

Animal Research Protocols Involving Hazardous Chemicals

I. OVERVIEW

Hazardous Chemicals: Known or suspected carcinogens, reproductive toxins or other highly toxic substances (e.g., anti-neoplastic agents), and nanomaterials may be used in laboratory animal research protocols. Reference the SU Chemical Hygiene Plan for hazardous chemical [definitions](#).

Potential Exposures: Research staff may be exposed to these hazardous chemicals during preparation, handling, and animal dosing. These substances may be excreted and/or secreted from the animal and, therefore, be present in the animal's bedding in extremely low concentrations. Animal husbandry staff and veterinarians may be exposed to these hazardous chemicals or their toxic metabolites during cage handling or when handling medicated water or feed.

How to Use this Guide: This guidance provides information for Principal Investigators to consider when **planning** and **conducting** their animal protocol involving hazardous chemicals so that appropriate controls are established in order to minimize potential exposure of laboratory personnel, husbandry staff, and veterinarians. See Section IV for a quick guide summarizing the general safety practices for: hazardous chemical preparation and handling; animal dosing; and cage management.

II. PLANNING YOUR ANIMAL PROTOCOL

1 Identify Hazards of Chemicals

SU Chemical Hygiene Plan

Hazardous chemicals usage in animal research protocols falls under the [SU Chemical Hygiene Plan](#).

As with any laboratory operation, the Principal Investigator (PI) and researchers must identify and understand the hazards associated with the chemical (e.g., toxicity, reactivity, flammability, corrosivity, etc.) before they begin their work so that appropriate controls can be established.

Intrinsic Hazards of Chemical

Review Safety Data Sheets (SDSs) and other sources of safety information to understand the hazards of the chemical and any other special considerations.

Suggested Sources of Safety Information on Hazardous Chemicals

- SU's SDS database: <http://msds.stanford.edu>
- SU's Chemical Hazard Class Definitions: <https://ehs.stanford.edu/reference/chemical-hazard-class-definitions>
- SU's reproductive & developmental health protection program: <https://ehs.stanford.edu/topic/health-wellness/reproductive-and-developmental-health-protection>
- SU's nanomaterials safety page: <https://ehs.stanford.edu/topic/hazardous-materials/nanomaterials>

- California Proposition 65 list: <http://oehha.ca.gov/prop65.html>
- NIH PubChem search: <https://pubchem.ncbi.nlm.nih.gov/>
- National Toxicology Program Report on Carcinogens: <https://ntp.niehs.nih.gov/pubhealth/roc/index-1.html>
- Common drugs considered hazardous by OSHA: <https://www.osha.gov/SLTC/hazardousdrugs/index.html>

Animal Metabolism of the Chemical

It is important to understand how the chemical is metabolized in a specific animal species so that appropriate controls can be implemented for safe animal and cage management after dosing. A review of peer-reviewed literature may yield this information, but it is often not documented. In the absence of such data, follow controls provided in Section III below.

Medical Surveillance

Medical surveillance and/or use of an antidote may, on the rare occasion, be required if the hazardous chemical used in an animal protocol is known to pose a serious health risk, such as diphtheria toxin or 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP). The PI must identify these chemicals during the safety literature review for the experiment and consult with EH&S's Laboratory Safety Program at 723-0448.

② Submit Protocol for APLAC Review

- Complete the Administrative Panel on Laboratory Animal Care (APLAC) [eProtocol form](#).
 - Describe the proposed use of hazardous chemicals in question #8 of the "Are You Using?" section.
 - Indicate that controls provided in Section III below will be implemented or its equivalent as described in your lab's Standard Operating Procedure (SOP) in Section III below.

Failure to properly identify hazardous chemical use may result in inadequate provision of chemical safety measures and may delay APLAC approval.

③ Coordinate with the Veterinary Service Center

- Contact the [Veterinary Service Center](#) (VSC) at 723-3876 at least two weeks before beginning the project to obtain:
 - Permission to use the facility
 - Room assignment
 - Provisions for appropriate cage labeling and waste management
- Provide a copy of the SOP, SDS or other hazard information so the VSC can ensure their personnel have chemical-specific hazard training.

III. CONDUCTING YOUR ANIMAL PROTOCOL

① Hazardous Chemical Preparation and Handling

- Follow the Standard Operating Procedure (SOP) established by the Principal Investigator. A [VSC SOP template](#) can be modified to reflect the experimental procedures. At minimum, handle hazardous chemicals using:
 - Laboratory fume hood or other appropriate engineering control.
 - Appropriate personal protective equipment (PPE): safety eyewear, chemical-resistant gloves appropriate for the chemical, and lab coat over appropriate street clothing (long pants and closed-toe shoes).
 - When filtering solutions by syringe, use a Luer lock syringe with the syringe filter to reduce risk of splash/spray.
- Ensure research personnel are trained on the SOPs and specific hazards associated with the chemicals. Ensure proper waste management. Maintain training documentation for at least one year.

② Animal Dosing and Care

- Wear appropriate personal protective equipment: disposable solid-front gown, head and shoe coverings, safety glasses/goggles, and chemical-resistant gloves (double gloving recommended).
- Appropriately restrain or sedate animals per your APLAC protocol to reduce the possibility of accidental self-inoculation. Contact the VSC if your procedure does not allow for restraints or sedation.
- If administering hazardous chemical by:
 - **Injection:** Use safety syringe and follow [sharps handling procedures](#) as described in the Biosafety Manual. If unable to use a safety syringe, you must document the reasons for this.
 - **Tablet:** Avoid liberating dust.
 - **Topical Application:** Avoid direct dermal contact with animal's application site.
 - **Water/Feed:** Minimize aerosolization (e.g., do not shake feed into dispenser).
 - **Aerosolization:** Use the fume hood or biosafety cabinet ducted to the outdoors. If unable to use these equipment, contact EH&S for a respirator assessment.
- Place animals back into cage and label cage with "Pink Card" (see below).
- Decontaminate lab surfaces and equipment using wet wiping methods with appropriate cleaning agent.
- Dispose sharps, chemical waste and PPE properly. Wash hands after removing gloves.

3 Cage Management

HOUSING

- If feasible, consider using disposable cages or alternative bedding (e.g., paper liner) to minimize potential aerosolization of the hazardous chemical during cage changing.
- Maintain cages on ventilated racks or with microisolator lids.

SIGNAGE

- Label cages with the “Pink Card” as follows:
 - Indicate the following information: “Animals treated with [name of chemical]. Excreta/bedding may be contaminated.” Affix “Hazardous Drug” sticker to card.
 - Indicate dosage and date/time animal was dosed.
 - Also label water bottle/feeder if hazardous chemical is administered via water/feed.
- Maintain label on cage for 72 hours after last dosing AND until contaminated bedding is changed, unless longer time frames are required as identified in the risk assessment during the planning phase.

CAGE CLEANING/BEDDING MANAGEMENT

(For all cage cleanings/bedding disposals performed up to 72 hours after animal dosing AND until contaminated bedding is changed, unless risk assessment requires longer time frame).

- Wear appropriate personal protective equipment (PPE): long-sleeved lab coat or disposable gown, chemical-resistant gloves, and safety glasses. Also use goggles/face shield, plastic apron, rubber boots or disposable plastic booties, where splash potential exists during cage washing.
- Place contaminated cage (with bedding, water and feed) into the bin specially marked “Chemotherapy Waste – For Incineration Only” at the ventilated dump station to ensure proper disposal by the VSC. Outside the VSC, a laboratory fume hood should be used to dump contaminated bedding (thoroughly wet down bedding to help minimize dust generation) into a bag and collected in a bin specially marked “Chemotherapy Waste – For Incineration Only” or tagged as chemical waste. To obviate this disposal requirement, contact the EH&S Environmental Programs Manager at 723-0448 for an assessment.
 - Respirators may be required if any of the aforementioned engineering controls are not feasible. Contact EH&S at 723-0448 for guidance.
 - Do not use laminar flow hoods which are commonly found in VSC animal rooms. These units do not provide personnel protection.
- For large animal pens (e.g., pig/sheep runs) follow VSC procedures: hose down waste into the sewer, do not direct jet stream at excreta, etc.
- Manage animal carcasses as pathological waste (i.e., tissues must be incinerated).
- Remove gloves and wash hands after working with animals, cages, and contaminated bedding.

CLEANUP OF WATER/FOOD SPILLS

(If hazardous chemical has been added to water/feed)

Assuming that the person is knowledgeable about the hazards of the chemical and has the appropriate spill cleanup materials, proceed as follows for [small spills](#) (less than 30 ml):

- Wear appropriate personal protective equipment (PPE): long-sleeved lab coat, chemical-resistant gloves, and safety glasses. Also use goggles/face shield, plastic apron, rubber boots or disposable plastic booties, where splash potential exists during cage washing.
- Transfer animals to clean cages via VSC procedures.
- At a ducted ventilated dump station or laboratory fume hood, dump contaminated material in the bin specially marked “Chemotherapy Waste – For Incineration Only” to ensure proper disposal.
 - Respirators may be required if any of the aforementioned engineering controls are not feasible. Contact EH&S at 723-0448 for guidance.
 - Do not use laminar flow hoods which are commonly found in VSC animal rooms. These units do not provide personnel protection.
- If unable to or not prepared to clean up a spill, call EH&S at 725-9999.

IV. SUMMARY OF HAZARDOUS CHEMICAL EXPOSURE CONTROLS:

	Hazardous Chemical Prep and Handling	Animal Dosing	Cage Management
Personal Protective Equipment	<ul style="list-style-type: none"> • Safety goggles/glasses • Chemical-resistant gloves • Long sleeved lab coat • Appropriate street clothing (long pants and closed-toe shoes) 	<ul style="list-style-type: none"> • Disposable solid-front gown with lab coat • Head and shoe coverings • Safety goggles/glasses • Chemical-resistant gloves (double-gloving) • Appropriate street clothing 	<ul style="list-style-type: none"> • Long sleeved lab coat or gown • Safety glasses/goggles • Chemical-resistant gloves • Also use face shield, plastic apron, rubber boots or disposable plastic booties when splash potential exists; e.g. hosing down large animal cages, pens and runs <p>Note: If engineering controls described below are not feasible, contact EH&S for respirator assessment.</p>
Work Practices/ Engineering Controls	<p>Prepare and handle hazardous chemical in a laboratory fume hood, including weighing, mixing, filtering and heating.</p> <p>NOTE: Do not use positive laminar flow hoods (commonly found in VSC animals rooms) - air flows towards worker.</p> <p>Ensure fume hood and eyewash/safety shower are currently certified and maintained.</p> <p>Ensure personnel are trained on the SOP and the specific chemical hazards.</p> <p>Ensure proper disposal of sharps, PPE and chemical waste.</p> <p>Wash hands after removing gloves.</p>	<p>For injections: Ensure animals are appropriately restrained per your research protocol to reduce possibility of accidental self-inoculation and use safety syringe. Follow sharps handling procedures per Biosafety Manual.</p> <p>Use fume hood when administering hazardous chemicals by aerosolization. If tablets are administered, avoid liberating dust. Consult EH&S for respirator assessment if fume hood is not used.</p> <p>For topical application, avoid dermal contact with animal's application site.</p> <p>Ensure proper disposal of sharps, PPE and chemical waste.</p> <p>Wash hands after removing chemical-resistant gloves.</p>	<p>Maintain cages on ventilated racks or with microisolator lids.</p> <p>Follow VSC guidelines on transporting animals.</p> <p>Consider using disposable cages or using alternative bedding (e.g., paper liner) to minimize aerosolization of bedding containing hazardous chemicals.</p> <p>Cage cleaning: Dump cages with hazardous chemicals contained in the bedding, food and/or water at the ventilated dump station into collection bin labeled "Chemotherapy waste – For incineration only" or in the fume hood, thoroughly wet down bedding to help minimize dust generation; gently dump into bag and place in collection bin labeled "Chemotherapy waste – For incineration only."</p> <p>For large animal pens (e.g., pig/sheep runs) follow VSC cleaning protocols (e.g. hose down sewer, do not direct jet stream at excreta).</p> <p>Wash hands after removing chemical-resistant gloves.</p>
Labeling/ signage	<ul style="list-style-type: none"> • Ensure proper storage and labeling of hazardous chemical. • Consult chemical manufacturer's instructions and/or SU's Chemical Safety Database. 		<p>If hazardous chemical will be present in cage:</p> <ul style="list-style-type: none"> • Label the cage with "Pink card" and Hazardous Drug sticker with the following information: <i>Animals treated with "name of chemical." Excreta/ bedding/ water/ feed may be contaminated. Do not change cage without wearing appropriate personal protective equipment per the SOP.</i> • Indicate date and time animal was dosed. • Maintain pink card for 72-hours after last dosing and until contaminated bedding/water/feed is changed.
Disinfection	Decontaminated lab surfaces and equipment with appropriate cleaning agents.		