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USP<800>

HAZARDOUS DRUGS- HANDLING IN OPHTHALMIC HEALTHCARE SETTINGS

LINDA KALATA RN BSN CNOR(E)

Purpose

Glaukos is providing this resource as an educational aid and reference for ophthalmic healthcare settings in the implementation of and compliance with requirements found in USP<800>. The scope of this document intentionally does not include the pharmacy or compounding facilities.

It is recommended that each facility consults with appropriate personnel, such as the consultant pharmacist, to ultimately determine applicability of the standards and receive guidance in preparing for compliance. Each facility is responsible for its compliance with USP<800>.

For additional information, the following resources are available:

USP<800>- Hazardous Drugs-Handling in Healthcare Settings

https://www.usp.org/products/usp-compounding-compendium

USP<800> FAQs- Updated January 21, 2026

https://www.usp.org-frequently-asked-questions

NIOSH List of Hazardous Drugs in Healthcare Setting, 2024

https://doi.org/10.26616/NIOSHPUB2025103

Mitomycin C and Ophthalmic Surgery

Mitomycin C (MMC) is a drug that has become a mainstay in many ophthalmic surgeries. It was first introduced by Japanese physicians in 1963 to treat pterygia. The first reported use of adjuvant MMC during trabeculectomy surgery was in 1983. Its ability to inhibit proliferation of fibroblasts prevents scarring of blebs created during glaucoma procedures, significantly increasing success rates.[1] MMC is an antineoplastic (chemotherapy) hazardous drug requiring strict protocols for handling to prevent worker exposure and environmental contamination.

What is USP <800>?

US Pharmacopeia (USP) is a nonprofit, scientific organization that publishes standards for quality, strength, purity, and consistency of medicines, ingredients and dietary supplements. The USP is published in a combined volume with the National Formulary (a formulary) as the USP-NF. Chapter 800 of the USP (USP <800>) describes practice and quality standards for handling hazardous drugs (HDs). The goal is to promote personal and patient safety, as well as environmental protection.

Studies throughout the 1980s and 1990s found that pharmacy and patient care areas were regularly contaminated by hazardous drugs (HDs), even in some cases when it was thought that standards were being followed.[2] Residue has been found in areas where HDs are compounded and administered, as well as on items such as pens, keyboards, and elevator buttons.[3]

A study by Falck et al.,1979, showed nurses who prepared and administered antineoplastic drugs had higher indicators of mutagenic substances in their urine than unexposed workers. The study suggested that nursing personnel were occupationally exposed to antineoplastic drugs.[4]
Numerous studies have shown elevations in biomarkers of genetic damage in HCWs who routinely handle antineoplastic drugs. A meta-analysis of 39 studies on occupational exposure to antineoplastic drugs confirmed a significant association between occupational exposure and increases in chromosomal aberrations in HCWs.[5] Given the potential for increased cancer risk linked to increases in chromosomal aberrations as well as other effects of exposure, the results support the need to limit exposure to HDs as much as possible.

When healthcare workers (HCWs) and other staff are uneducated about HDs and their risks, an attitude of complacency can develop.[6] Some health care facility policies may not include procedures for the OR where HDs may be used. When policies do exist, staff may be unaware of them. Although spills are a significant source of environmental contamination, proper cleaning and decontamination are often not performed.[7]

USP <800> establishes guidelines for standards of practice and covers all aspects of HD handling, which includes, but is not limited to, receipt, storage, containment, administration, compounding, and disposal.
USP <800> applies to all healthcare personnel who handle HDs and all facilities where HDs are stored, prepared, transported and/or administered.

Hazardous Drugs

The National Institute of Occupational Safety and Health (NIOSH) define hazardous drugs as having one or more of the following characteristics:

- Carcinogenicity- causes cancer
- Teratogenicity- causes birth defects
- Reproductive toxicity- affects fertility
- Organ toxicity in low doses
- Genotoxicity- causes genetic mutations
- New drugs that mimic existing drugs deemed hazardous by the above criteria are also considered hazardous

No permissible exposure levels have been established for HDs.[8] Despite the relatively small quantity of HDs used, for example, in ophthalmologic procedures, the risks associated with exposure in any amounts have not been determined. Due to this uncertainty, **guidelines have consistently warned against any exposure, regardless of volume or concentration.**[9]

Examples of Hazardous Drugs

- Antineoplastics- e.g. cancer chemotherapy
- Antiviral medications
- Hormones
- Some bioengineered drugs-
- Drugs with safe handling guidelines from manufacturer

Types of Exposure

Listed below are the routes of unintentional exposure when handling HDs:

- Skin absorption
- Mucosal absorption
- Inhalation of the liquid, powder or evaporated HD
- Injection
- Ingestion- i.e.; mouth contact from contaminated hands

Opportunities for Exposure

- Receiving drug from manufacturer
- Manipulation
    - Reconstitution
    - Expelling air from syringes
    - Cleaning items contaminated with HDs
    - Administration- generating aerosols during administration
    - Exposure to vapors coming from a drug in a cup on the sterile field
- Spills- spill generation, management and disposal
- Transport- transporting HDs within a healthcare setting
- Disposal- collecting and disposing of contaminated waste

List of Hazardous Drugs

NIOSH maintains a list of antineoplastic and other HDs used in healthcare. **Facilities where HDs are used must maintain a list of HDs** that are stocked that appear in the NIOSH List of Antineoplastic and Other Hazardous Drugs in Healthcare Settings.[10]

The list maintained by each facility must:

1. Be reviewed and edited as needed at least every 12 months
2. Be made available to all personnel with potential exposure to HDs, and personnel must be educated as to the location and nature of the list
3. Be updated when any new drug or dosage form is brought into the facility for use and must be checked against the NIOSH list

The common HDs used in the operating room for ophthalmic procedures are Mitomycin C (MMC) and 5-Fluorouracil (5-FU).

Responsibilities of Personnel Handling HDs

The facility must assign a designated person to ensure that all personnel who handle HDs understand the fundamental practices and precautions and are continually evaluating these procedures to prevent harm to patients, minimize exposure to personnel, and minimize contamination of the work and patient- care environment.

In summary, the designated person is responsible for:

- Developing and implementing standard operating procedures (SOPs), and reviewing every 12 months
- Overseeing compliance with USP 800 and other regulations and standards
- Understanding rationale for risk prevention policies
- Documenting and reporting potentially hazardous situations to management and follow-up
- Overseeing and documenting monitoring
- Overseeing and documenting training- ensuring competency of personnel

Hazard Communication Program

Facilities are required to establish policies and procedures that ensure employee safety during all aspects of HD handling.

Elements of the Hazard Communication Program plan must include:

- A written plan that describes how the standard will be implemented
- All containers of hazardous chemicals must be labeled with the identity of the material and appropriate hazard warnings
- Safety Data Sheets (SDS) required for all HDs and each hazardous chemical used in the facility
- SDSs must be readily accessible to all personnel
- Personnel who may be exposed to HDs must receive appropriate training based on job function before being assigned to work with the HD
- **Personnel of reproductive capability must sign a confirmation stating that they understand the risks of handling HDs -applies to women and men**

Staff Training

All personnel who handle HDs must be fully trained based on their job functions (e.g., in receipt, storage, transporting, administration and disposal of HDs).

- All personnel must be trained before handling HDs independently
- Competency for handling must be demonstrated and documented
- Competency must be reassessed and documented every 12 months
- Training must be documented

Training must include:

- Overview of the facility's list of HDs and risks
- Review of SOPs related to HDs
- Proper use of personal protective equipment (PPE)
- Proper use of closed system transfer devices (required for administration)
- Spill management
- Proper disposal of HDs and trace-contaminated materials

Risk Assessment

Some dosage forms of drugs defined as HDs may not pose a significant risk of exposure due to their dosage formulation. An assessment of risk may be performed for these dosage forms to determine if alternative containment strategies or work practices can be implemented. The assessment of risk must consider the following:

- Type of HD (e.g., antineoplastic, non-antineoplastic or reproductive risk only)
- Dosage form- physical form of drug made available for use
- Risk of exposure
- Packaging
- Manipulation required

If a risk assessment is not performed, all HDs must be handled with the containment strategies defined in USP800. If a risk assessment is performed, the facility must document what alternative containment strategies and work practices will be employed for specific dosage forms to minimize the risk of occupational exposure. This risk assessment must be reviewed and documented at least every 12 months, and whenever there are significant changes in processes, facilities or equipment.

Facilities and Engineering Controls

Facilities and engineering controls are implemented to ensure patient and employee safety and environmental protection.

- Signs designating that HDs are in use must be prominently displayed before the entrance to the HD handling areas.
- Areas where hazardous drugs are handled should be equipped with a sink available for hand washing, an eyewash station, and/or other emergency and safety precautions that meet applicable laws and regulations.

These controls would include:

Receipt- USP<800> states that HDs must be unpacked (i.e., removal from shipping containers) in an area that is neutral/normal or negative pressure while wearing at least one pair of ASTM D6978 chemotherapy-tested gloves. Full PPE, including 2 pairs of chemo-tested gloves, must be considered if receiving compounded antineoplastic drugs, such as MMC, to protect the employee due to the possibility of leaking inside the package. HDs must not be unpacked from their external shipping containers in sterile areas or in positive pressure areas.

Storage- USP<800> states that HDs must be stored in a manner that prevents any environmental contamination or exposure to healthcare personnel. For example, this could happen if a drug were to leak from its container in a refrigerator. Antineoplastic HDs that require refrigeration must be stored in a **dedicated** refrigerator in a negative pressure area with at least 12 air changes per hour (ACPH**).** Combining HDs with other medications in a refrigerator is prohibited and HDs and medications should never be stored in a refrigerator designated for food. **Areas where HDs are stored MUST be locked and labeled.**

Containment- Containment supplemental engineering controls, such as **closed-system transfer devices (CSTDs)**, provide additional levels of protection during administration.
CSTDs **must** be used when administering antineoplastic HDs when the dosage form allows.
CSTDs known to be physically or chemically incompatible with a specific HD must not be used for that HD.
There are several CSTDs on the market and users should carefully evaluate the performance claims associated with available CSTDs based on independent, peer-reviewed studies and demonstrated containment reduction.[11]

Labeling, Transport and Disposal

The facility must establish SOPs for the labeling, transport and disposal of HDs. The SOPs must address:

- Prevention of accidental exposures or spills
- Personnel training on response to exposure
- Use of a spill kit

Labeling

HDs and any HD containers (i.e. chemo bin) must be labeled at all times.
Areas where HDs are stored must be labeled.

Transport

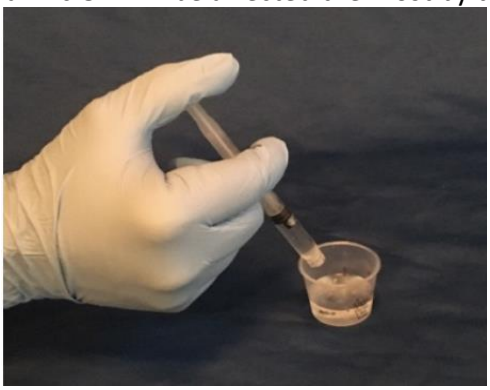
HDs must be transported in containers that minimize the risk of breakage or leakage. Pneumatic tubes must not be used to transport any liquid HDs or antineoplastic HDs because of the potential for breakage and contamination. USP 800 states that appropriate PPE should be worn when handling HDs, including during transport. i.e.; chemo-tested gloves.

Disposal

All personnel who perform routine custodial waste removal and cleaning activities in HD handling areas must be trained in appropriate procedures to protect themselves and the environment from contamination by HDs. Disposal of all HD waste, including, but not limited to, unused HDs and trace-contaminated PPE and other materials, must comply with all federal laws, which **require disposal in an appropriate HD bin. It is not acceptable to dispose of HD waste or trace-contaminated materials in regular trash, biohazard or medication bins.**

Administration

The facility must establish a SOP for the administration of HDs. HDs must be administered safely using protective medical devices and techniques.
Closed-system transfer devices (CSTDs) are now required for the administration of anti-neoplastic HDs when the dosage form allows to minimize contamination and exposure to personnel. **When utilizing sponges for administration, the CSTD must encompass both the sponges and the delivery of the antineoplastic HD to the sponges.**
This offers additional levels of protection during administration and reduces the potential for spills, aerosolization and hazardous vapors.
This section is where the ophthalmic OR will be affected the most by the standards set forth in USP 800.



Note: Squirting MMC into a cup on the sterile field is no longer an acceptable practice.

Appropriate PPE must be worn when administering HDs. **After use, PPE must be removed and disposed of in an HD waste container approved for trace-contaminated HD waste.** Devices used to administer HDs (i.e.; CSTDs, syringes, needles, etc.) are considered trace-contaminated and must be disposed of in an appropriate HD bin.

Personal Protective Equipment

The facility's SOP must describe the appropriate PPE to be worn based on its occupational safety plan and assessment of risk (if used). The entity must develop SOPs for PPE based on the risk of exposure (see Types of Exposure) and activities performed. Disposable PPE must not be reused.
While traditional OR garb is designed for sterility and to varying degrees protection against bodily fluids, USP 800 requires specialized PPE that protects against HDs.

This is a section where a risk assessment would be valuable in determining the PPE requirements. Keep in mind that you must use the criteria listed in the "Risk Assessment" section to assess the true risk of exposure to an HD. Risk assessments must be documented.

• **Gloves**: Two pairs of **ASTM 6978-05-tested** chemotherapy gloves are required.
• **Gowns:** USP 800 requires gowns that have been tested against HDs. Gowns must be closed in the front, allow for closing in the back, have long sleeves with elastic or knit cuffs. USP 800 states that disposable sleeve covers may be used to protect areas of the arm that may come in contact with HDs. Disposable sleeve covers made of polyethylene-coated polypropylene or other laminate materials offer better protection than those made of uncoated materials. Gowns are considered single use and disposable and cannot be washed or reused.
• **Eye/Face:** Appropriate eye and face protection must be worn if there is a risk of splashing. Eyeglasses or safety glasses with side shields do not provide adequate protection from a splash. USP 800 states that face shields in combination with goggles provide a full range of protection against splashes to the face and eyes and that face shields alone do not provide full eye and face protection. Once again, a risk assessment of exposure would be beneficial in this case to determine the best option for eye/face protection.
• **Masks:** A fit-tested, NIOSH-certified N95 respirator is required when handling HDs, however, **CDC/NIOSH states that no special respiratory protection is required for ophthalmologic applications.**[10] If N95 masks are used, fit testing must be done annually.
• **Shoes:** Shoe covers worn in areas where HDs are handled must be removed prior to leaving the area. This prevents tracking HD residue out of the area in which it was compounded or, in the case of the OR, where the drug was administered.

USP<800> states that gowns must be changed every 2-3 hours if information for permeation is not available from the manufacturer, and gloves must be changed every 30 minutes. This may be a situation where a risk assessment could determine if these times are applicable. Gloves must always be changed after cleaning a spill on the sterile field.
Appropriate PPE must be worn when handling HDs including during:

- Receipt
- Storage
- Transport
- Administration
- Deactivation/Decontamination, Cleaning, and Disinfecting

• Spill Control • Waste disposal

Deactivating, Decontaminating, Cleaning and Disinfecting

Surfaces that may become contaminated with HDs must undergo appropriate deactivation, decontamination, cleaning and disinfection.

Deactivation renders a compound inert or inactive. Residue from deactivation must be removed by decontaminating the surface.

Decontamination occurs by neutralizing or physically removing HD residue from non-disposable surfaces and transferring it to absorbent, disposable materials (e.g., wipes, pads, or towels). There is no one proven method for deactivating all compounds. For this reason, the use of disposable devices is recommended as they can be disposed of with the other hazardous waste. Products that have known deactivation properties (EPA-registered oxidizing agents that are appropriate for the intended use) should be used when possible.

Cleaning is a process that results in the removal of contaminants (e.g., soil, bioburden, microbial contamination, HD residue) from objects and surfaces using water, detergents, surfactants, solvents, and/or other chemicals. Cleaning of HD-contaminated ophthalmic instruments requires additional steps.

Surgical instruments that have come into contact with HDs must be handled and cleaned as follows:

- Instruments that come into contact with MMC including, but not limited to, the forceps used to apply and remove a sponge soaked with MMC and the speculum, must be isolated from the other instruments on the surgical field.
- These instruments should be wiped with an instrument wipe designed for ophthalmic instruments to remove MMC residue **prior to leaving the OR** for processing.
- These instruments must be soaked in a facility-approved, **non-enzymatic detergent** for 10 minutes. After soaking, the detergent should be poured down the drain of an empty sink, and the sink should be rinsed well. The instruments should be rinsed well, then cleaned and processed as usual per facility policy.[11]

- PPE must be worn when pre-washing MMC-contaminated instruments. Disposable gloves must be worn and immediately disposed of as contaminated waste.
- Distilled or deionized water should be used for the final rinse.
- A system must be in place to alert the Sterile Processing department that the OR instruments are contaminated with HDs to avoid potentially spreading HD contamination to other departments or facilities and to protect the sterile processing employee from exposure.

Disinfection must be performed for sterile manipulations. The purpose of disinfection is to inhibit or destroy microorganisms. Before disinfection can be adequately performed, surfaces must be cleaned.

Spill Control

HD spills must be contained and cleaned immediately only by qualified personnel trained in spill cleanup. All HD spills must be disposed of as hazardous waste. Personnel who may be required to clean an HD spill must receive proper training in spill management and proper use of PPE.

Cleaning a HD spill ON the sterile field:

1. While double-gloved with chemotherapy-tested gloves, place a stack of 4x4 gauze pads onto the spill- HOLD AND BLOT.
2. Immediately dispose of contaminated 4x4 gauze pads into appropriate chemotherapy bag or bin.
3. Change gloves.
4. Cover area where spill occurred with a folded disposable towel to contain the drug residue.
5. Contaminated drape and disposable towel must be disposed of into chemotherapy bin.

Cleaning a HD spill OFF the sterile field:

Circulating nurse or other disignated individual should utilize a chemotherapy spill kit to clean the spill. The kit contains proper items, including PPE, and instructions to clean the spill. All contaminated items must be disposed of into chemotherapy bin.

Documentation of HD spills:

Documentation of HD spills must contain the following:

1. Circumstances of how the spill occurred.
2. Details of how the spill was cleaned and disposed of.
3. An action plan to prevent this type of spill from occurring again.

Utilize your facility's existing documenting forms that are used for unusual occurrences (i.e.; incident reports).

SOPs must be developed to prevent spills and to direct the clean-up of HD spills:

- SOPs must address who is responsible for spill management and the type of PPE required.
- The SOP must address the location of spill kits and clean-up materials.
- The SOP address steps for cleanup on sterile field.

Documentation and Standard Operating Procedures

All sites must maintain SOPs for the safe handling of HDs for all situations in which these HDs are used throughout a facility. The SOPs must be reviewed at least every 12 months by the designated person and the review must be documented. Revisions in forms or records must be made as needed and communicated to all personnel handling HDs.
The recommended SOPs for USP<800> Compliance are:

- List of HDs and process for re-evaluation
- Receiving and storage
- Packaging and delivery
- Use of proper engineering controls (e.g.; CSTDs)
- Hand hygiene and use of PPE based on activity
- Administration of HDs
- Cleaning, deactivating, decontaminating, and disinfecting HDs
- Disposal of HDs
- HD spill prevention and control
- Training, education and competency requirements

Personnel who handle, transport, or administer HDs must have their training documented according to OSHA standards (see OSHA Standard 1910.120 Hazardous Waste Operations and Emergency Response) and other applicable laws and regulations.[12]

Medical Surveillance and Follow-Up Plan

It is recommended, but not required, to institute a medical surveillance program to identify any problems to healthcare workers from potential exposure to HDs as early as possible and to remediate if necessary.
Also, it is recommended, but not required, to institute a follow-up post HD exposure that evaluates the health of the exposed worker and addresses any deficiencies in exposure control mechanisms.[13]

Environmental Quality and Control

USP 800 recommends, but does not require, the performance of environmental wipe sampling to evaluate the effectiveness of containment strategies and work practices. Currently, there is no standard for acceptable limits for HD contamination of surfaces.[14]

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