

Antineoplastic Agents Lab Safety

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1. Purpose and Applicability

1. This generic chemical safety guidance describes a basic prudent safety practice for handling antineoplastic agents, including bulk drugs and formulated solutions in research labs.
2. This guidance is applicable to all researchers who handle antineoplastic agents in research labs and animal handling facilities, including OAR.
3. This guidance is not applicable to UIHC patient care areas or pharmaceuticals formulation areas.
4. The principal investigator (PI) or lab manager is solely responsible for developing and implementing standard operating procedures (SOPs) for specific hazardous drug(s) used in their research lab.
5. Researchers should review the product specific safety data sheets (SDSs) and/or pharmaceutical product inserts before handling any hazardous drug, including agents listed herein.
6. The antineoplastic drug list identified within this guidance is not exhaustive. Therefore, researchers are advised to refer to [OSHA safety guidance](#) and references listed therein. The [NIOSH list](#) of antineoplastic agents and other hazardous agents includes cancer chemotherapy agents, antiviral agents, hormones, and other miscellaneous agents.

2. Health Effects of Antineoplastic Agents

Danger:

Antineoplastic agents are typically used as cancer chemotherapeutic agents. The majority of antineoplastic agents are carcinogenic in animals or humans. Such agents can damage chromosomes (mutagens) and/or the fetus (teratogens).

NIOSH defines “Pharmaceutical Drugs” as “Hazardous Drugs” if toxicology studies in animals or humans indicate that exposures to these drugs can cause carcinogenic, teratogenic, or reproductive toxic effects on target organs or cellular mechanisms.

Antineoplastic agents are “**anti-cancer pharmaceutical drugs**” used for the treatment of cancer. These agents are highly toxic to living cells and therefore known as “cytotoxic drugs”. Antineoplastic agents are also described as chemotherapeutic agents, and oncology drugs. Antineoplastic hazardous agents are genotoxic, teratogenic, carcinogenic, or toxic to other target organs even at very low concentrations. Antineoplastic agents may also be used to treat other medical conditions such as rheumatoid arthritis, multiple sclerosis, and other auto-immune disorders.

Antineoplastic agents are classified into seven groups as below:

- A. **Alkylating agents:** Alkylating agents undergo alkylation by a nucleophilic substitution reaction with cellular constituents, such as DNA base pairs, cell membranes, proteins, and proteins.
- B. **Antitumor antibiotics:** The antitumor antibiotics are synthesized from microorganisms. The antitumor antibiotics either break-up DNA strands, slow, or stop DNA synthesis.
- C. **Antimetabolites:** Antimetabolites are structurally similar to metabolites required for normal biochemical reactions. Antimetabolites interfere with cellular processes such as cell division.

- D. **Nitrosoureas:** Nitrosoureas act similar to that of alkylating agents and slow down or stop enzymes that help repair DNA.
- E. **Mitotic agents (plant alkaloids):** Plant alkaloids break DNA strands and prevent cell replication.
- F. **Hormonal agents:** Steroids lyse lymphoblasts and thus directly cause lymphoid malignancies.
- G. **Miscellaneous agents:** Though mechanisms of miscellaneous agents are not well understood, these agents probably inhibit DNA, RNA, and protein synthesis.

All antineoplastic or cytotoxic agents are universally identified by a purple symbol. This symbol represents a cell late in the process of division known as telephase.



Universal warning symbol for antineoplastic agents

Examples of antineoplastic agents, along with potential occupational exposure hazards, are summarized in Appendices A to H. However, caution must be exercised, as antineoplastic agents classified in a specific group may belong to a different group based on biochemical interactions with cells.

If researchers do not handle or conduct experiments with antineoplastic agents within proper engineering controls or do not use appropriate personnel protective equipment (PPE), adverse health effects may result from occupational exposures to these hazardous drugs. Potential health effects include:

- Abnormal cell formation and mutagenic activity,
- Alterations to normal blood cell counts,
- Fetal loss in pregnant women,
- Liver damage,
- Hair loss,
- Skin or mucous membrane irritation or an allergic reaction,
- Abdominal pain, and
- Nausea and vomiting.

3. Emergency/Medical Treatment

Antineoplastic agents should be washed off immediately after exposure (even at very low concentrations). These chemicals can be irritating to the respiratory tract, eyes, and skin.

- The affected area should be immediately rinsed off with copious amounts of cold water for at least 15-20 minutes using the safety shower or eyewash, as appropriate. Then, researchers should seek **medical attention** by going to the [UI HealthWorks](#) or [UIHC emergency treatment center \(ETC\)](#), as appropriate.
- If the spill occurs near or around the eyes, irrigate eyes with cold water for at least 20 minutes. Then proceed to UIHC emergency treatment center (ETC) for **medical treatment**.
- Call 911 for medical emergency.

4. Engineering Controls

Warning:

If your research does not permit handling of antineoplastic agents in a fume hood or a biological safety cabinet, researchers should contact EHS at 335-8501 for risk assessment before conducting work.

Fume hoods and biosafety cabinets provide the best protection against exposure to reproductive hazards and carcinogens and are the preferred engineering control devices in research labs. Therefore, manipulation of antineoplastic agents should be carried out in a fume hood as depicted below.



- Antineoplastic agents formulated in volatile solvents should not be used in a biological safety cabinet, unless the biosafety cabinet is vented outside of the lab.
- A face-shield is strongly recommended when there is a risk of splash hazard, even if the work is performed within the fume hood or biosafety cabinet.
- Placement of a portable process safety shield within the antineoplastic drug handling hood or on the designated workbench will provide protection to the researcher and their research colleagues who may be working nearby.

- Avoid exposure to aerosol sprays from solutions and solids. Before opening, sterile gauze should be wrapped around the neck of the ampoule, injectable vial, or reagent bottle containing dry/lyophilized antineoplastic powder.
- Manipulation of antineoplastic agents outside the fume hood may require special ventilation devices to minimize exposure. Any specialized engineering controls should be designed and/or approved by experts.

5. Safety Equipment

Eyewash

Whenever eyes or skin is exposed to antineoplastic agents, flush eyes and skin with water at least for 15 to 20 minutes. Ensure an eyewash station is available for immediate use within research lab areas. Periodic testing of eyewashes is recommended.



Safety shower

Ensure a safety shower is available in research labs or nearby corridors or in washrooms in certain locations.

6. Personal Protective Equipment (PPE)

At minimum, a disposable lab coat, long sleeved clothing or a coverall, safety glasses with side shields, closed toed shoes, and double Nitrile (or Latex) gloves should be worn when handling antineoplastic agents.

Gloves

Wear double Nitrile gloves (or Latex gloves) when handling antineoplastic agents or when there is a potential for contact with antineoplastic agents contaminated items or work surfaces. Kimberly Clark KC500 Purple Nitrile gloves or other equally or more protective gloves are recommended for handling antineoplastic agents.

Coverall

Wear disposable gowns/coveralls made of low permeability fabric with a closed front, long sleeves, and elastic or knit cuffs while preparing antineoplastic agents or conducting other hazardous drug

handling activities. At the end of hazardous drug handling activities, researchers should remove and dispose of gowns/coveralls as if they were contaminated with hazardous drug. Disposable gowns/coveralls should be periodically replaced based on the hazardous drug handling activity, or at least at the end of the work day. Disposable gowns/coveralls should be replaced immediately after a splash or spill occurs.

Eye protection and face shield

Safety glasses with side shields or goggles should be worn at all times when handling antineoplastic agents. Wear a face shield with goggles or safety glasses to protect against splashes to the eyes, nose, and mouth.

Dust Masks/Respirators

A N95, R95, P95 dust mask, or more protective half/full face piece respirator should be worn for respiratory protection during a spill cleanup. A dust mask/respirator should also be worn whenever there is significant risk of exposure through inhalation during preparation and administration of antineoplastic agents. Disposable dust masks should be disposed of after each use or at least at the end of the work day. Before any planned respirator or dust mask use in the research lab, a **respirator use evaluation is needed** by EHS. Please contact EHS at 335-8501 to request a dust mask/respirator use evaluation.

The use of a full face piece respirator with appropriate chemical cartridge is strongly recommended for handling large spills of hazardous drugs including hazardous drug solutions reconstituted in aqueous-organic solvent mixture or intravenous (IV) solutions. If half/full face respirators are used, cartridges should be replaced as per manufacturer recommendations.

7. Prudent Work Practices

Prudent safety precautions should be exercised to eliminate or minimize hazardous drug exposure to respiratory, skin, alimentary, and gastrointestinal/digestive systems. Researchers handling antineoplastic agents in research labs should anticipate these occupational risks.

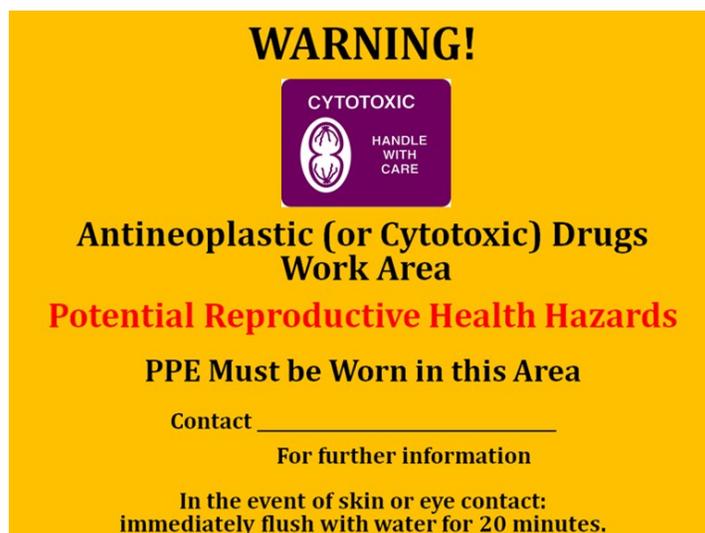
- Label hazardous drug containers in accordance with OSHA hazard communication standards and the Chemical Hygiene Plan.
- Prepare antineoplastic agents in designated work areas to limit or minimize occupational exposures in research labs.
- Use a plastic lined absorbent sheet to cover antineoplastic agents work area.
- Store and transport antineoplastic agents in a manner that minimizes the risk of breakage.
- When antineoplastic drug preparation is completed, seal the hazardous drug product in a container for safe transport before removing the drug out of a chemical fume hood or biosafety cabinet.

Designated Work Area

Antineoplastic use labs should provide a "Designated work area". Any area where antineoplastic agents are stored or manipulated should be defined and communicated to other lab staff. The intent of a designated work area is to inform others about the hazardous drug work so they can avoid the area if they are not fully trained. Communicate with other lab members about the

antineoplastic drug work so they understand its hazards and use precautions near the area where hazardous agents are being handled.

Antineoplastic agents should be manipulated over disposable plastic-backed absorbent sheet work surfaces to minimize work area contamination and to simplify clean up and disposal of waste.



Example Sign for Designated Work Area for Handling Antineoplastic Agents

Hazards Evaluation and Process Risks Reduction Assessment

- A hazard evaluation should be conducted prior to working with the antineoplastic agents. Steps to reduce potential exposure and risk should be identified.
- These steps including safe work practices, protective equipment and engineering controls should be incorporated into a standard operating procedure for the materials used.
- Researchers should contact EHS at 335-8501 for any questions related to safe handling of antineoplastic agents in research labs.

Standard Operating Procedures (SOPs)

A written SOP for safe handling of antineoplastic agents should include: laboratory staff training, PPE, receiving and storage, labeling, preparation and manipulation of antineoplastic agents in physicochemical studies or animals, equipment used, housekeeping practices, glassware decontamination, spill cleanup, and disposal of antineoplastic agents as hazardous waste.

SOPs for handling different forms of antineoplastic agents (i.e. tablet, injectable liquid, etc.) should also include anticipated exposures from different work activities or processes (e.g., weighing dry powder, standard solution preparation/dilution, concentration, evaporation or lyophilization of formulated solutions, drug release/diffusion study, etc.) and duration of such exposures in a typical work day (e.g., weighing 15 minutes).

Training

All researchers, including students, who handle the antineoplastic drug should receive training initially and as needed as a refresher. Basic safety training module on 'Antineoplastic Agents in Research Labs' can be accessed through the UI Employee Self Service website.

Storage

Antineoplastic agents should be stored in a designated lab area or in refrigerator. An updated chemical inventory should be maintained for antineoplastic or hazardous agents used or stored in a research lab.

Housekeeping

- Clean work surfaces and contaminated equipment and glassware within engineering controls before and after each handling activity and at the end of the work day.
- Eating or drinking is not allowed in areas where hazardous agents are handled.
- Wash hands with soap and water before donning gloves, immediately after removal, and whenever hands become contaminated with antineoplastic agents.

8. Decontamination

Precaution:

At a minimum, all contaminated (and potentially contaminated) work surfaces should be cleaned with detergent solution followed by several rinses with clean water.

There is no universal chemical reagent for the deactivation or decontamination all antineoplastic agents and formulated antineoplastic agents.

- Surfaces may be wiped with an appropriate deactivating agent such as paper towel wetted with diluted bleach, water containing surfactants, isopropyl alcohol, etc. or using the manufacturer's recommended cleanup procedures.
- Similarly, the outer surface of contaminated equipment should be wiped using isopropanol and water before removing them from the designated area.
- Glassware should be decontaminated and cleaned in a designated location.
- Wash hands and arms with soap and water immediately after handling antineoplastic agents.
- Waste materials generated from the decontamination procedures should be treated as hazardous waste and disposed of through EHS.

9. Spill Response

Precaution:

A N95, R95, P95 dust mask, or more protective half/full face respirators should be worn during an antineoplastic drug spill cleanup.

Please consult the EHS spill response guide, antineoplastic drug specific product insert, or safety data sheets for appropriate clean-up materials prior to the purchase and use of any antineoplastic agents. This is especially true when working with reproductive hazards.

- Spill kits should include spill cleanup materials and PPE, instructions, and waste containment bags.
- Antineoplastic spill kit may be purchased from commercial vendors, but are not required.
- Commercial vendors include Thermo-Fisher, Govidien, and Safetek, etc.

Depiction of Commercially available Spill Kit for Antineoplastic agents



(Govidien® Chemosafety Kit)

In the event of a spill, alert everyone in the immediate work area in the lab and the lab manager. Then, clean the spilled materials as per decontamination or spill procedures described in your Lab SOP

For spills of less than 5 ml solution or 5 mg solid outside a hood should be cleaned by wearing disposable gowns made of less permeable fabric, double Nitrile gloves, eye protection, and a N95, R95, or P95 dust mask. Spilled injectable liquids including HPLC autosampler vials should be wiped with absorbent gauze pads and solids should be wiped with wet absorbent gauze or towels. Then, spill areas should be cleaned using a detergent solution followed by copious amount of clean water.

For spills of larger than 5 ml solution, spread of the spill should be contained by covering with absorbent sheets or spill-control pads or pillows. For spills of larger than 5 g solid or powder, the spill should be contained with damp cloths or towels.

Broken glass fragments containing antineoplastic agents, contaminated absorbent material, gloves, etc. should be placed in a puncture resistant cardboard or plastic containers and these containers placed inside a sturdy waste bag (double bagging). Place this waste bag in a hard-sided sealable plastic container. Affix a completed large EHS hazardous waste label on the plastic container. Each of these containers should be marked or labeled as CYTOTOXIC WASTE.

Unbroken glassware or other contaminated reusable plastic-ware or tools should be placed in a plastic bag/receptacle and washed in a sink with detergent wearing double Nitrile gloves.

10. Waste disposal

All materials contaminated with antineoplastic agents must be disposed of as hazardous chemical waste.

- Antineoplastic drug waste solids and solutions should be contained separately from other hazardous chemical waste.
- Laboratory waste that is contaminated with trace amounts of antineoplastic agents (also known as trace contaminated hazardous drug waste and trace chemotherapy waste) should be contained separately and also disposed of as hazardous chemical waste, not as biohazardous waste in red tubs.
- Outer gloves and sleeve covers should be bagged and collected with antineoplastic drug contaminated laboratory waste.
- Containerize the waste that is contaminated with trace amounts of antineoplastic agents by placing the waste in a plastic bag, double bag; seal the bag and place in a hard-sided sealable plastic container. Label and seal the box for disposal.
- Needles and syringes must not be capped or bent, but must be directly placed in sharps container, also for disposal as hazardous chemical waste.
- Antineoplastic containing arsenic trioxide should be collected separately from any other antineoplastic agents.



Depiction of Example Label for Antineoplastic Agents/Cytotoxic Waste

- The outside of antineoplastic agent waste containers must be cleaned and free of contamination for disposal through EHS.
- Antineoplastic drug waste must be disposed of in accordance with EHS chemical waste policies and procedures including use of the hazardous waste label.
- Request waste pick up from EHS by completing the [online request form](#).

11. References

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18. T. Queruau Lamerie et al. Decontamination Efficacy of Cleaning Solutions Contaminated by Antineoplastic Agents. Ann. Occup. Hyg., Vol. 57, No. 4, pp. 456–469, 2013.
19. Handling Cytotoxic Drugs; A Health And Safety Review

12. Appendix

Note: Summary of physiochemical hazard and toxicity information has been extracted, if available, from chemical specific safety data sheets, internet key word search engines, and references identified herein.

- [Appendix A. Significant Antineoplastic Alkylating Agents](#)
- [Appendix B. Significant Antineoplastic Antitumor Antibiotics](#)
- [Appendix C. Significant Antineoplastic Antimetabolites](#)
- [Appendix D. Significant Antineoplastic Nitrosoureas](#)
- [Appendix E. Significant Antineoplastic Mitotic Agents \(Plant alkaloids\)](#)
- [Appendix F. Significant Antineoplastic Hormonal Agents](#)
- [Appendix G. Significant Antineoplastic Miscellaneous Agents](#)
- [Appendix H. Other Significant Cytotoxic Agents](#)
- [Appendix I. Example Sign for Designated Work Area](#)

13. Acknowledgement

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