USP <800> Must(s)

1. Introduction & Scope

Entities that handle HDs **must** incorporate the standards in this chapter into their occupational safety plan.

The entity's health and safety management system **must**, at a minimum, include:

- A list of HDs
- Facility and engineering controls
- Competent personnel
- Safe work practices
- Proper use of appropriate Personal Protective Equipment (PPE)
- Policies for HD waste segregation and disposal

2. List of Hazardous Drugs

An entity must maintain a list of HDs, which **must** include any items on the current NIOSH list that the entity handles.

The NIOSH list of antineoplastic and other HDs provides the criteria used to identify HDs. These criteria **must** be used to identify HDs that enter the market after the most recent version of the NIOSH list, or that the entity handles as an investigational drug.

Drugs on the NIOSH list that **must** follow the requirements in this chapter include:

- Any HD API
- Any antineoplastic requiring HD manipulation

If an assessment of risk is not performed, all HDs **must** be handled with all containment strategies defined in this chapter.

- The assessment of risk **must**, at a minimum, consider the following:
    - Type of HD (e.g., antineoplastic, non-antineoplastic, reproductive risk only)
    - Dosage form
    - Risk of exposure
    - Packaging
    - Manipulation

If an assessment of risk approach is taken, the entity **must** document what alternative containment strategies and/or work practices are being employed for specific dosage forms to minimize occupational exposure.

If used, the assessment of risk **must** be reviewed at least every 12 months and the review documented.

4. Responsibilities of Personnel Handling Hazardous Drugs

Each entity **must** have a designated person who is qualified and trained to be responsible for developing and implementing appropriate procedures; overseeing entity compliance with this chapter and other applicable laws, regulations, and standards; ensuring competency of personnel; and ensuring environmental control of the storage and compounding areas.

- The designated person **must** thoroughly understand the rationale for risk prevention policies, risks to themselves and others, risks of noncompliance that may compromise safety, and the responsibility to report potentially hazardous situations to the management team.
- The designated person **must** also be responsible for the oversight of monitoring the facility and maintaining reports of testing/sampling performed in facilities and acting on the results.

5. Facilities and Engineering Controls

HDs **must** be handled under conditions that promote patient safety, worker safety, and environmental protection. Signs designating the hazard **must** be prominently displayed before the entrance to the HD handling areas. Access to areas where HDs are handled **must** be restricted to authorized personnel to protect persons not involved in HD handling. HD handling areas **must** be located away from breakrooms and refreshment areas for personnel, patients, or visitors to reduce risk of exposure.

Designated areas **must** be available for:

- Receipt and unpacking
- Storage of HDs
- Nonsterile HD compounding (if performed by the entity)
- Sterile HD compounding (if performed by the entity)

Antineoplastic HDs and all HD APIs **must** be unpacked (i.e., removal from external shipping containers) in an area that is neutral/normal or negative pressure relative to

the surrounding areas. HDs **must not** be unpacked from their external shipping containers in sterile compounding areas or in positive pressure areas.

HDs **must** be stored in a manner that prevents spillage or breakage if the container falls. In areas prone to specific types of natural disasters (e.g., earthquakes) the manner of storage **must** meet applicable safety precautions, such as secure shelves with raised front lips.

Antineoplastic HDs requiring manipulation other than counting or repackaging of final dosage forms and any HD API **must** be stored separately from non-HDs in a manner that prevents contamination and personnel exposure. These HDs **must** be stored in an externally ventilated, negative-pressure room with at least 12 air changes per hour (ACPH).

Refrigerated antineoplastic HDs **must** be stored in a dedicated refrigerator in a negative pressure area with at least 12 ACPH [e.g., storage room, buffer room, or containment segregated compounding area (C-SCA)].

Sterile and nonsterile HDs **must** be compounded within a C-PEC located in a C-SEC. The C-SEC used for sterile and nonsterile compounding **must**:

- Be externally vented
- Be physically separated (i.e., a different room from other preparation areas)
- Have an appropriate air exchange (e.g., ACPH)
- Have a negative pressure between 0.01 and 0.03 inches of water column relative to all adjacent areas

The C-PEC **must** operate continuously if it supplies some or all of the negative pressure in the C-SEC or if it is used for sterile compounding.

If there is any loss of power to the C-PEC, or if repair or moving occurs, all activities occurring in the C-PEC **must** be suspended immediately.

A sink **must** be available for hand washing. An eyewash station and/or other emergency or safety precautions that meet applicable laws and regulations **must** be readily available. Care **must** be taken to locate water sources and drains in areas where their presence will not interfere with required ISO classifications. Water sources and drains **must** be located at least 1 meter away from the C-PEC.

For entities that compound both nonsterile and sterile HDs, the respective C-PECs **must** be placed in separate rooms, unless those C-PECs used for nonsterile compounding are sufficiently effective that the room can continuously maintain ISO 7 classification throughout the nonsterile compounding activity. If the C-PECs used for sterile and nonsterile compounding are placed in the same room, they **must** be placed at least 1 meter apart and particle-generating activity **must** not be performed when sterile compounding is in process.

The C-PECs used for manipulation of nonsterile HDs must be either externally vented (preferred) or have redundant-HEPA filters in series. Nonsterile HD compounding **must** be performed in a C-PEC that provides personnel and environmental protection, such as a Class I Biological Safety Cabinet (BSC) or Containment Ventilated Enclosure (CVE).

- A Class II BSC or a compounding aseptic containment isolator (CACI) may also be used.

For occasional nonsterile HD compounding, a C-PEC used for sterile compounding (e.g., Class II BSC or CACI) may be used but **must** be decontaminated, cleaned, and disinfected before resuming sterile compounding in that C-PEC.

- A C-PEC used only for nonsterile compounding does not require unidirectional airflow because the critical environment does not need to be ISO classified.

The C-PEC **must** be placed in a C-SEC that has at least 12 ACPH.

Due to the difficulty of cleaning HD contamination, surfaces of ceilings, walls, floors, fixtures, shelving, counters, and cabinets in the nonsterile compounding area **must** be smooth, impervious, free from cracks and crevices, and non-shedding.

In addition to this <800>, sterile compounding **must** follow standards in <797>.

All C-PECs used for manipulation of sterile HDs **must** be externally vented. Sterile HD compounding must be performed in a C-PEC that provides an ISO Class 5 or better air quality, such as a Class II or III BSC or CACI. Class II BSC types A2, Bl, or B2 are acceptable.

A laminar airflow workbench (LAFW) or compounding aseptic isolator (CAI) **must not** be used for the compounding of an antineoplastic HD.

A BSC or CACI used for the preparation of HDs **must not** be used for the preparation of a non-HD unless the non-HD preparation is placed into a protective outer wrapper during removal from the C-PEC and is labeled to require PPE handling precautions.

The C-PEC **must** be located in a C-SEC, which may either be an ISO Class 7 buffer room with an ISO Class 7 ante-room (preferred) or an unclassified containment segregated compounding area (C-SCA).

- If the C-PEC is placed in a C-SCA, the beyond-use date (BUD) of all compounded sterile preparations (CSPs) prepared must be limited as described in <797> for CSPs prepared in a segregated compounding area.

The buffer room **must** be externally vented.

A hand-washing sink must be placed in the ante-room at least 1 meter from the entrance to the HD buffer room to avoid contamination migration into the negative pressure HD buffer room.

- If the negative-pressure HD buffer room is entered though the positive-pressure non-HD buffer room, the following is also required:
    - A line of demarcation **must** be defined within the negative-pressure buffer room for donning and doffing PPE
    - A method to transport HDs, HD CSPs, and HD waste into and out of the negative pressure buffer room to minimize the spread of HD contamination. This may be accomplished by use of a pass-through chamber between the negative-pressure buffer area and adjacent space. The pass-through chamber must be included in the facility's certification to ensure that particles are not compromising the air quality of the negative-pressure buffer room. A refrigerator pass-through **must not** be used. Other methods of containment (such as sealed containers) may be used.

The C-SCA **must** be externally vented.

A hand-washing sink **must** be placed at least 1 meter from C-PEC and may be either inside the C-SCA or directly outside the C-SCA.

Only low and medium risk HD CSPs may be prepared in a C-SCA. HD CSPs prepared in the CSCA **must not** exceed the BUDs described in <797> for CSPs prepared in a segregated compounding area.

A CSTD **must not** be used as a substitute for a C-PEC when compounding. 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.

7. Personal Protective Equipment
Disposable PPE **must** not be re-used.

Reusable PPE **must** be decontaminated and cleaned after use.

The entity **must** develop SOPs for PPE based on the risk of exposure activities performed.

Appropriate PPE **must** be worn when handling HDs including during:

- Receipt
- Storage
- Transport
- Compounding (sterile and nonsterile)
- Administration
- Deactivation/decontamination, cleaning, and disinfecting
- Spill control
- Waste disposal

When chemotherapy gloves are required, they **must** meet American Society for Testing and Materials (ASTM) standard D6978 (or its successor).

Chemotherapy gloves **must** be powder-free

When used for sterile compounding, the outer chemotherapy gloves **must** be sterile.

Chemotherapy gloves **must** be changed when torn, punctured, or contaminated.

Hands **must** be washed with soap and water after removing gloves.

When gowns are required, they **must** be disposable and shown to resist permeability by HDs.

Gowns **must** be selected based on the HDs handled.

Gowns **must** close in the back (i.e., no open front), be long sleeved, and have closed cuffs that are elastic or knit.

Gowns **must** not have seams or closures that could allow HDs to pass through.

Potentially contaminated clothing **must** not be taken home under any circumstances.

Gowns **must** be changed per the manufacturer's information for permeation of the gown.

- If no permeation information is available for the gowns used, change them every 2-3 hours or immediately after a spill or splash.

Gowns worn in HD handling areas **must not** be worn to other areas in order to avoid spreading HD contamination and exposing other healthcare workers.

When compounding HDs, a second pair of shoe covers **must** be donned before entering the CSEC and doffed when exiting the C-SEC.

Shoe covers worn in HD handling areas **must not** be worn to other areas to avoid spreading HD contamination and exposing other healthcare workers.

Appropriate eye and face protection **must** be worn when there is a risk for spills or splashes of HDs or HD waste materials when working outside of a C-PEC (e.g., administration in the surgical suite, working at or above eye level, or cleaning a spill).

Goggles **must** be used when eye protection is needed.

Surgical masks do not provide respiratory protection from drug exposure and **must** not be used when respiratory protection from HD exposure is required.

Chemotherapy gloves and sleeve covers (if used) worn during compounding **must** be carefully removed and discarded immediately into a waste container approved for trace contaminated waste inside the C-PEC or contained in a sealable bag for discarding outside the C-PEC.

8. Hazard Communication Program

The entity **must** develop SOPs to ensure effective training regarding proper labeling, transport, storage, and disposal of the HDs and use of Safety Data Sheets (SDS),

based on the Globally Harmonized System of Classification and Labeling of Chemicals (GHS).

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, tagged, or marked with the identity of the material and appropriate hazard warnings
- Entities must have an SDS for each hazardous chemical they use (29 CFR 1910.1200)
- Entities must ensure that the SDSs for each hazardous chemical used are readily accessible to personnel during each work shift and when they are in their work areas
- Personnel who may be exposed to hazardous chemicals when working must be provided information and training before the initial assignment to work with a hazardous chemical, and also whenever the hazard changes
- Personnel of reproductive capability must confirm in writing that they understand the risks of handling HDs

9. Personnel Training

All personnel who handle HDs **must** be trained based on their job functions (e.g., in the receipt, storage, compounding, repackaging, dispensing, administrating, and disposing of HDs).

Training **must** occur before the employee independently handles HDs.

The effectiveness of training for HD handling competencies **must** be demonstrated by each employee.

Personnel competency **must** be reassessed at least every 12 months.

Personnel **must** be trained prior to the introduction of a new HD or new equipment and prior to a new or significant change in process or SOP.

All training and competency assessment **must** be documented.

The training must include at least the following:

- Overview of entity's list of HDs and their risks
- Review of the entity's SOPs related to handling of HDs
- Proper use of PPE

- Proper use of equipment and devices (e.g., engineering controls)
- Response to known or suspected HD exposure
- Spill management

10. Receiving
The entity **must** establish SOPs for receiving HDs

HDs **must** be delivered to the HD storage area immediately after unpacking.

PPE, including chemotherapy gloves, **must** be worn when unpacking HDs

A spill kit **must** be accessible in the receiving area.

The entity **must** enforce policies that include a tiered approach, starting with visual examination of the shipping container for signs of damage or breakage (e.g., visible stains from leakage, sounds of broken glass).

Damaged packages or shipping cartons **must** be considered spills that must be reported to the designated person and managed according to the entity's SOPs.

Clean-up **must** comply with established SOPs.

11. Labeling, Packaging, Transport, and Disposal
The entity **must** establish SOPs for the labeling, packaging, transport, and disposal of HDs.

- The SOPs **must** address prevention of accidental exposures or spills, personnel training on response to exposure, and use of a spill kit.

HDs identified by the entity as requiring special HD handling precautions **must** be clearly labeled at all times during their transport.

Personnel **must** ensure that the labeling processes for compounded preparations do not introduce contamination into the non-HD handling areas.

Personnel **must** select and use packaging containers and materials that will maintain physical integrity, stability, and sterility (if needed) of the HDs during transport.

Packaging materials **must** protect the HD from damage, leakage, contamination, and degradation while protecting healthcare workers who transport HDs.

The entity **must** have written SOPs to describe appropriate shipping containers and insulating materials, based on information from product specifications, vendors, and mode of transport.

HDs that need to be transported **must** be labeled, stored, and handled in accordance with applicable federal, state, and local regulations.

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 any antineoplastic HDs because of the potential for breakage and contamination.

When shipping HDs to locations outside the entity, the entity **must** consult the Transport Information on the SDS.

The entity **must** ensure that labels and accessory labeling for the HDs include storage instructions, disposal instructions, and HD category information in a format that is consistent with the carrier's policies.

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 to prevent HD contamination.

Disposal of all HD waste, including, but not limited to, unused HDs and trace-contaminated PPE, and other materials, **must** comply with all applicable federal, state, and local regulations.

12. Dispensing Final Dosage Forms

Counting or repackaging of HDs **must** be done carefully.

Tablet and capsule forms of antineoplastic HDs **must not** be placed in automated counting or packaging machines, which subject them to stress and may create powdered contaminants.

13. Compounding
Entities and personnel involved in compounding HDs **must** be compliant with the appropriate USP standards for compounding, Including <795> and <797>.

Compounding **must** be done in proper engineering controls as described in *Compounding*.

Disposable or clean equipment for compounding (such as mortars and pestles, and spatulas) **must** be dedicated for use with HDs.

Bulk containers of liquid and API HD **must** be handled carefully to avoid spills.

- If used, APIs or other powdered HDs must be handled in a C-PEC to protect against occupational exposure, especially during particle-generating activities (such as crushing tablets, opening capsules, and weighing powder).

14. Administering
HDs **must** be administered safely using protective medical devices and techniques.

Appropriate PPE **must** be worn when administering HDs.

After use, PPE **must** be removed and disposed of in a waste container approved for trace contaminated HD waste at the site of drug administration.

Equipment (such as tubing and needles) and packaging materials **must** be disposed of properly, such as in HD waste containers, after administration.

CSTDs **must** be used for administration of antineoplastic HDs when the dosage form allows.

Techniques and ancillary devices that minimize the risk posed by open systems **must** be used when administering HDs through certain routes.

If HD dosage forms do require manipulation such as crushing tablet(s) or opening capsule(s) for a single dose, personnel **must** don appropriate PPE and use a plastic pouch to contain any dust or particles generated.

15. Deactivating, Decontamination, Cleaning, and Disinfecting
All areas where HDs are handled and all reusable equipment and devices **must** be deactivated, decontaminated, and cleaned.

Additionally, sterile compounding areas and devices **must** be subsequently disinfected.

The entity **must** establish written procedures for decontamination, deactivation, and cleaning, and for sterile compounding areas disinfection.

Additionally, cleaning of nonsterile compounding areas **must** comply wth <795> and cleaning of sterile compounding areas **must** comply with <797>.

Written procedures for cleaning **must** include procedures, agents used, dilutions (if used), frequency, and documentation requirements.

All personnel who perform deactivation, decontamination, cleaning, and disinfection activities in HD handling areas **must** be trained in appropriate procedures to protect themselves and the environment from contamination.

All personnel performing these activities **must** wear appropriate PPE resistant to the cleaning agents used, including two pairs of chemotherapy gloves and impermeable disposable gowns (see Personal Protective Equipment). Additionally, eye protection and face shields **must** be used if splashing is likely.

If warranted by the activity, respiratory protection **must** be used.

The deactivating, decontaminating, cleaning, and disinfecting agents selected **must** be appropriate for the type of HD contaminant(s), location, and surface materials.

The products used **must** be compatible with the surface material.

All disposable materials **must** be discarded to meet EPA regulations and the entity's policies.

Residue from deactivation **must** be removed by decontaminating the surface.

To prevent corrosion, sodium hypochlorite **must** be neutralized with sodium thiosulfate or by following with an agent to remove the sodium hypochlorite (e.g., sterile alcohol, sterile water, germicidal detergent, or sporicidal agent).

The solution used for wiping HD packaging **must not** alter the product label.

The work surface of the C-PEC **must** be decontaminated between compounding of different HDs.

The C-PEC **must** be decontaminated at least daily (when used), any time a spill occurs, before and after certification, any time voluntary interruption occurs, and if the ventilation tool is moved.

C-PECs may have areas under the work tray where contamination can build up. These areas **must** be deactivated, decontaminated, and cleaned at least monthly to reduce the contamination level in the C-PEC.

Disinfection is a process of inhibiting or destroying microorganisms. Before disinfection can be adequately performed, surfaces **must** be cleaned.

Disinfection **must** be done for areas intended to be sterile, including the sterile compounding areas.

16. Spill Control

All personnel who may be required to clean up a spill of HDs **must** receive proper training in spill management and the use of PPE and NIOSH-certified respirators (see Personal Protective Equipment).

Spills **must** be contained and cleaned immediately only by qualified personnel with appropriate PPE.

Qualified personnel **must** be available at all times while HDs are being handled.

Signs **must** be available for restricting access to the spill area.

Spill kits containing all of the materials needed to clean HD spills **must** be readily available in all areas where HDs are routinely handled.

If HDs are being prepared or administered in a non-routine healthcare area, a spill kit and respirator **must** be available.

All spill materials **must** be disposed of as hazardous waste.

The circumstances and management of spills **must** be documented.

SOPs **must** be developed to prevent spills and to direct the clean up of HD spills.

SOPs **must** address the size and scope of the spill and specify 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 as well as the capacity of the spill kit.

17. Documentation and SOPs

The entity **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.

Personnel who transport, compound, or administer HDs **must** document their training according to OSHA standards (see OSHA Standard 1910.120 Hazardous Waste Operations and Emergency Response) and other applicable laws and regulations.