



# Chemotherapeutic Drugs in Research Fact Sheet

***This fact sheet is for general safety awareness. Individual Standard Operating Procedures for all experiments and processes involving chemotherapeutic hazards must be developed by the laboratory.***

## **INTRODUCTION**

The hazards inherent in chemotherapy drugs (cancer chemotherapeutic drugs, antineoplastic agents or cytotoxic drugs) makes them harmful to healthy cells and tissues as well as cancerous cells. For cancer research using rodents, use of these agents can be necessary. However, for researchers who may be exposed to chemotherapy drugs as part of their work, precautions must be taken to eliminate or reduce the potential for exposure as much as possible. In a research laboratory setting, researchers may be exposed to chemotherapy drugs by skin contact, inhalation of agent, or aerosol produced during preparation, administration or rodent bedding cleanup activities.




Principal Investigators are required to assess the exposure hazards of their work with chemotherapeutic drugs to determine the appropriate precautions and controls to be taken to develop a safe procedure. Principal investigators must provide researchers laboratory-specific training for the specific agents they are working with. Work with particularly hazardous substances requires special provisions for employee protection. Materials designated as particularly hazardous substances include chemotherapeutic drugs. The following is required when working with chemicals having these designations:

- Prior approval required from principal investigator before use
- Establishment of a designated area

These items should be addressed in your lab’s procedure-specific standard operating procedures that require use and handling of chemotherapeutic drugs.

## **PROPERTIES & HAZARDS**

Chemotherapeutic drugs have various hazards depending on the type of drug that are listed on the safety data sheet (SDS). In Section 2 – Hazard Identification of the SDS, a combination of the following hazard classifications, pictograms and hazard statements will be listed for chemotherapeutic drugs. More information on material hazards can be found in complete hazard and precautionary statements.

<b>Hazard Classification and Category</b>	<b>Pictogram</b>	<b>Hazard Statement</b>
Toxic to Reproduction – Category 1A, 1B and 2		May damage fertility or the unborn child Suspected of damaging fertility or the unborn child May cause harm to breast-fed children
Carcinogenicity – Category 1A, 1B and 2		May cause cancer Suspected of causing cancer
Germ Cell Mutagenicity – Category 1A, 1B and 2		May cause genetic defects Suspected of causing genetic defects

## **CHEMOTHERAPEUTIC DRUGS**

The following table contains some of the typical chemotherapeutic drugs used in research using rodents and the length of time it takes a mouse to fully metabolize the drug after final administration. This list is not all inclusive. These times should be used to specify the length of time during which cage bedding becomes contaminated with the drug from mouse excreta. During the stated

times, cage bedding shall be treated as hazardous waste. Where no data was found on metabolism times for a given drug, a conservative estimate of period of 5 days was used. As these metabolism times are for mice, shorter or longer times may be more appropriate for other animals.

<b>Chemotherapeutic Drug</b>	<b>Mouse Metabolism Time After Final Administration</b>
Streptozotocin (STZ) <sup>4,5</sup>	3 days
Doxorubicin <sup>6,7</sup>	4 days
Tamoxifen <sup>9</sup>	3 days
Bromodeoxyuridine (BrdU) <sup>9</sup>	2 days
5-Fluorouracil (5-FU) <sup>10</sup>	4 days
Cyclophosphamide*	5 days
Busulfan <sup>12</sup>	5 days
Estradiol**	3 days
Progesterone**	3 days
Methotrexate (MTX)*	5 days
Fluvastatin*	5 days
Testosterone**	3 days
Fadrozole*	5 days

- Drugs for which metabolism time references were not found for presence in the urine or feces were given a default time period of 5 days which is the longest time period from a drug with a reference. This is denoted with a \*.
- When administered hormones create no greater than physiologic levels in the body no special treatment of animal bedding is required. Above these levels the designated metabolism time is denoted with a \*\*.

### **DRUG HANDLING AND PREPARATION**

Handling and preparation include any weighing, solution preparation, mixing of doses and dilution of the drug. Safe handling and preparation of the drug requires the following controls and personal protective equipment.

#### **Engineering Controls**

##### Liquid Drugs

- Chemical fume hood
- Biological Safety Cabinet, Class II, Type B2 (100% exhaust)
- Glovebox

##### Solid Drugs

- Chemical fume hood (recirculating or exhausted)
- Biological Safety Cabinet
- Glovebox

These engineering controls provide the best protection against exposure in the laboratory. Generally, chemical fume hoods are the preferred ventilation control device in laboratories unless a glovebox or biosafety cabinet is warranted.

#### **Personal Protective Equipment**

- Double Gloves – Generally nitrile or neoprene provide adequate protection against minor splashes/contact for most chemicals. Consult glove manufacturer’s chemical compatibility guides for best glove selection, or alternative glove types if needed for specific chemicals that penetrate nitrile or neoprene. SDS recommendations on glove type should be reviewed.
- Splash goggles
- Lab Coat
- Clothing that leaves no exposed skin on legs or feet
- Closed-toe shoes that fully cover the top of the foot

#### **Waste**

Non-animal waste that contains chemotherapeutic drug shall be submitted as hazardous waste following standard labeling protocol to ESSR, Environmental Affairs. For questions involving waste, contact Environmental Affairs at [envaffairs@umd.edu](mailto:envaffairs@umd.edu).

## **ANIMAL PROCEDURES AND MANIPULATION**

The following shall be considered during administration of doses, cage manipulations and animal handling. Chemotherapeutic drugs will be excreted in the feces and urine of the mouse after drug administration for the period specified in the above table and contaminate cage bedding and the animal itself. Instructions must be followed when handling animals during the specified time periods until the first cage cleaning following the specified metabolism times after final administration.

### **Signage**

Cages of animals treated with chemotherapeutic drugs must be clearly labeled with pink cage stickers saying "Chemotherapeutic Agent - Caution" and the date of the last administration of the drug. To get additional information on pink cage stickers contact the Biosafety Group at [biosafety@umd.edu](mailto:biosafety@umd.edu).

### **Engineering Controls**

Administration of doses, cage manipulations and handling of animals that could cause bedding dust to become airborne must be performed in a chemical fume hood, biological safety cabinet, or HEPA filtered change station during the metabolism times indicated in the table above and until the first bedding change thereafter.

### **Personal Protective Equipment**

- Gloves
- Splash goggles
- Lab Coat
- Clothing that leaves no exposed skin on legs or feet
- Closed-toe shoes that fully cover the top of the foot
- N95 Disposable Facemask - If activities are conducted outside of an engineering control device. To wear a facemask researchers will need to be enrolled in the UMD Respiratory Protection Program as voluntary users. To enroll contact the Occupational Safety Group at [osh@umd.edu](mailto:osh@umd.edu).

### **Waste**

Non-animal waste containing chemotherapeutic drug shall be submitted as hazardous waste following standard labeling protocol to ESSR, Environmental Affairs. For questions involving waste contact Environmental Affairs at [envaffairs@umd.edu](mailto:envaffairs@umd.edu).

## **CAGE CLEANING**

Cages should not be initially cleaned by autoclave or standard cage washing. If autoclaving or standard cage washing is eventually desired, the following cleaning measures must be done first. Any cage bedding change within the metabolism time periods specified in the table above, and the first cage bedding change thereafter, must be performed using the controls and procedures listed below.

### **Engineering Controls**

A chemical fume hood, biological safety cabinet, or HEPA filtered cage change station should be used while removing all bedding materials and conducting initial cleaning activities. If cage cleaning activities occur outside of an engineering control N95 disposable facemasks must be worn and the surfaces of the area cleaned after the activity using the materials described under "Initial Cleaning" below.

### **Initial Cleaning**

The interior of cages shall be cleaned with a towelette or wipe saturated with an acceptable cleaning agent such as 1:10 sodium hypochlorite and water solution, or Clidox-S per manufacturer mixing instructions, followed by a wipe down with 70% isopropyl alcohol.

### **Personal Protective Equipment**

- Double Gloves
- Safety Glasses
- Lab Coat
- Clothing that leaves no exposed skin on legs or feet
- Closed-toe shoes that fully cover the top of the foot

- N95 Disposable Facemask - If activities are conducted outside of an engineering control device. To wear a facemask researchers will need to be enrolled in the UMD Respiratory Protection Program as voluntary users. To enroll contact the Occupational Safety Group at [osh@umd.edu](mailto:osh@umd.edu).

### **Animal Waste and Bedding**

Bedding material and cleaning wipes and waste must be double bagged in a red biohazard bag and placed in a biohazard burn box. The biohazard burn box shall be labeled with pink stickers, Chemotherapeutic Agent – Caution, and be submitted to ESSR, Environmental Affairs for disposal. To get additional information on pink cage stickers contact the Biosafety Group at [biosafety@umd.edu](mailto:biosafety@umd.edu). For questions regarding waste management contact ESSR, Environmental Affairs at [envaffairs@umd.edu](mailto:envaffairs@umd.edu).

### **REFERENCES AND ADDITIONAL RESOURCES**

1. OSHA [A Guide to the Globally Harmonized System of Classification and Labeling of Chemicals \(GHS\)](#)
2. OSHA [Occupational Exposure to Hazardous Chemicals in Laboratories](#)
3. Prudent Practices in the Laboratory: Handling and Disposal of Chemical, National Academy Press, Washington, DC, 1995.
4. [Preparation, Administration, Handling and Care of Streptozotocin](#), Texas Tech University
5. [SOP #708 Use of Streptozotocin in Rodents](#), McGill University
6. [SOP Doxorubicin Safe Handling, Disposal, and Storage Procedures](#), Laurentian University
7. [Working with Doxorubicin and Treated Animals](#), University of Toronto
8. [Animals Administered a Hazardous Substance Requiring Containment](#), University of Michigan
9. [Exposure assessment of laboratory workers to hazardous waste from mice treated with tamoxifen and bromodeoxyuridine](#), Journal of Chemical Health and Safety
10. [The Physiological Disposition of 5-Fluorouracil in Mice Bearing Solid L1210 Lymphocytic Leukemia](#), Cancer Research
11. [Waste Handling and Patient Excreta](#), International Society of Oncology Pharmacy Practitioners Standards of Practice
12. [Clarifying Busulfan Metabolism and Drug Interactions to Support New Therapeutic Drug Monitoring Strategies: A Comprehensive Review](#), National Institutes of Health, National Library of Medicine, PubMed