TECHNICAL INFORMATION PAPER

U.S. ARMY PUBLIC HEALTH CENTER

SAFE HANDLING OF HAZARDOUS DRUGS
HAZARD COMMUNICATION

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PURPOSE. This Technical Information Paper provides guidance for the safe handling of the National Institute for Occupational Safety and Health (NIOSH) list of Hazardous Drugs (HD). It does not change any existing Department of the Army (DA) directives, policies, or procedures related to handling of HD or HD usage at DA medical treatment facilities (MTFs).

REFERENCES.

DA. 2017. Technical Bulletin, Medical 515, Occupational Health and Industrial Hygiene Guidance for the Management, Use and Disposal of Hazardous Drugs.

U.S. Department of Health and Human Services (DHHS). 2012. U.S. Public Health Service, National Institute for Occupational Safety and Health (NIOSH). June 2012. DHHS (NIOSH) Publication No. 2012-150—NIOSH List of Antineoplastic and other Hazardous Drugs in Healthcare Settings, 2012

U.S. Pharmacopeia Convention (USP). 2016. *USP Compounding Compendium.* Rockville, Maryland: USP

DHHS. U.S. Public Health Service, NIOSH. 2008. DHHS (NIOSH) Publication No. 2009-106—Personal Protective Equipment for Health Care Workers Who Work with Hazardous Drugs

DA. 2013. Army Regulation 11-34, The Army Respiratory Protection Program.

APPLICABILITY

This TIP addresses the safe handling practices associated with HD use at DA MTFs. This TIP is applicable to all DA MTF personnel and all DA Industrial Hygienists.

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BACKGROUND

In the healthcare setting, it would appear counter-intuitive that there would be drugs regularly prescribed that are considered hazardous since the primary goal of all healthcare workers is to "do no harm." Unfortunately there are a large number of drugs that are prescribed that can do harm when people are unintentionally exposed. In 1990, the American Society of Hospital Pharmacists initially coined a definition for HD. Shortly afterwards, NIOSH took the pharmaceutical societies' definition of HD and refined it to—

> *Drugs considered Hazardous include those that exhibit one or more of the following six characteristics in humans or animals:*
> - *Carcinogenicity*
> - *Tetrogenicity or other developmental toxicity*
> - *Reproductive toxicity*
> - *Organ toxicity at low doses*
> - *Genotoxicity*
> - *Structure and toxicity profiles of new drugs that mimic existing drugs determined hazardous by the above criteria*

From this definition, NIOSH developed a list of drugs that are considered hazardous, and the list is continually expanding. Due to the exposure possibility in Army MTFs, Technical Bulletin, Medical 515 was published to provide guidance.

The U.S. Army Public Health Center (APHC) has worked to ensure that these lifesaving, yet dangerous drugs are handled appropriately and safely in the MTF. To understand the extent of potential exposure across the U.S. Army, a team from APHC has been conducting sampling at Army-owned MTFs since 2014. During this time, it became evident that even with the most stringent handling practices, residual HD contamination on surfaces is possible. There exists the potential for residual HD contamination anywhere within the MTF where HD travelled.

SAFE HANDLING OF HAZARDOUS DRUGS

a. General Guidelines.

Due to the nature of HD, special care must be given to the proper receiving, storage, handling, and dispensing of this type of medication. Anyone who is to handle HD must be trained to ensure the minimal exposure to work personnel, proper exposure to patients, and to minimize possible contamination.

Although eliminating use of HD would protect the work personnel with the greatest efficiency, these HD are essential to the modern practice of medicine. Therefore, following proper administrative and engineering controls, as well as the judicious employment of personal protective equipment (PPE), will ensure the least possible exposure of work personnel.

Any MTF that has HD must establish policies and procedures to ensure that all HD handling is done in a manner that ensures worker safety. These policies and procedures must be written and accessible by the workforce at the MTF. Additionally, a listing of all HD used at the MTF, as well as their respective Safety Data Sheets (SDS), must be provided. Prior to any personnel initially conducting work with HD or before use of a new HD, all personnel must be trained on the proper handling and hazards of the HD. All personnel of reproductive capacity must confirm their understanding of the risks associated with handling HD in writing.

b. Administrative Controls.

The use of administrative controls is essential to help promote a proper understanding of HD. Administrative controls should include the following:

- Designated HD storage areas within the MTF pharmacy
- Designated HD counting areas within the MTF pharmacy
- Signs designating HD areas
- Controlled access to designated HD areas
- Signs demarcating HD specific counting trays

Several administrative controls are required for employment by USP <800>: Hazardous Drugs—Handling in Healthcare Settings.

- Drugs designated to be HD must be stored separately from non-HD medications.
- Refrigerated HD must be stored in a dedicated HD refrigerator in a negative pressure area with a minimum of 12 air exchanges per hour.
- Unpacking shipments of HD cannot take place within a positive-pressure room.
- Unpacking shipments of HD cannot take place in sterile-compounding areas.

c. Engineering Controls.

Engineering controls provide the most reliable protection from unintended exposure to HD, as long as the systems are well maintained. Depending on the type of work, different engineering controls are needed.

General Hazardous Drug Storage

All HD should be segregated from the general drug population within the MTF. This location should be well labeled with general signage, and each HD should be prominently labeled as HD. For HD requiring refrigeration, the refrigerator must be located in a negatively pressured room, with a minimum of twelve (12) air exchanges an hour.

General Counting of Hazardous Drugs

For HD that are not manipulated (that is those HD that are counted or dispensed without producing particles), no engineering controls are necessary. Even though no specific engineering controls are necessary, a separate counting tray should be used only for HD. This tray should be well labeled and stored in a unique location away from general drug counting trays.

Compounding of Hazardous Drugs

While compounding activities occur, USP <800> requires both primary and secondary engineering controls to be in place. Two types of compounding are recognized by USP <800>, sterile and non-sterile, each with different requirements. Regardless of type of compounding all HD compounded, the following requirements should be followed:

- Primary engineering controls (PEC) should be located within a secondary engineering control (SEC).
- Secondary engineering control should be externally vented.
- Exhaust from the engineering controls should be high-efficiency particulate air (HEPA) filtered prior to venting.
- Secondary engineering control, which is an identified, signed room, should be physically separated from other preparation areas.
- Secondary engineering controls should be at negative pressure relative to all adjacent areas.

Non-Sterile Compounding of Hazardous Drugs

For compounding of HD that does not require a sterile environment, the SEC should have at minimum 12 air exchanges an hour. Additionally, the PEC should be externally vented or at minimum have exhaust air redundant HEPA filtered in series. The PEC can be a Class I or Class II biological safety cabinet (BSC) or a compounding aseptic containment isolator (CACI).

Sterile Compounding of Hazardous Drugs

Hazardous drugs that are compounded sterilely can be compounded in either of two SEC environments. The preferred SEC is an International Organization of Standardization (ISO) Class 7 “Clean” room with the unclassified dedicated room as the non-preferred SEC. In either type of SEC, the room must be externally ventilated and be negatively pressurized relative to adjacent rooms. For an ISO Class 7 room, a minimum of 30 air exchanges per hour is required. For a non-classified SEC room, a minimum of 12 air exchanges per hour is required.

For sterile compounding of HD, the PEC can either be a Class II BSC or a CACI. With either a Class II BSC or a CACI, an ISO Class 5 environment must be maintained to ensure sterile compounding. The PEC must be negatively pressured relative to the SEC. Additionally, after each use, sterilization and decontamination must take place.

PERSONAL PROTECTIVE EQUIPMENT

Use of PPE is considered to be the least preferred means of protection against HD. This is due to the effectiveness of the protection being fully dependent upon the employee using the proper PPE. Although it is the least preferred, it is an essential portion of the daily use of HD within the MTF.

Due to the primary route of unintended exposure to HD contacting unprotected skin, proper chemotherapy tested gloves must be worn while handing HD. During compounding activities, further PPE should be worn to meet the criteria of the location of compounding. Additionally during a spill clean-up, additional PPE should be worn, including but not limited to, eye protection, airway protection, and additional body protection in the form of gowns or coveralls.

At any point, the worker may employ more than the minimally required PPE while working with HD.

CLEANING

Cleaning of areas that are in contact with HD should occur regularly to ensure the minimal amount of residual HD on surfaces where contact can be made. The cleaning must ensure that the HD agent has been sufficiently removed and disinfected to ensure patient safety.

Cleaning of counting and storage areas must ensure that all residual HD at the location are rendered inert or inactive and are removed along with any other organic or inorganic compounds. During the cleaning of compounding areas, an additional disinfection step must be completed.

a. Counting Areas.

Areas within the pharmacy that are used for counting solid forms of HD should be cleaned at least daily when HD is being dispensed. For pharmacies with a high volume of HD traffic, more frequent cleanings are recommended. These areas include, but are not limited to, HD counting trays, HD counting workbenches, and HD prescription confirmation locations. See table 1 for suggested cleaning procedure.

Table 1. Cleaning Procedure for HD Counting Areas

Cleaning Step	Purpose	Suggested Agents
1. Deactivation	Render HD inert or inactive	- Agent listed on HD labeling - Sodium Hypochlorite (Bleach) - U.S. Environmental Protection Agency (EPA)-Registered Oxidizer
2. Decontamination	Remove inactivated HD	- Sterile alcohol - Sterile water - Peroxide - Sodium Hypochlorite (Bleach)
3. Cleaning	Remove additional organic or inorganic material	Germicidal detergent and sterile water

b. Compounding Areas.

Areas within the pharmacy that compound HD should be cleaned at least daily when HD is being dispensed. Those pharmacies with a large demand for compounded HD should consider cleaning multiple times a day, to prevent cross contamination of compounded materials. Locations that are considered compounding areas include, but are not limited to, “clean rooms,” laminar flow hoods, compounding aseptic containment is Table 2 for cleaning procedures for compounding areas.

Table 2. Cleaning Procedure for HD Compounding Areas

Cleaning Step	Purpose	Suggested Agents
1. Deactivation	Render HD inert or inactive	- Agent listed on HD labeling - Sodium Hypochlorite (Bleach) - EPA-Registered Oxidizer
2. Decontamination	Remove inactivated HD	- Sterile alcohol - Sterile water - Peroxide - Sodium Hypochlorite (Bleach)
3. Cleaning	Remove additional organic or inorganic material	Germicidal detergent and sterile water
4. Disinfection	Destroy Microorganisms	- Sterile alcohol - EPA-Registered Disinfectant

c. Storage Areas.

Hazardous drug storage areas become contaminated via transfer of HD from the exterior surface of HD storage containers. These locations should be on a rotation of cleaning at least quarterly. The areas to be cleaned include the physical storage location (i.e., bench, storage shelf, or refrigerator) as well as the secondary containment for the drug. See Table 3 for suggested cleaning procedure.

Table 3. Cleaning Procedure for HD Counting Areas

Cleaning Step	Purpose	Suggested Agents
1. Deactivation	Render HD inert or inactive	- Agent listed on HD labeling - Sodium Hypochlorite (Bleach) - EPA-Registered Oxidizer
2. Decontamination	Remove inactivated HD	- Sterile alcohol - Sterile water - Peroxide - Sodium Hypochlorite (Bleach)
3. Cleaning	Remove additional organic or inorganic material	Germicidal detergent and sterile water

SPILL PROCEDURES

A spill of HD requires immediate action to help prevent unintended exposure. Due to nature of the HD, untrained persons should be encouraged to not attempt to clean spills. Spill clean-up procedure varies depending on state of spilled HD (i.e. liquid, powder, tablet) and container type.

a. Personal Protective Equipment.

To ensure limited exposure of HD to personnel responsible for cleaning spills appropriate, PPE should be worn during clean-up procedures. This PPE consists of, but is not limited to:

- Disposable gown
- Disposable gloves (chemotherapeutic grade or two pairs of nitrile)
- Face shield
- Appropriate respiratory protection (employees must complete all required Respiratory Protection Program elements prior to use (see Army Regulation 11-34))

Upon completion of cleanup, all PPE should be disposed of in appropriate chemotherapy waste containers. Additionally, care should be taken to properly clean any exposed body parts with soap and water.

b. Liquid Spills.

Spills of liquid HD materials can often be accompanied by broken glass and sharps. Care should be taken not to create injuries from broken materials accompanying the spilled liquid HD. The following procedure is recommended for cleaning of a spill of liquid HD materials:

- Carefully remove any sharps from site of spill, place into appropriate sharps container.
- Carefully remove any broken glass or plastic, place into appropriate chemotherapy waste container.
- Use an absorbent pad to absorb liquid HD materials. Dispose of used absorbent pad in appropriate chemotherapy waste container.
- Follow appropriate deactivating, decontaminating, and cleaning procedures from above.

c. Powder/Tablet Spills.

Spills of dry materials, powders, or tablets should be cleaned up with a damp cloth. Care should be taken not to allow dry HD materials to become airborne; therefore, do not use a broom to clean these materials. The following procedure is recommended for cleaning a spill of solid dry HD materials:

- Remove any non-powdered solid materials (e.g., pills, tablets, caplets) and place in chemotherapy waste containers.

- Take damp gauze or disposable dampened cloths and collect powdered material. Use multiple dampened materials to collect all visible material.
- Follow appropriate deactivating, decontaminating, and cleaning procedures from above.

ROUTINE SURVEILLANCE VIA SAMPLING

Periodic surveillance via wipe sampling is a requirement of Technical Bulletin, Medical 515. This surveillance is used to determine the level of residual surface contamination and the effectiveness of engineering controls, work practices, and cleanup procedures from daily use of HD.

The industrial hygienist (IH) will conduct periodic sampling. The frequency of surveying will be dependent on the changes to HD being used, procedures, operations, equipment, and environmental controls, as well as upon the IH's professional judgement. Generally, sampling is conducted no less frequently than annually. Initial sampling will be conducted as a baseline to determine the initial levels of HD to be expected.

The IH may conduct two different types of sampling: screening sampling or specific sampling. During the periodic sampling, the IH will screen for a number of the drugs specifically used at the facility. If any of those drugs are above the action limit, as set forth in TB MED 515, the IH will ask the facility to clean the locations and conduct a specific sampling for those HD that were above the action limit.

All sampling is to be coordinated with the APHC Laboratory Sciences Division (LAB). The LAB will supply all sampling materials needed, to include wetting agent, sampling swabs, collection vials, and sampling templates. The IH will be responsible for coordinating with the individual pharmacies to conduct the sampling. Upon completion of sampling, the samples will be returned to LAB for analysis.

The installation IH will receive an analytical report of the results of sampling. Any sample location that has a result above the action limit for any of the selected HD, must clean and resample that location. If contamination persists, cause analysis must be conducted.

MEDICAL SURVEILLANCE

Although enrollment in medical surveillance is not a requirement, NIOSH recommends that all workers, who may be exposed to HD either directly or by

waste products, be enrolled into an HD medical surveillance program. The goal of the program is to minimize adverse health effects of HD by identifying the earliest reversible biological effects in individuals who may be exposed. The intended enrollees to the program include the following roles:

- Pharmacists
- Pharmacy Technicians
- Nurses
- Physicians
- Physician Assistants

Prior to beginning work with HD, the medical surveillance should include a general and reproductive health questionnaire. Additionally, a baseline clinical evaluation should also be conducted prior to beginning of work with HD. This evaluation should include a physical examination, laboratory testing, and a targeted medical history. Annual surveillance should include a history of handling HD and any known exposures during the intervening time period. A plan must be in place for workers who show a negative change due to exposure to HD.

CONTACTS

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