinet (ducted only) or a chemical fume hood. This includes cage-changing, animal care, or other experiment-related purpose.
c. Bedding will be removed in a B2 biological safety cabinet or chemical fume hood.

3. Personal Protective Equipment (PPE):

a. Standard PPE includes:
    i. Nitrile exam gloves (4-mil or higher)
    ii. Lab coat, gown, or coveralls (closed in front)
    iii. Shoe covers
    iv. Cover open cuts/irritated skin during animal care
b. Additional PPE to be used based on procedure:
    i. Splashing:
        - Safety goggles and/or face shield ***OR***
        - Powered Air Purifying Respirator (PAPR)
    ii. Open or unventilated cages containing contaminated bedding – ventilated racks not in use and not covered with microisolator lids; opening/changing cages with contaminated bedding while not using engineering controls mentioned above
        - PAPR ***OR*** N-95 (or better) respirator – Note: N-95 respirator use requires medical clearance, fit testing, and training
    iii. Cage dumping of any contaminated bedding unless using an engineering control as mentioned above
        - PAPR ***OR*** N-95 (or better) respirator ***PLUS***
        - Face shield or safety goggles

4. Work Practices:

a. For cage changing, label the bag with the hazardous chemical
b. Use disposable cages, water bottles, and low-no dust producing bedding when possible
c. Change gloves at minimum every 2 hours, when they are torn or contaminated ***AND*** before handling animals in other experimental groups.
d. Wash hands after removing gloves

e. Safety glasses, goggles, or reusable face shields must be cleaned with soap and water, and stored in a clean place before reuse
f. Decontamination of work surfaces such as that of a biosafety cabinet consists of wiping with 10% bleach then a rinsing with clean water. Clean/disinfect from least to most contaminated areas.
g. Waste bags must be closed for transport
h. Animal carcasses and contaminated bedding must be handled and discarded as hazardous material to be incinerated. Materials will be sent as either biological hazard or chemical hazard waste depending on the contaminant.

5. Disposal Procedures:

NOTE: Autoclaving does not destroy most toxic chemicals and hazardous drugs. Do not autoclave toxic chemical waste.

UND uses two separate vendors for hazardous material disposal. Veolia is the contractor for hazardous chemical and radioactive waste. Chemicals considered to be acutely toxic or those falling under the Resource Conservation and Recovery Act (RCRA) must be disposed as hazardous chemical waste. Those chemicals not falling within this category AND considered to be in minute/diluted quantities may be processed for disposal as biological waste. Contact the Office of Safety for assistance.

- Used bedding will be bagged in a chemical fume hood or B2 biological safety cabinet, securely closed and labeled with the chemical contaminant. Bedding will be disposed as either chemical or biological waste dependent on the hazard.
- Contaminated water must be collected as hazardous waste, labeled with the chemical contaminant, and picked up by the Office of Safety for disposal.
- Contaminated animal carcasses must be bagged, sealed, labeled with the chemical contaminant, and sent for disposal as either chemical or biological hazardous waste.
- Contaminated sharps must be placed in an appropriate puncture and leak proof container and collected as either chemical or biological hazardous waste dependent on the chemical contaminant.

6. Work-related Injury/Illness/Exposure:

- If medical assistance is required, go to Altru Occupational Health for non-emergency care or Altru Emergency Room as needed.
- Submit an incident reporting form to the Office of Safety within 24 hours and notify a supervisor.

Responsibilities:

Researchers Will:

- Follow this SOP when dosing animals with hazardous chemicals exhibiting health hazards stated above.
- Maintain a copy of this SOP in their lab.
- Submit a written chemical-specific SOP to IACUC, CBR, and the Office of Safety. Contact the Biological Safety Officer for a SOP template.
- Submit chemical SDS and chemical hazard door sign.
- Ensure ALL personnel to include research staff and animal care staff read, understand, and follow this SOP **AND** the chemical-specific SOP.

Animal Handlers Will:

- Follow this SOP when handling or performing husbandry with animals dosed with hazardous chemicals.
- Acknowledge they have read and understand the procedures in this SOP.

I have read and understand this SOP.

Last Name	First Name	Signature	Date

Remove this door sign and chemical cage card once chemical hazard is no longer present.

Use the manufacturer's Safety Data Sheet to identify the GHS hazard(s) and check the appropriate box(s) below:

Chemical Hazards for:

		
Toxic ☐ or Harmful ☐ by: ☐ Skin contact ☐ Inhalation ☐ Ingestion	☐ Reproductive ☐ Carcinogen ☐ Mutagen ☐ Sensitizer (inhalation)	☐ Skin sensitizer ☐ Unknown ☐ Other:

Who is responsible for changing cages?: ☐**CBR** ☐**Research Staff**

Principal Investigator:	**Protocol Number:**
Dosing date/time:	**Building/Room #:**

Safety Data Sheet (provided by PI) available in CBR office or Office of Safety

For 72 hours after administration/exposure AND until bedding is changed, wear **STANDARD** PPE as well as additional PPE for specific tasks as indicated below:

Standard	If splashing may occur ADD	Open or unventilated cages* ADD	Cage dumping (unless chemical fume hood or B2-ducted BSC is used) ADD	Double glove IF CHECKED
 Change gloves every 2 hours or when torn and/or contaminated.	 And/or  **OR** 	 **OR** 	 or  + or	☐  Change gloves every 2 hours or when torn and/or contaminated.

*Cages should be opened in ventilated cage-changing station, B2 (ducted) biological safety cabinet (BSC), or chemical fume hood.

Emergency Contact	Name	Work Phone	Afterhours Number
Primary			
Secondary			