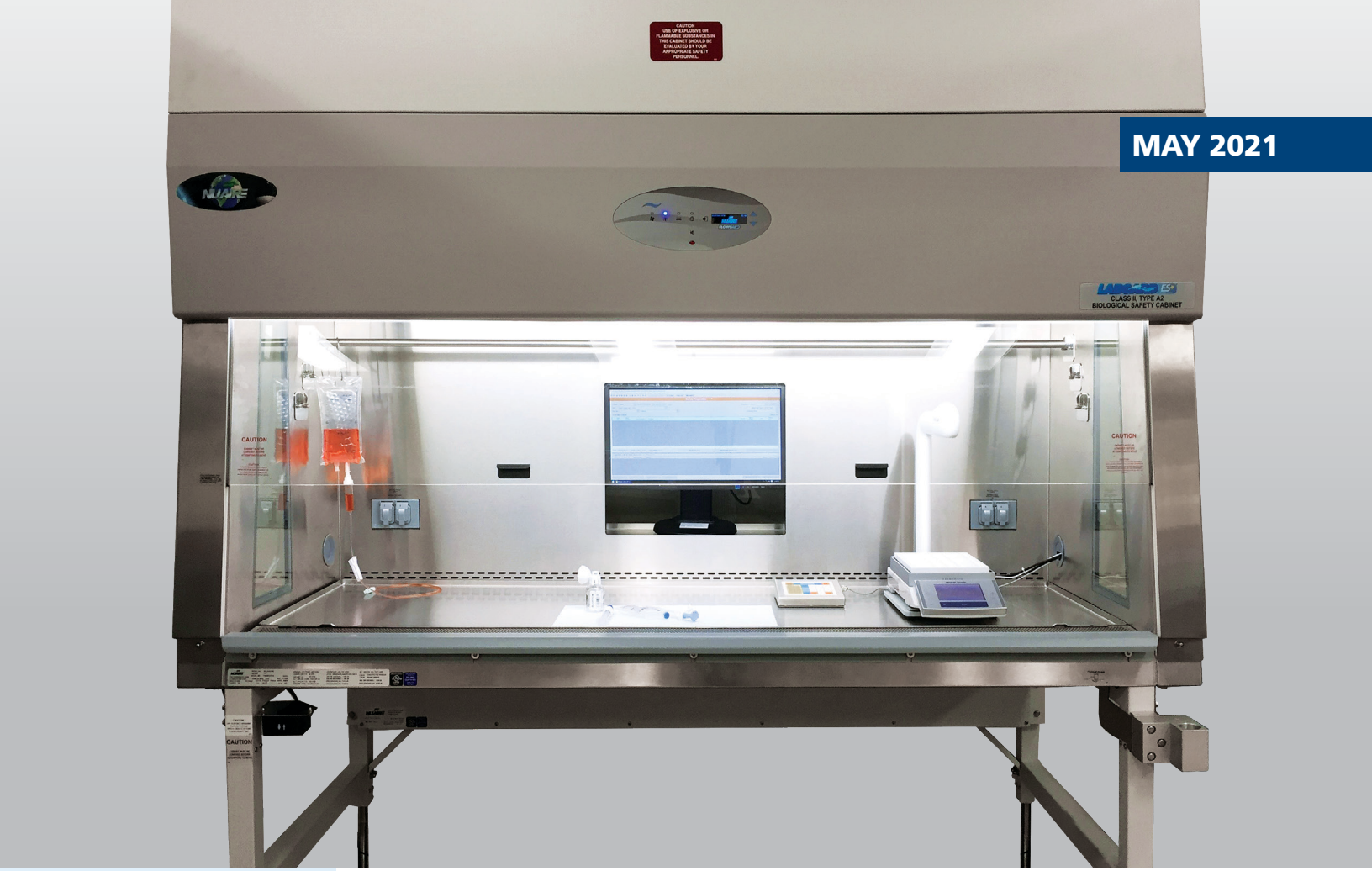


MAY 2021

Patricia C. Kienle, RPh, MPA, BCSCP, FASHP

Director of Accreditation and Medication Safety
Cardinal Health

Best Practices for HD Handling

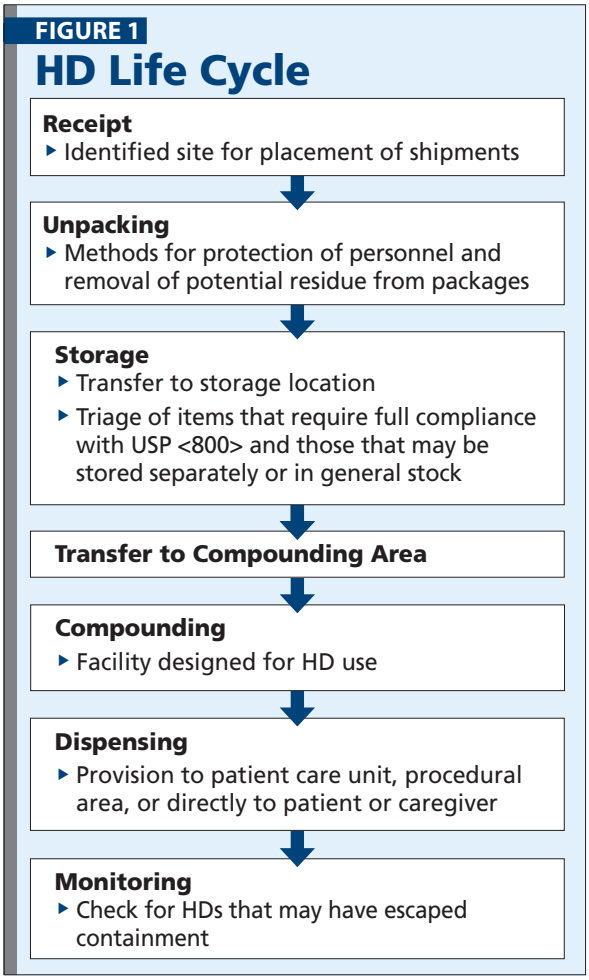
Some drugs used for treatment of cancers and other conditions may have adverse effects on the clinicians who care for the patients being treated. Hazardous drugs (HDs) are those that are carcinogenic or genotoxic, cause teratogenicity or other developmental toxicity, cause reproductive toxicity, or organ toxicity at low doses in humans.[1] As new therapeutic agents are developed, those that mimic the existing structure or toxicities of known HDs must also be considered hazardous until definitive information is known.[2]

Proper handling of HDs is essential for safe workplace practices. While the patient will be exposed to the HD as part of therapy, health care personnel need to be protected from potential contamination. Although mitigating factors to exposure have been published for over 20 years, universal compliance has not yet occurred.[2]

Steps to Mitigate Risk

Strategies for improving HD handling can be implemented in a manner similar to the way many organizations assess safe medication practices: incorporate safety steps into the medication use cycle. Applying best practices throughout the cycle serves to mitigate risks to health professionals who handle HDs. Among the most practical approaches to workplace safety for health care personnel is the use of containment devices—such as biological safety cabinets (BSCs), compounding aseptic containment isolators (CACIs), externally

Best Practices for HD Handling



vented negative pressure rooms, and closed system drug-transfer devices (CSTDs)—in addition to establishing robust policies & procedures, and utilizing PPE.

It is important to remember that not all HDs need to be handled the same way. When medications are purchased in final dosage forms that do not require manipulation prior to administration, some mitigation of risk is already present. Creating an Assessment of Risk as defined in USP <800> allows an organization to triage risks and implement practices that differ from those listed in USP <800> for those HDs that are not active pharmaceutical ingredients (APIs) or NIOSH Table 1 antineoplastics that must be manipulated prior to patient administration.[3]

USP <800> Hazardous Drugs—Handling in Healthcare Settings is the standard that has been official since December 2019, and has been available as in draft format and as final documents since March 2014.[3] While many organizations have implemented key elements of the chapter, more work remains to achieve full compliance. Pragmatic approaches to addressing the safety components of each step of the medication use cycle include the following:

- **Education & training:** policies and procedures, comprehensive orientation, and requalification using the tests defined in USP chapters
- **Selection:** identification of the HDs handled in the organization, and strategies to mitigate exposure defined in the organization's Assessment of Risk
- **Storage:** placement of HDs in appropriate storage
- **Ordering:** therapeutic and safety issues defined in the organization's policies, approved orders and protocols, and quality oversight
- **Dispensing:** compounding and repackaging dosage forms consistent with USP <800> and associated best practices
- **Administering:** use of closed system drug-transfer devices (CSTDs) and other closed systems and personal protective equipment (PPE)
- **Monitoring:** performing wipe sampling of receiving, storage, compounding, and administration areas to detect HDs that have escaped containment
- **Evaluation:** use of a quality system, such as *Plan-Do-Check-Act* (PDCA) for continuous improvement of practices

Defining these processes requires a clear understanding of the movement of HDs throughout the workplace. Emphasis has often been limited to areas where the drugs are compounded, but the entire life cycle of the HDs in an organization must be evaluated, from receipt, through compounding, to dispensing and monitoring (see **FIGURE 1**).

Receiving, Unpacking, and Storing HDs

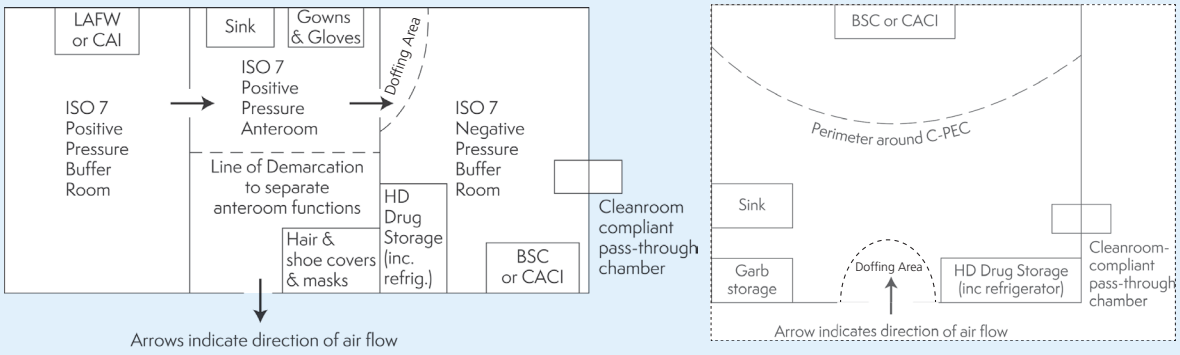
Proper handling must start when the HDs are delivered to your organization. If HDs are delivered to a location other than the area where they will be stored and compounded, they must be transferred to the storage/compounding area as soon as possible. Receipt of HDs may occur in your general receiving area. Do not place external shipping containers or other packages of NIOSH Table 1 HDs in a positive pressure area (such as an anteroom or positive pressure buffer room). Unpacking NIOSH Table 1 antineoplastics and other HDs you have not exempted in your Assessment of Risk should occur in negative or neutral/normal pressure.

Compliant Facility Design

Active pharmaceutical ingredients (APIs) of any HD on the NIOSH list and any NIOSH Table 1 antineoplastic must be

FIGURE 2

Examples of HD Compounding Rooms



Sample designs for both a cleanroom suite and a C-SCA for HD production.

handled under the containment and work practices listed in USP <800>. Other HDs may be included in an Assessment of Risk to establish alternative handling strategies. The dosage forms of HDs that have been deemed entity-exempt by the organization must be stored and compounded as indicated on the Assessment of Risk. Some non-antineoplastic HDs that have been deemed entity-exempt may be prepared in laminar air flow workbenches (LAFWs) if precautions detailed in the Assessment of Risk are followed. HDs that must follow all containment listed in USP <800> must be compounded in externally vented negative pressure PECs within an externally vented negative pressure room.

Containment primary engineering controls (C-PECs) used for compounding HDs must be negative pressure devices. The C-PEC (informally called a chemo hood) used for compounding nonsterile HDs must meet the definition of a 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.[3] CVEs (often called powder containment hoods) are designed to protect the worker and the environment. CVEs should be vented to the outside, but may instead have redundant HEPA filters in the event that external venting is not possible.

The C-PEC for compounding sterile HDs must be one that protects the preparation as well as protecting the worker and the environment. Two kinds of C-PECs for sterile compounding are available: a BSC and a CACI. Two types of BSCs are common, and both must be vented to the outside: the Type A2 cabinet recirculates a portion of the air in the working area, and the Type B2 cabinet is totally exhausted to the outside. All C-PECs used for compounding sterile HDs must have unidirectional flow and be vented to the outside.

Unless entity-exempt, HDs requiring refrigeration must be kept in a refrigerator dedicated to HD storage that is placed within the containment secondary engineering control (C-SEC), commonly referred to as the negative-pressure room or chemo room.

The C-SECs used for storage or compounding of HDs that have not been entity-exempt have four criteria:

1. Room that is separate from non-HD storage or compounding
2. Negative pressure between 0.010" and 0.030" water column to adjacent areas
3. Vented to the outside
4. An appropriate number of air changes per hour (ACPH). Storage, nonsterile compounding areas, and containment segregated compounding areas (C-SCAs) must have at least 12 ACPH. Sterile compounding suite rooms must have at least 30 ACPH.

Ideally, sterile compounding should occur in a cleanroom suite, consisting of at least an anteroom (which must be at least ISO 7 and positive pressure) and a buffer room (which must be at least ISO 7 and negative pressure). Minimally, a C-SCA may be used, which can be a single negative room with a defined area for the C-PEC. **FIGURE 2** provides examples of common facility designs.

HDs that must be handled with all the precautions listed in USP <800> may be stored in a negative pressure storage room or inside the chemo room (negative buffer room or

Best Practices for HD Handling

TABLE
Key Design Criteria

- Air handling system
- Ceiling HEPA filters
- Ports for testing HEPA filter integrity
- Exhausts that are low on the wall
- Cleanable surfaces that can withstand frequent decontamination
- Doffing area prior to leaving the room
- Placement of equipment (eg, printers) that does not interfere with air flow or material transfer
- Areas for storage of drugs and supplies
- Consideration for cleanroom-compliant pass-through chambers
- Room for trash segregation and removal

C-SCA). Carefully evaluate the areas where HDs will be stored, since storage in the negative buffer room or C-SCA must be cleaned at least monthly.

In addition to the basic design of the facility, many structural requirements must be met. The **TABLE** lists some of the considerations for design. Refer to USP <800>[3] and your certifier to include all appropriate design criteria. Once your initial construction or renovation plans are established, consider taping off the full dimensions and equipment placement to simulate your work processes.

Cleaning Requirements

Key to maintaining safe workspaces is the cleaning process. USP <800> outlines the four steps necessary to remove HD residue:

1. **Deactivation.** When possible, deactivate the HD. Since the solution to use is often unknown, this step is generally combined with decontamination.
2. **Decontamination.** All HD surfaces must be decontaminated with a solution known to remove HDs. Solutions should be ready-to-use (to avoid the need to dilute toxic chemicals and maintain the required documentation) and should be designed for use with HDs.
3. **Cleaning.** A properly diluted (if necessary) detergent must be used to clean the area.
4. **Sanitizing.** Sterile 70% isopropyl alcohol must be used to sanitize the area. Note that this is the only solution which must be sterile, since it is the final solution applied to surfaces.

Do not use any spray solution containers in negative rooms, as spraying could aerosolize HD residue.

CSTD Use

The technique used to compound HDs differs from that used for non-hazardous drugs so that over-pressurization of vials does not allow spray of contents when removing needles from the vials. Use of CSTDs for compounding makes this process safer. If a CSTD is not used when compounding, a negative pressure technique must be used.[4] Training kits are available that contain a dye and a black light to detect potential exposure by simulating negative pressure compounding procedures.

Monitoring for HD Contamination

USP <800> recommends wipe sampling be conducted for areas that could be contaminated with HD residue.[3] Sterile compounders are familiar with microbiological monitoring of hoods and rooms where visible contamination can be viewed on media plates. Issues of HD contamination are generally not visible so possible contamination needs to be monitored via a wipe sampling process. Wipe sampling provides clear data to assess employee exposure to HDs in the areas where these products are stored, compounded, and administered. It can be further leveraged to support staff training and assess the organization's HD spill response.[5]

Summary

Antineoplastics and other HDs are important therapies that successfully treat many medical conditions. Inadvertent exposure of health care workers to HDs must be as low as reasonably achievable. Use of containment (appropriately designed and used hoods, cleanrooms, and CSTDs), PPE designed for use with HDs, and robust policies and work practices are essential to providing a safe workplace. Pharmacy leadership must address and overcome any barriers to the implementation of best practices.

References

1. US Centers for Disease Control and Prevention and National Institute for Occupational Safety and Health. NIOSH List of Antineoplastics and Other Hazardous Drugs in Healthcare Settings, 2016. www.cdc.gov/niosh/docs/2016-161/default.html. Accessed April 1, 2021.
2. US Centers for Disease Control and Prevention and National Institute for Occupational Safety and Health. Hazardous Drug Exposures in Healthcare. www.cdc.gov/niosh/topics/hazdrug/default.html. Accessed April 1, 2021.
3. United States Pharmacopeial Convention. USP General Chapter <800> Hazardous Drugs – Handling in Healthcare Settings. www.usp.org/compounding/general-chapter-hazardous-drugs-handling-healthcare. Accessed April 1, 2021.
4. Wilson JP, Solimando DA. Aseptic technique as a safety precaution in the preparation of antineoplastic agents. *Hosp Pharm*. 1981;16(11):575-81.
5. Gabay M, Johnson P, Fanikos J, et al. Report on 2020 Safe to Touch Consensus Conference on Hazardous Drug Surface Contamination. *Am J Health Syst Pharm*. https://doi.org/10.1093/ajhp/zxab134. Accessed April 5, 2021.

20-1594-N-G-EN-1-0621