BRIEFING

〈800〉 Hazardous Drugs—Handling in Healthcare Settings, *PF* 40(3) [May–Jun. 2013]. Based on the public comments received for the proposed 〈800〉 in *PF* 40(3), the USP Compounding Expert Committee has developed a revised chapter. This chapter has been created to identify the requirements for receipt, storage, compounding, dispensing, and administration of hazardous drugs (HDs) to protect the patient, healthcare personnel, and environment. Facility requirements that differ from *Pharmaceutical Compounding—Sterile Preparations* 〈797〉 and this chapter will be harmonized through an upcoming revision of 〈797〉, which will include the following:

- Elimination of the current allowance in 〈797〉 for facilities that prepare a low volume of HDs that permits placement of a Biological Safety Cabinet (BSC) or Compounding Aseptic Containment Isolator (CACI) in a non-negative pressure room. All HD compounding must be done in a separate area designated for HD compounding.
- Addition of an allowance in 〈800〉 for a Containment Segregated Compounding Area (C-SCA), a separate, negative pressure room with at least 12 air changes per hour (ACPH) for use when compounding HDs. Low- and medium-risk HD compounded sterile preparation (CSP) may be prepared in a BSC or compounding aseptic containment isolator (CACI) located in a C-SCA, provided the beyond-use date of the CSP does not exceed 12 hours.

Major changes from the proposal of 〈800〉 in *PF* 40(3) include:

- Clarified wording in many sections.
- Removed statement concerning no acceptable level of HDs.
- Revised section on list of HDs, to allow entities to perform an assessment of risk for non-antineoplastic drugs and final dosage forms to determine alternative containment strategies and/or work practices.
- Clarified that HDs may be unpacked in either a neutral/normal or negative pressure area.
- Allowance for either external venting or redundant high-efficiency particulate air (HEPA) filtration of containment primary engineering controls (C-PECs) used for nonsterile compounding.

The proposed chapter is posted online at www.usp.org/usp-nf/notices/general-chapter-hazardous-drugs-handling-healthcare-settings with line numbers. Please provide the line numbers corresponding to your comments when submitting comments to *CompoundingSL@usp.org*.

(CMP: J. Sun.) Correspondence Number—C151881

Add the following:

‹ 800 › HAZARDOUS DRUGS—HANDLING IN HEALTHCARE SETTINGS

1. INTRODUCTION AND SCOPE

This chapter describes practice and quality standards for handling hazardous drugs (HDs) to promote patient safety, worker safety, and environmental protection. Handling HDs includes, but is not limited to, the receipt, storage, compounding, dispensing, administration, and disposal of sterile and nonsterile products and preparations.

This chapter applies to all healthcare personnel who handle HD preparations and all entities which store, prepare, transport, or administer HDs (e.g., pharmacies, hospitals and other healthcare institutions, patient treatment clinics, physicians' practice facilities, or veterinarians' offices). Personnel who may potentially be exposed to HDs include, but are not limited to: pharmacists, pharmacy technicians, nurses, physicians, physician assistants, home healthcare workers, veterinarians, and veterinary technicians.

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:

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

The chapter is organized into the following main sections:

2. LIST OF HAZARDOUS DRUGS

The National Institute for Occupational Safety and Health (NIOSH) maintains a list of antineoplastic and other HDs used in healthcare. An entity must maintain a list of HDs, which may include items on the current NIOSH list in addition to other agents not on the NIOSH list. The entity's list must be reviewed at least annually and whenever a new agent or dosage form is used.

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 enter the entity as an investigational drug. If the information available on this drug is deemed insufficient to make an informed decision, consider the drug hazardous until more information is available.

Box 1: Containment Requirements

- Any antineoplastic HD requiring manipulation and HD Active Pharmaceutical Ingredients (API) on the NIOSH list must follow the requirements in this chapter.

  - Final antineoplastic dosage forms that do not require any further manipulation other than counting final dosage forms may be dispensed without any further requirements for containment unless required by the manufacturer.

- For dosage forms of other HDs on the NIOSH list, the entity may perform an assessment of risk to determine alternative containment strategies and/work practices.

Some dosage forms of drugs defined as hazardous may not pose a significant risk of direct occupational exposure because of their dosage formulation (e.g., tablets or capsules—solid, intact medications that are administered to patients without modifying the formulation). However, dust from tablets and capsules may present a risk of exposure by skin contact and/or inhalation. An assessment of risk may be performed for these dosage forms to determine alternative containment strategies and/or work practices.

The assessment of risk must, at a minimum, consider the following:

- Type of HD (e.g., antineoplastic, non-antineoplastic, reproductive risk)
- 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 annually and the review documented.

3. TYPES OF EXPOSURE

Routes of unintentional entry of HDs into the body include dermal and mucosal absorption, inhalation, injection, and ingestion (e.g., contaminated foodstuffs, spills, or mouth contact with contaminated hands). Both clinical and nonclinical personnel may be exposed to HDs when they handle HDs or touch contaminated surfaces. *Table 1* lists examples of potential routes of exposure based on activity.

Table 1. Examples of Potential Routes of Exposure Based on Activity

Activity	Potential Route of Exposure
Dispensing	• Counting tablets and capsules from bulk containers
Compounding	• Crushing tablets or opening capsules • Pouring oral or topical liquids from one container to another • Weighing or mixing components • Constituting or reconstituting powdered or lyophilized HDs • Withdrawing or diluting injectable HDs from parenteral containers • Expelling air or HDs from syringes • Contacting HD residue present on PPE or other garments • Deactivating, decontaminating, cleaning, and disinfecting areas contaminated with or suspected to be contaminated with HDs • Maintenance activities for potentially contaminated equipment and devices
Administration	• Generating aerosols during administration of HDs by various routes (e.g. injection, irrigation, oral, inhalation, or topical application) • Performing certain specialized procedures (e.g., intraoperative intraperitoneal injection or bladder instillation) • Priming an IV administration set
Patient-care activities	• Handling body fluids (e.g., urine, feces, sweat, or vomit) or body-fluid-contaminated clothing, dressings, linens, and other

Activity	Potential Route of Exposure
	materials
Spills	• Spill generation, management, and disposal
Receipt	• Contacting with HD residues present on drug container, individual dosage units, outer containers, work surfaces, or floors
Transport	• Moving HDs within a healthcare setting

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

All personnel who handle HDs are responsible for understanding the fundamental practices and precautions and for continually evaluating these procedures and the quality of final HDs to prevent harm to patients, minimize exposure to personnel, and minimize contamination of the work and care environment.

5. FACILITIES

HDs must be handled under conditions that promote patient safety, worker safety, environmental protection, and infection prevention. 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. Signs designating the hazard must be prominently displayed before the entrance to the HD handling areas.

Designated areas must be available for:

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

5.1 Receipt

Antineoplastic HDs and 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 shipping containers in sterile compounding areas or in positive pressure areas.

5.2 Storage

HDs must be stored in a manner that prevents spillage or breakage if the container falls. Do not store HDs on the floor. 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.

Non-antineoplastic, reproductive risk only, and final dosage forms of antineoplastic HDs may be stored with other inventory. Antineoplastic HDs requiring manipulation other than counting 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 a negative-pressure room with at least 12 air changes per hour (ACPH).

Sterile and nonsterile HDs may be stored together. Depending upon facility design, HDs may be stored within a negative pressure buffer room with at least 12 ACPH. However, only HDs used for sterile compounding may be stored in the negative pressure buffer room.

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)]. If a refrigerator is placed in a negative pressure buffer room, an exhaust located adjacent to the refrigerator's compressor and behind the refrigerator should be considered.

5.3 Compounding

Engineering controls are required to protect the preparation from cross-contamination and microbial contamination (if preparation is intended to be sterile) during all phases of the compounding process. Engineering controls for containment are divided into three categories representing primary, secondary, and supplementary levels of control. A containment primary engineering control (C-PEC) is a ventilated device designed to minimize worker and environmental HD exposure when directly handling HDs. Containment secondary engineering controls (C-SEC) is the room in which the C-PEC is placed. Supplemental engineering controls [e.g., closed-system drug-transfer device (CSTD)] are adjunct controls to offer additional levels of protection. *Appendix B* provides examples for designs of HD compounding areas.

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 through high-efficiency particulate air (HEPA) filtration
- Be physically separated (i.e., a different room from other preparation areas)
- Have a negative pressure between 0.01 and 0.03 inches of water column

The C-PEC must operate continuously if used for sterile compounding or if the C-PEC supplies the negative pressure. If there is any loss of power to the unit, or if repair or moving occurs, all activities occurring in the C-PEC must be suspended immediately. If necessary, protect the unit by covering it appropriately per the manufacturer's recommendations. Once the C-PEC can be powered on, decontaminate, clean, and disinfect (if used for sterile compounding) all interior surfaces and wait the manufacturer-specified recovery time before resuming compounding.

A sink must be available for hand washing as well as emergency access to water for removal of hazardous substances from eyes and skin. An eyewash station and/or other emergency or safety precautions that meet applicable laws and regulations must be readily available. However, care must be taken to locate them in areas where their presence will not interfere with required ISO classifications.

For entities that compound both nonsterile and sterile HDs, the respective C-PECs must be placed in segregated rooms separate from each other, 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.

5.3.1 NONSTERILE COMPOUNDING

In addition to this chapter, nonsterile compounding must follow standards in *Pharmaceutical Compounding—Nonsterile Preparations* ⟨795⟩. A C-PEC is not required if manipulations are limited to handling of final dosage forms (e.g., tablets and capsules) that do not produce particles, aerosols, or gasses.

The C-PECs used for manipulation of nonsterile HDs must be either externally vented (preferred) or redundant–HEPA filtered 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 be 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 need to have 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. *Table 2* summarizes the engineering controls required for nonsterile HD compounding.

Due to the difficulty of cleaning HD contamination from surfaces, the architectural finish requirements (e.g., smooth, seamless, and impervious surfaces) described in *Pharmaceutical Compounding—Sterile Preparations* ⟨797⟩ also apply to nonsterile compounding areas.

Table 2. Engineering Controls for Nonsterile HD Compounding

C-PEC	C-SEC Requirements
• Externally vented (preferred) or redundant–HEPA filtered in series	• 12 ACPH • Externally vented

C-PEC	C-SEC Requirements
• Examples: CVE, Class I or II BSC, CACI	• Negative pressure between 0.01 and 0.03 inches of water column

5.3.2 STERILE COMPOUNDING

In addition to this chapter, applicable sterile compounding standards in 〈797〉 must be followed.

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 a Class 5 or better air quality, such as a Class II or III BSC, or CACI. Class II BSC types A2, B1, or B2 are all acceptable. For most known HDs, type A2 cabinets offer a simple and reliable integration with the ventilation and pressurization requirements of the C-SEC. Class II type B2 BSCs are typically reserved for use with volatile components. *Appendix C* describes the different types of BSCs.

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 (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 defined in 〈797〉 for CSPs prepared in a segregated compounding area. *Table 3* summarizes the engineering controls required for sterile HD compounding.

Table 3. Engineering Controls for Sterile HD Compounding

Configuration	C-PEC	C-SEC	Maximum BUD
ISO Class 7 Buffer Room	• Externally Vented • Examples: Class II BSC or CACI	• 30 ACPH • Externally vented • Negative pressure between 0.01 and 0.03 inches of water column	As described in 〈797〉
C-SCA	• Externally Vented • Examples: Class II BSC or CACI	• 12 ACPH • Externally vented • Negative pressure between 0.01 and 0.03 inches of water column	As described in 〈797〉 for segregated compounding area

ISO class 7 buffer room: The C-PEC may be placed in an ISO Class 7 buffer room that has a negative pressure between 0.01 and 0.03 inches of water column and has a minimum of 30 ACPH of HEPA-filtered supply air.

Because the room through which entry into the HD buffer room (e.g., ante-area or non-HD buffer room) plays an important role in terms of total contamination control, the following is required:

- Minimum of 30 ACPH of HEPA-filtered supply air
- Maintain a positive pressure of 0.02 inches of water column relative to all adjacent unclassified spaces
- Maintain an air quality of ISO Class 7 or better

This provides for inward air migration of equal cleanliness classified air into the negative pressure buffer room to contain any airborne HD. A hand-washing sink must be placed at least 1 meter from the entrance of the buffer room to avoid contamination migration into the negative pressure HD buffer room.

Although not a recommended facility design, if the negative-pressure HD buffer room is entered though the positive-pressure non-HD buffer room, the following is required:

- A line of demarcation must be defined within the negative-pressure buffer area for garbing and degarbing
- A method to transport HDs, CSPs, and 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 between the negative-pressure buffer area and adjacent space. The pass-through must be included in the facility's certification to ensure that particles are not compromising the air quality of the negative-pressure buffer room. Do not use a refrigerator pass-through. Other methods of containment (such as sealed containers) may be used if the entity can demonstrate HD containment and appropriate environmental control.

HD CSPs prepared in an ISO Class 7 buffer room may use the BUDs described in 〈797〉, based on the categories of CSP, sterility testing, and storage temperature.

Containment segregated compounding area (C-SCA): The C-PEC may be placed in an unclassified C-SCA that has a negative pressure between 0.01 and 0.03 inches of water column relative to all adjacent spaces and has a minimum of 12 ACPH of HEPA-filtered supply air. A hand-washing sink must be placed at least 1 meter from C-PEC.

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

5.4 Containment Supplemental Engineering Controls

Containment supplemental engineering controls, such as CSTDs, provide adjunct controls to offer additional levels of protection during compounding or administration. Some CSTDs have been shown to limit the potential of generating aerosols during compounding. However, there is no certainty that all CSTDs will perform adequately.

Since there is no published universal performance standard for evaluation of CSTD containment, users should carefully evaluate the performance claims associated with available CSTDs based on independent studies and demonstrated containment reduction.

A CSTD must not be used as a substitute for a C-PEC when compounding. CSTDs should be used when compounding HDs when the dosage form allows. CSTDs must be used when administering HDs when the dosage form allows.

6. ENVIRONMENTAL QUALITY AND CONTROL

Environmental wipe sampling should be performed routinely (e.g., initially as a benchmark and at least every 6 months, or more often as needed, to verify containment). Surface wipe sampling should include:

- Interior of the C-PEC and equipment contained in it
- Staging or work areas near the C-PEC
- Areas adjacent to C-PECs (e.g., floors directly under staging and dispensing area)
- Patient administration areas

There are currently no studies demonstrating the effectiveness of a specific number or size of wipe samples in determining levels of HD contamination. Wipe sampling kits should be verified before use to ensure the method and reagent used have been tested to recover a specific percentage of known marker drugs from various surface types found in the sampled area. There are currently no certifying agencies for vendors of wipe sample kits.

There is currently no standard for acceptable limits for HD surface contamination. Common marker HDs that can be assayed include cyclophosphamide, ifosfamide, methotrexate, fluorouracil, and platinum-containing drugs. An example of measurable contamination would be cyclophosphamide levels >1.00 ng/cm^2, which were shown in some studies to result in uptake of the drug in exposed workers. If any measurable contamination is found, the compounding supervisor must identify, document, and contain the cause of contamination. Such action may include reevaluating work practices, re-training personnel, performing thorough deactivation/decontamination and cleaning, and improving engineering controls. Repeat the wipe sampling to validate that the deactivation/decontamination and cleaning steps have been effective.

7. PERSONAL PROTECTIVE EQUIPMENT

Personal Protective Equipment (PPE) provides worker protection to reduce exposure to HD aerosols and residues. When performing a task in situations where C-PECs are not generally available, such as treating a patient or cleaning a spill, additional PPE may be required. The NIOSH list of antineoplastic and other HDs provides some general guidance on PPE for possible scenarios that may be encountered in healthcare settings.

Gloves, gowns, head, hair, and shoe covers are required for compounding sterile and nonsterile HDs. Gloves are required for administering antineoplastic HDs. Gowns are

required when administering injectable antineoplastic HDs. For all other activities, the entity'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.

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

7.1 Gloves

When required, chemotherapy gloves must be tested to American Society for Testing and Materials (ASTM) standard D6978 (or its successor). Chemotherapy gloves must be powder-free because powder can contaminate the work area and can adsorb and retain HDs. Gloves must be inspected for physical defects before use. Do not use gloves with pin holes or weak spots.

Chemotherapy gloves must be changed every 30 min or when torn, punctured, or contaminated.

7.2 Gowns

When required, disposable gowns must be tested and shown to resist permeability by HDs. Gowns must be selected based on the HDs handled. Disposable gowns made of polyethylene-coated polypropylene or other laminate materials offer better protection than those made of uncoated materials. 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.

Cloth laboratory coats, surgical scrubs, isolation gowns, or other absorbent materials are not appropriate outerwear when handling HDs because they permit the permeation of HDs and can hold spilled drugs against the skin, thereby increasing exposure. Clothing may also retain HD residue from contact, and may transfer to other healthcare workers or various surfaces. Washing of non-disposable clothing contaminated with HD residue may transfer drug residue to other clothing.

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 avoid spreading HD contamination and exposing other healthcare workers.

7.3 Head, Hair, Shoe, and Sleeve Covers

Head and hair covers (including beard and moustache, if applicable) and shoe covers provide protection from contact with HD residue on surfaces and floors. When compounding sterile HDs, a second pair of shoe covers must be donned before entering

the buffer room and removed when exiting the buffer room. Shoe covers worn in HD handling areas must not be worn to other areas to avoid spreading HD contamination and exposing other healthcare workers.

Disposable sleeve covers constructed of coated materials may be used to protect areas of the arm that may come in contact with HDs. If used, sleeve covers must be carefully removed and properly disposed of after the task is completed.

7.4 Eye and Face Protection

Many HDs are irritating to the eyes and mucous membranes. 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). A full-facepiece respirator provides eye and face protection. Goggles must be used when eye protection is needed. Eye glasses alone or safety glasses with side shields do not protect the eyes adequately from splashes. Face shields in combination with goggles provide a full range of protection against splashes to the face and eyes. Face shields alone do not provide full eye and face protection.

7.5 Respiratory Protection

For most activities requiring respiratory protection, a fit-tested NIOSH-certified N95 or more protective respirator is sufficient to protect against airborne particles. However, N95 respirators offer no protection against gases and vapors and little protection against direct liquid splashes (see the Centers for Disease Control and Prevention's (CDC's) Respirator Trusted-Source Information).

Surgical masks do not provide respiratory protection from drug exposure and must not be used when respiratory protection is required. A surgical N95 respirator provides the respiratory protection of an N95 respirator, and like a surgical mask, provides a barrier to splashes, droplets, and sprays around the nose and mouth.

Personnel who are unpacking HDs that are not contained in plastic should wear an elastomeric half-mask with a multi-gas cartridge and P100-filter. If the type of drug can be better defined, then a more targeted cartridge can be used.

Fit test the respirator and train workers to use respiratory protection. Follow all requirements in the Occupational Safety and Health Administration (OSHA) respiratory protection standard (29 CFR 1910.134). An appropriate full-facepiece, chemical cartridge-type respirator must be worn when attending to HD spills larger than what can be contained with a spill kit, or when there is a known or suspected airborne exposure to powders or vapors.

7.6 Disposal of Used Personal Protective Equipment

Consider all PPE worn when handling HDs to be contaminated with, at minimum, trace quantities of HDs. PPE must be placed in an appropriate waste container and further disposed of per local, state, and federal regulations. PPE used during compounding should be disposed of in the proper waste container before leaving the C-SEC. Chemotherapy gloves worn during compounding must be carefully removed and discarded immediately in an approved HD waste container inside the C-PEC or contained in a sealable bag for discarding outside the C-PEC. Potentially contaminated clothing must not be taken home under any circumstances.

8. HAZARD COMMUNICATION PROGRAM

Entities are required to establish policies and procedures that ensure worker safety during all aspects of HD handling. The entity must develop SOPs to ensure effective training regarding proper labeling, transport, and storage 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 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.
- 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.

9. PERSONNEL TRAINING

All personnel who handle HDs must be fully trained based on their job functions (e.g., in the receipt, storage, handling, compounding, dispensing, and disposal 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 and when a new HD or new equipment is used or a new or significant change in process or SOP occurs. 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)
- Spill management
- Response to known or suspected HD exposure

10. RECEIVING

The entity must establish SOPs for receiving HDs. HDs should be received from the supplier sealed in impervious plastic to segregate them from other drugs and to improve safety in the receiving and internal transfer process. HDs must be delivered to the HD storage area immediately upon arrival.

PPE, including ASTM-tested, powder-free chemotherapy gloves, must be worn when unpacking HDs (see *Personnel Protective Equipment*). 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 containers). *Table 4* summarizes the steps for receiving and handling of damaged shipping containers.

Table 4. Summary of Requirements for Receiving and Handling Damaged HD Shipping Containers

If the shipping container appear damaged	• Seal container without opening and contact the supplier for instructions • If the unopened package is to be returned to the supplier, enclose the package in an impervious container and label the outer container "Hazardous" • If the supplier declines return, dispose of properly
If a damaged shipping container must be opened	• Seal the container in plastic or an impervious container • Transport it to a C-PEC and place on a plastic-backed preparation mat • Open the package and remove usable items. • Wipe the outside of the usable items with a disposable wipe. • Enclose the damaged item(s) in an impervious container and label the outer container "Hazardous" • If the supplier declines return, dispose of properly • Decontaminate/deactivate and clean the C-PEC (see *Deactivation/Decontamination, Cleaning, and Disinfection*) and discard the mat and cleaning disposables as hazardous waste

When opening damaged shipping containers, they should preferably be transported to a C-PEC designated for nonsterile compounding. If a C-PEC designated for sterile compounding is the only one available, it must be thoroughly disinfected after the decontamination/deactivation and cleaning step before returning to any sterile compounding activity.

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, AND TRANSPORT

The entity must establish SOPs for the labeling, handling, packaging, and transport of HDs. The SOPs must address prevention of accidental exposures or spills, personnel training on response to exposure, and use of a spill kit. Examples of special exposure-reducing strategies include small-bore connectors (such as Luer Lock) and syringes,

syringe caps, CSTDs, the capping of container ports, sealed impervious plastic bags, impact-resistant and/or water-tight containers, and cautionary labeling.

11.1 Labeling

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

11.2 Packaging

Compounding 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, mode of transport, and experience of the compounding personnel.

11.3 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 or 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 courier's policies.

12. DISPENSING FINAL DOSAGE FORMS

HDs that do not require any further manipulation other than counting final dosage forms may be dispensed without any further requirements for containment unless required by the manufacturer or if visual indicators of HD exposure hazards (e.g., HD dust or leakage) are present.

Counting of HDs should be done carefully. Clean equipment should be dedicated for use with these drugs. Tablet and capsule forms of HDs must not be placed in automated counting or packaging machines, which subject them to stress and may introduce powdered contaminants into the work area.

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*. When compounding nonsterile and sterile HD preparations in a C-PEC, a plastic-backed preparation mat must be placed on the work surface of the C-PEC. The mat should be changed immediately if a spill occurs and regularly during use, and should be discarded at the end of the daily compounding activity. Disposable or clean

equipment for compounding (such as mortars and pestles, and spatulas) must be dedicated for use with HDs. Compounding personnel must ensure that the labeling processes for compounded preparations do not introduce contamination into non-HD handling areas.

When compounding nonsterile HD preparations, use commercially available products as starting ingredients whenever possible. Liquid formulations are preferred over crushing tablets or opening capsules. APIs should only be used when there are no other options. When compounding sterile HD preparations, APIs should be avoided if a suitable manufactured product is available and appropriate for use (e.g., use an injectable product rather than API).

Bulk containers of liquid and API HD must be handled carefully to avoid spills. If used, APIs should 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. Examples of protective medical devices include needleless and closed systems. Examples of protective techniques include spiking or priming of IV tubing in a C-PEC and crushing tablets in plastic sleeves.

Appropriate PPE must be worn when administering HDs. After use, PPE must be removed and disposed of in an approved HD waste container 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 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. Administration into certain organs or body cavities (e.g., the bladder, eye, peritoneal cavity, or chest cavity) often requires equipment for which locking connections may not be readily available or possible.

Healthcare personnel should avoid manipulating HDs such as crushing tablets or opening capsules if possible. Liquid formulations are preferred if solid oral dosage forms are not appropriate for the patient. 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 sleeve to contain any dust or particles generated.

The Oncology Nursing Society (ONS) Safe Handling of Hazardous Drugs publication contains additional information on handling HDs for administration.

15. DEACTIVATION/DECONTAMINATION, CLEANING, AND DISINFECTION

All areas where HDs are handled (e.g., such as during receiving, compounding, transport, administering, and disposal) and all reusable equipment and devices (e.g., C-PEC, carts, and trays) must be routinely deactivated/decontaminated and cleaned. Additionally, sterile compounding areas and devices must be subsequently disinfected.

All healthcare 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 ASTM-tested chemotherapy gloves and impermeable disposable gowns. Consult manufacturer or supplier information for compatibility with cleaning agents used. Additionally, eye protection and face shields must be used if splashing is possible. Respiratory protection must be used if warranted by the activity.

The entity must establish written procedures for decontamination, deactivation, cleaning, and disinfection (for sterile compounding areas). Cleaning of nonsterile and sterile compounding areas must also comply with 〈795〉 and 〈797〉. Written procedures for cleaning must include procedures, agents used, dilutions used, frequency, and documentation requirements. *Table 5* summarizes the purpose and example agents for each step.

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 not contaminate the surfaces with substances that are toxic, volatile, corrosive, or otherwise harmful to the surface material. Perform cleaning in areas that are sufficiently ventilated to prevent accumulation of hazardous airborne drug concentrations and decontamination agents.

Table 5. Summary of Cleaning Steps

Cleaning Step	Purpose	Agents
Deactivation	Render compound inert or inactive	As listed in the HD labeling or if no specific information available, sodium hypochlorite or other Environmental Protection Agency (EPA)-registered oxidizer
Decontamination	Remove inactivated residue	Sterile alcohol, sterile water, peroxide, or sodium hypochlorite
Cleaning	Remove organic and inorganic material	Germicidal detergent and sterile water
Disinfection	Destroy microorganisms	Sterile alcohol or other EPA-registered disinfectant appropriate for use

15.1 Deactivation/Decontamination

Deactivation renders a compound inert or inactive. Decontamination occurs by physically removing HD residue from non-disposable surfaces and transferring it to absorbent, disposable materials (e.g., wipes, pads, or towels) appropriate to the area being cleaned. All disposable materials must be discarded as contaminated HD waste.

Chemical deactivation of HD residue is preferred, but no single process has been found to deactivate all currently available HDs. Studies have examined oxidizing agents such as potassium permanganate, hydrogen peroxide, and sodium hypochlorite; vaporized hydrogen peroxide and detergents; and high- and low-pH solutions, all with varying results. Some potential deactivators have produced byproducts that are as hazardous as the original drug. Other deactivators have respiratory effects or result in caustic damage to surfaces. Note that sodium hypochlorite is corrosive to stainless steel surfaces if left untreated; therefore, sodium hypochlorite must be neutralized with sodium thiosulfate or followed by use of a germicidal detergent.

A multi-component deactivation system is theoretically more efficient than a single-agent system because of the diverse nature of HDs. One commercially available product provides a system for decontamination and deactivation using sodium hypochlorite, surfactant, and thiosulfate neutralizer. This combination product, followed by rinsing, has been shown to be effective for cleaning HD-contaminated surfaces. Other products use combinations of deactivating agents and/or cleaning agents, followed by rinsing and disinfecting. Because of the growing number of assays available for HDs, additional surface wipe sampling is now possible and should be done to document the effectiveness of any agent used for decontamination of HD residue from work surfaces (see *Environmental Quality and Control*).

15.2 Cleaning and Disinfection

Cleaning is a process that results in the removal of contaminants (e.g., soil, microbial contamination, HD residue) from objects and surfaces using water, detergents, surfactants, solvents, and/or other chemicals. Disinfection is a process of destroying microorganisms. Disinfection must be done for areas intended to be sterile including the sterile compounding areas.

15.3 Cleaning the Compounding Area

The *Cleaning and Disinfecting the Compounding Area* section in 〈797〉 applies to both sterile and nonsterile HD compounding areas. Cleaning agents used on compounding equipment should not introduce microbial contamination.

All C-PEC used for either nonsterile or sterile compounding must be decontaminated between compounding of different HDs, any time a spill occurs, before and after certification, any time voluntary interruption occurs, and if the ventilation tool is moved. No cleaning step may be performed when compounding activities are occurring.

The amount of HD contamination introduced into the C-PEC may be reduced by surface decontamination (i.e., wiping down) of HD containers. Although no wipe-down procedures have been studied, the use of disposable material moistened with alcohol, sterile water, peroxide, or sodium hypochlorite solutions may be effective. To avoid spreading HD residue, spray the wiper, not the HD container. The solution used for wiping HD packaging must not alter the product label.

C-PECs may have areas under the work tray where contamination can build up. These areas must be cleaned at least monthly to reduce the contamination level in the C-PEC. Accessing this area may be difficult. Clean as much as possible of the C-PEC surfaces before accessing the area under the work tray. When cleaning the area under the work tray of a C-PEC, the containment airflows are compromised by opening the cabinets. To provide protection to the worker performing this task, respiratory protection may be required. An NIOSH-approved respirator worn by a worker who has been fit tested and cleared to use a respirator would be appropriate.

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 in entities handling HDs. 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. Personnel who are potentially exposed during the spill or spill clean-up or who have direct skin or eye contact with HDs require immediate evaluation. Non-employees exposed to an HD spill should report to the designated emergency service for initial evaluation and also complete an incident report or exposure form.

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 management of the spill (e.g., decontamination, deactivation, and cleaning) may be dependent on the size and type of spill. The SOP must address the location of spill kits and clean-up materials as well as the capacity of the spill kit. Written procedures should address use of appropriate full-facepiece, chemical cartridge-type respirators if the capacity of the spill kit is exceeded or if there is known or suspected airborne exposure to vapors or gases.

17. DISPOSAL

Disposal of all HD waste (including unused and unusable HDs) must comply with all applicable federal, state, and local regulations. 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.

18. DOCUMENTATION AND STANDARD OPERATING PROCEDURES

Activities that must be documented include, but are not limited to, the acquisition, preparation, and dispensing of an HD; personnel training; and the use and maintenance of equipment and supplies. These records must be available for review. 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.

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 annually by the designated responsible individual, and the review must be documented. Revisions in forms or records must be made as needed and communicated to all personnel handling HDs.

The SOPs for handling of HDs should include:

- Hazard communication program
- Occupational safety program
- Labeling of HDs
- Procurement of HDs
- Use of proper engineering controls (e.g., C-PECs, C-SECs)

- Use of PPE based on activity (e.g., receipt, transport, compounding, administration, spill, and disposal)
- Decontamination/deactivation, cleaning, and disinfection
- Transport
- Environmental monitoring
- Spill control
- Medical surveillance

19. MEDICAL SURVEILLANCE

Medical surveillance is part of a comprehensive exposure control program complementing engineering controls, safe work processes, and use of PPE. Entities should ensure that healthcare workers who handle HDs as a regular part of their job assignment are enrolled in a medical surveillance program. The general purpose of surveillance is to minimize adverse health effects in personnel potentially exposed to HDs. Medical surveillance programs involve assessment and documentation of symptom complaints, physical findings, and laboratory values (such as a blood count) to determine whether there is a deviation from the expected norms.

Medical surveillance can also be viewed as a secondary prevention tool that may provide a means of early detection if a health problem develops. Tracking personnel through medical surveillance allows the comparison of health variables over time in individual workers, which may facilitate early detection of a change in a laboratory value or health condition. Medical surveillance programs also look for trends in populations of workers. Examining grouped data compared with data from unexposed workers may reveal a small alteration or increase in the frequency of a health effect that would be obscured if individual workers' results alone were considered.

Medical surveillance evaluates the protection afforded by engineering controls, other administrative controls, safe work processes, PPE, and worker education about the hazards of the materials they work with in the course of their duties. The data-gathering elements of a medical surveillance program are used to establish a baseline of workers' health and then to monitor their future health for any changes that may result from exposure to HDs.

Elements of a medical surveillance program should be consistent with the entity's Human Resource policies and should include:

- Development of an organized approach to identify workers who are potentially exposed to HDs on the basis of their job duties
- Use of an 'entity-based' or contracted employee health service to perform the medical surveillance while protecting the confidentiality of the employees' personal medical information
- Initial baseline assessment (pre-placement) of a worker's health status and medical history. Data elements collected include a medical (including reproductive) history and work history to assess exposure to HDs, physical examination, and laboratory testing. Methods used to assess exposure history include a review of:

- Records of HDs handled, with quantities and dosage forms

- Number of HD preparations/administrations per week

- Estimates of hours spent handling HDs per week and/or per month

- Performance of a physical assessment and laboratory studies linked to target organs of commonly used HDs, such as a baseline complete blood count. Note that biological monitoring to determine blood or urine levels of specific HDs is not currently recommended in surveillance protocols, but may have a role in the follow-up of acute spills with a specific agent.

- Medical records of surveillance should be maintained according to OSHA regulation concerning access to employee exposure and medical records
- Monitoring workers' health prospectively through periodic surveillance using the elements of data gathering described above (updated health and exposure history, physical assessment, and laboratory measures, if appropriate)
- Monitoring of the data to identify prevention failure leading to health effects; this monitoring may occur in collaboration with the employee health service
- Development of a follow-up plan for workers who have shown health changes suggesting toxicity or who have experienced an acute exposure. This follow-up should include evaluation of current engineering and administrative controls and equipment to ensure that all systems are appropriately and accurately implemented (see *Follow-Up Plan* below).
- Completion of an exit examination when a worker's employment at the entity ends, to document the information on the employee's medical, reproductive, and exposure histories. Examination and laboratory evaluation should be guided by the individual's history of exposures and follow the outline of the periodic evaluation.

19.1 Follow-Up Plan

The occurrence of exposure-related health changes should prompt immediate re-evaluation of primary preventive measures (e.g., administrative and engineering controls, PPE, and others). In this manner, medical surveillance acts as a check on the effectiveness of controls already in use.

The entity should take the following actions:

- Perform a post-exposure examination tailored to the type of exposure (e.g., spills or needle sticks from syringes containing HDs). An assessment of the extent of exposure should be conducted and included in a confidential database and in an incident report. The physical examination should focus on the involved area as well as other organ systems commonly affected (i.e., the skin and mucous membranes for direct contact or inhalation; the pulmonary system for aerosolized HDs). Treatment and laboratory studies will follow as indicated and be guided by emergency protocols.

- Compare performance of controls with recommended standards; conduct environmental sampling when analytical methods are available.
- Verify and document that all controls are in proper operating condition.
- Verify and document that the worker complied with existing policies. Review policies for the use of PPE and employee compliance with PPE use and policies. Review availability of appropriate PPE (see *Personal Protective Equipment*).
- Develop and document a plan of action that will prevent additional exposure of workers.
- Ensure confidential, two-way communication between the worker and the employee health unit(s) regarding notification, discussions about a change in health condition, or detection of an adverse health effect.
- Provide and document a follow-up medical survey to demonstrate that the plan implemented is effective.
- Ensure that any exposed worker receives confidential notification of any adverse health effect. Offer alternative duty or temporary reassignment.
- Provide ongoing medical surveillance of all workers at risk for exposure to HDs to determine whether the plan implemented is effective.

APPENDIX A: ACRONYMS AND DEFINITIONS

Acronyms

ACPH	Air changes per hour
API	Active pharmaceutical ingredient
ASTM	American Society for Testing and Materials
BSC	Biological safety cabinet
BUD	Beyond-use date
CACI	Compounding aseptic containment isolator
CAI	Compounding aseptic isolator
CDC	Centers for Disease Control and Prevention
C-PEC	Containment primary engineering control
C-SCA	Containment segregated compounding area
C-SEC	Containment secondary engineering control
CSP	Compounded sterile preparation
CSTD	Closed-system drug-transfer device
CVE	Containment ventilated enclosure
EPA	Environmental Protection Agency
GHS	Globally Harmonized System of Classification and Labeling of Chemicals
HD	Hazardous drug

HEPA	High-efficiency particulate air
IV	Intravenous
LAFW	Laminar airflow workbench
NIOSH	National Institute for Occupational Safety and Health
ONS	Oncology Nursing Society
OSHA	Occupational Safety and Health Administration
PPE	Personal protective equipment
SDS	Safety Data Sheet
SOP	Standard operating procedure
ULPA	Ultra-low particulate air

Definitions

Active pharmaceutical ingredient (API): Any substance or mixture of substances intended to be used in the compounding of a drug preparation, thereby becoming the active ingredient in that preparation and furnishing pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease in humans and animals or affecting the structure and function of the body.

Alternative duty: Performance of other tasks that do not include the direct handling of HDs.

Assessment of risk: Evaluation of risk to determine alternative containment strategies and/or work practices.

Beyond-use date (BUD): The date or time after which a compounded preparation must not be used, stored, or transported (see ⟨795⟩ and ⟨797⟩).

Biological safety cabinet (BSC): A ventilated cabinet often used for preparation of hazardous drugs. These cabinets are divided into three general classes (Class I, Class II, and Class III). Class II BSCs are further divided into types (Type A1, Type A2, Type B1, and Type B2). See *Appendix C* for details.

Buffer room: A type of C-SEC under negative pressure where the C-PEC is physically located. Activities that occur in this area are limited to the preparation and staging of components and supplies used when compounding HDs.

Chemotherapy glove: A medical glove that meets the ASTM Standard Practice for Assessment of Resistance of Medical Gloves to Permeation by Chemotherapy Drugs (D6978) or its successor.

Cleaning: The removal of soil (e.g., organic and inorganic material) from objects and surfaces, normally accomplished by manually or mechanically using water with detergents or enzymatic products.

Closed-system drug-transfer device (CSTD): A drug transfer device that mechanically prohibits the transfer of environmental contaminants into the system and the escape of HD or vapor concentrations outside the system.

Compounded preparation: A nonsterile or sterile drug or nutrient preparation that is compounded in a licensed pharmacy or other healthcare-related facility in response to or anticipation of a prescription or a medication order from a licensed prescriber.

Compounding aseptic containment isolator (CACI): A specific type of CAI that is designed for the compounding of sterile HDs. The CACI is designed to provide worker protection from exposure to undesirable levels of airborne drugs throughout the compounding and material transfer processes and to provide an aseptic environment with unidirectional airflow for compounding sterile preparations.
Compounding aseptic isolator (CAI): An isolator specifically designed for compounding sterile, non-hazardous pharmaceutical ingredients or preparations. The CAI is designed to maintain an aseptic compounding environment throughout the compounding and material transfer processes.
Compounding personnel: Individuals who participate in the compounding process.
Compounding supervisor: Individual(s) responsible for developing and implementing appropriate procedures; overseeing facility compliance with this chapter and other applicable laws, regulations, and standards; ensuring the competency of personnel; and maintaining environmental control of the compounding areas.
Containment primary engineering control (C-PEC): A ventilated device designed and operated to minimize worker and environmental exposures to HDs by controlling emissions of airborne contaminants through the following:

- The full or partial enclosure of a potential contaminant source
- The use of airflow capture velocities to trap and remove airborne contaminants near their point of generation
- The use of air pressure relationships that define the direction of airflow into the cabinet
- The use of HEPA filtration on all potentially contaminated exhaust streams

Examples of C-PECs include Class I, II, or III BSCs, CACIs, and CVE (e.g., powder hood). C-PECs used for nonsterile compounding do not need to have ISO Class 5 air quality, whereas C-PECs used for sterile compounding must have ISO Class 5 air quality (see *Table 2* and *3*).
Containment secondary engineering control (C-SEC): The C-SEC is the room in which the C-PEC is placed. It incorporates specific design and operational parameters required to contain the potential hazard within the compounding room.
Containment segregated compounding area (C-SCA): A type of C-SEC with nominal requirements for airflow and room pressurization as they pertain to HD compounding.
Containment ventilated enclosure (CVE): A full or partial enclosure that uses ventilation principles to capture, contain, and remove airborne contaminants through HEPA filtration and prevent their release into the work environment.
Deactivation: Treatment of an HD contaminant on surfaces with a chemical, heat, ultraviolet light, or another agent to transform the HD into a less hazardous agent.
Decontamination: Inactivation, neutralization, or removal of HD contaminants on surfaces, usually by chemical means.
Disinfectant: A chemical agent that destroys or inhibits the growth of microorganisms.
Engineering control: Primary, secondary, and supplemental devices designed to eliminate or reduce worker exposure to a chemical, biological, radiological, ergonomic, or physical hazard, and in the case of CSPs, to protect the compounded preparation

from environmental contamination.

Entity: Pharmacy, hospital, physician's office, clinic, veterinary office, or other location where HDs are received, stored, prepared, dispensed, administered, and/or distributed.

EPA-registered disinfectant: Antimicrobial products registered with the Environmental Protection Agency (EPA) for healthcare use against pathogens specified in the product labeling.

Externally vented: Exhausted to the outside

Globally Harmonized System of Classification and Labeling of Chemicals (GHS): A system for standardizing and harmonizing the classification and labeling of chemicals.

Goggles: Tight-fitting eye protection that completely covers the eyes, eye sockets, and facial area that immediately surrounds the eyes. Goggles provide protection from impact, dust, and splashes. Some goggles fit over corrective lenses.

Hazardous drug (HD): Any drug identified as hazardous or potentially hazardous on the basis of at least one of the following six criteria:

- Carcinogenicity
- Teratogenicity or developmental toxicity
- Reproductive toxicity in humans
- Organ toxicity at low doses in humans or animals
- Genotoxicity
- New drugs that mimic existing HDs in structure or toxicity

High-efficiency particulate air (HEPA) filtration: An extended-medium, dry-type filter in a rigid frame, having a minimum particle collection efficiency of 99.97% for particles with a mass median diameter of 0.3 µm when tested at a rated airflow in accordance with MIL STD 282 using IEST Recommended Standard RP-CC001.5.

Negative-pressure room: A room that is maintained at a lower pressure than the adjacent spaces; therefore the net flow of air is into the room.

Pass-through: An enclosure with interlocking doors that is positioned between two spaces for the purpose of reducing particulate transfer while moving materials from one space to another. A pass-through serving negative-pressure rooms needs to be equipped with sealed doors.

Personal protective equipment (PPE): Items such as gloves, gowns, respirators, goggles, faceshields, and others that protect individual workers from hazardous physical or chemical exposures.

Positive-pressure room: A room that is maintained at a higher pressure than the adjacent spaces; therefore, the net flow of air is out of the room.

Safety data sheet (SDS): An informational document that provides written or printed material concerning a hazardous chemical. The SDS is prepared in accordance with the HCS [previously known as a Material Safety Data Sheet (MSDS)].

Spill kit: A container of supplies, warning signage, and related materials used to contain the spill of an HD.

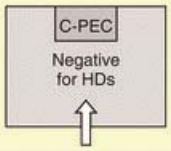
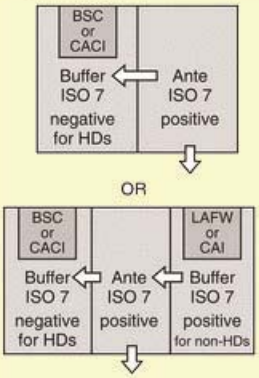
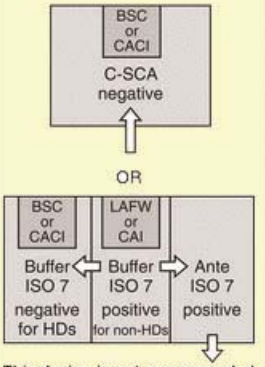
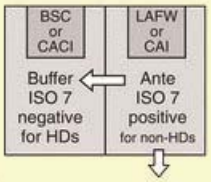
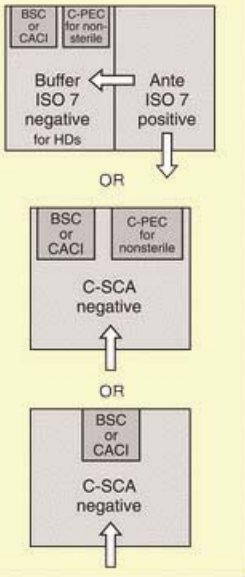
Standard operating procedure (SOP): Written procedures describing operations,

testing, sampling, interpretation of results, and corrective actions that relate to the operations that are taking place.

Supplemental engineering control: An adjunct control (e.g., CSTD) that may be used concurrently with primary and secondary engineering controls. Supplemental engineering controls offer additional levels of protection and may facilitate enhanced occupational protection, especially when handling HDs outside of primary and secondary engineering controls (e.g., during administering).

Trace contaminated waste: Items used in the handling, compounding, dispensing, administration, or disposal of antineoplastic agents that are not overtly contaminated (e.g., gowns, gloves, goggles, wipes).

APPENDIX B: EXAMPLES OF DESIGNS FOR HAZARDOUS DRUGS COMPOUNDING AREAS[A]

Use	Optimal Primary and Secondary Control	Minimum ACPH	Limitations Primary and Secondary Control	Minimum ACPH	Notes for limitations
Nonsterile HD compounding		12			
Sterile HD compounding		30	 **This design is not recommended**  Typically used in oncology clinic settings.	12 30 30	Maximum BUD as described in <797> for segregated compounding area. If this design is in place, measures must be taken to avoid contamination of the positive-pressure buffer room. Maximum BUD as described in <797>.
Both sterile HD and nonsterile HD compounding	A separate room for sterile and nonsterile compounding is recommended			30 12 12	For rooms used for both sterile and nonsterile compounding, particle-generating activity must not be performed when sterile compounding is in process. C-PECs must be at least 1 meter apart. Maximum BUD as described in <797> for segregated compounding area. Maximum BUD as described in <797> for segregated compounding area.

[a] The arrows indicate direction of airflow.

APPENDIX C: TYPES OF BIOLOGICAL SAFETY CABINETS

Class I: A BSC that protects personnel and the environment but does not protect the product/preparation. A minimum velocity of 75 linear feet/min of unfiltered room air is drawn through the front opening and across the work surface, providing personnel protection. The air is then passed through a HEPA/ULPA (ultra-low particulate air) filter, either into the room or to the outside in the exhaust plenum, providing environmental protection.

Class II: Class II (Types A1, A2, B1, and B2) BSCs are partial barrier systems that rely on the movement of air to provide personnel, environmental, and product/preparation protection. Personnel and product/preparation protection are provided by the combination of inward and downward airflow captured by the front grille of the cabinet. Side-to-side cross-contamination of products/preparations is minimized by the internal downward flow of HEPA/ULPA filtered air moving toward the work surface and then drawn into the front and rear intake grilles. Environmental protection is provided when the cabinet exhaust air is passed through a HEPA/ULPA filter.

- **Type A1 (formerly, Type A):** These Class II BSCs maintain a minimum inflow velocity of 75 feet/min; have HEPA-filtered, down-flow air that is a portion of the mixed down-flow and inflow air from a common plenum; may exhaust HEPA-filtered air back into the laboratory or to the environment through an exhaust canopy; and may have positive-pressure contaminated ducts and plenums that are not surrounded by negative-pressure plenums. Type A1 BSCs are not suitable for use with volatile toxic chemicals and volatile radionucleotides.
- **Type A2 (formerly, Type B3):** These Class II BSCs maintain a minimum inflow velocity of 100 feet/min; have HEPA-filtered, down-flow air that is a portion of the mixed down-flow and inflow air from a common exhaust plenum; may exhaust HEPA-filtered air back into the laboratory or to the environment through an exhaust canopy; and have all contaminated ducts and plenums under negative pressure or surrounded by negative-pressure ducts and plenums. If these cabinets are used for minute quantities of volatile toxic chemicals and trace amounts of radionucleotides, they must be exhausted through properly functioning exhaust canopies.
- **Type B1:** These Class II BSCs maintain a minimum inflow velocity of 100 feet/min; have HEPA-filtered, down-flow air composed largely of uncontaminated, recirculated inflow air; exhaust most of the contaminated down-flow air through a dedicated duct exhausted to the atmosphere after passing it through a HEPA filter; and have all contaminated ducts and plenums under negative pressure or surrounded by negative-pressure ducts and plenums. If these cabinets are used for work involving minute quantities of volatile toxic chemicals and trace amounts of radionucleotides, the work must be done in the directly exhausted portion of the cabinet.
- **Type B2 (total exhaust):** These Class II BSCs maintain a minimum inflow velocity of 100 feet/min; have HEPA-filtered, down-flow air drawn from the laboratory or the outside; exhaust all inflow and down-flow air to the atmosphere after filtration through a HEPA filter without recirculation inside the cabinet or return to the laboratory; and have all contaminated ducts and plenums under negative pressure or surrounded by directly exhausted negative-pressure ducts and plenums. These cabinets may be used with volatile toxic chemicals and radionucleotides.

Class III: The Class III BSC is designed for work with highly infectious microbiological agents and other hazardous operations. It provides maximum protection for the environment and the worker. It is a gas-tight enclosure with a viewing window that is secured with locks and/or requires the use of tools to open. Both supply and exhaust air are HEPA/ULPA filtered. Exhaust air must pass through two HEPA/ULPA filters in series before discharge to the outdoors.

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