USP Chapter 800 Hazardous Drugs — Handling in Healthcare Settings will increase protection for compounding personnel and other healthcare workers who come in contact with hazardous drugs, including all the antineoplastic and other hazardous drugs on the National Institute for Occupational Safety and Health (NIOSH) list.

Below are some tips and best practices regarding hazardous drug (HD) compounding:

Hand Hygiene and Garbing

- **Chapter <800>** only requires a “doffing area” inside a C-SEC that is inside or off of the nonhazardous buffer room. This doffing area can be similar to a 3-foot square with its outer edge along the door out of the C-SEC and 3 foot in all directions. It can be marked using yellow cleanroom tape.

- **Don 2 pairs of shoe covers at the line of demarcation when you will be entering the Containment Secondary Engineering Control (C-SEC) or Containment Segregated Compounding Area (C-SCA).** Wipe studies show that the floors of HD buffer rooms are contaminated. By wearing double shoe covers, the outer pair can be removed before leaving the C-SCA or C-SEC, thereby reducing HD residue that would be spread by walking. As it relates to the “doffing line,” remove the outer shoe cover of the first foot and then step into the doffing area (discarding the contaminated boot cover in the yellow trace waste). Carefully remove the other foot’s outer shoe cover and place it into the yellow trace waste as you step fully inside the doffing area.

- **Wear 2 pairs of powder-free, sterile gloves that have been tested to ASTM standard 6978-05 to protect yourself from hazardous drug residue which can permeate non-tested gloves.** Both pairs of gloves must be sterile, since the outer pair of gloves is removed inside the C-PEC (CACI or BSC) so that the final CSP that has been decontaminated can be removed from the C-PEC by gloves that are not contaminated with HDs.
• **When donning double gloves**, the inner pair of gloves of gloves is worn underneath the cuff of the chemo-rated gown (when using a BSC) and the 2nd is worn outside and pulled up over the cuff of the gown. Set 2 pairs of sterile gloves with their outer packaging removed on a clean flat surface in the C-SEC or C-SCA. Pull up sleeves. Open both pairs of gloves. Don first pair of sterile chemo gloves. Use the sterile paper from the first pair of gloves to grasp gown sleeves and pull them down over cuffs being careful not to contaminate gloves. Don second pair of gloves pulling cuffs of gloves up and over cuffs of the chemo gown.

• **Always use a chemo-rated gown which closes in the back and is made from materials that do not permit liquids to permeate the gown (in case of a spill).** Though there is not a specific ASTM standard for chemotherapy gowns it is wise to use gowns that have been tested to ASTM F1671 which tests gowns for penetration by blood-borne pathogens in the form of liquids. There are gowns sold as Chemo-rated gowns that are uncoated and those that are coated. In CriticalPoint’s testing, only coated chemo-rated gowns were able to successfully shield workers from airborne mists and powders used to simulate chemotherapy. Coated gowns make them far less permeable to liquids.

• **Gowns used for HD compounding must never be reused and should be changed if HD compounding is performed for more than 3 continuous hours.** Unlike gowns used for nonhazardous sterile compounding which can be reused for one shift as long as they don’t leave ISO class 8 air, gowns used during HD compounding are likely to be contaminated with HD residue and may not be reused because they become a source of HD contamination spread. Gowns are removed before the innermost gloves are removed.

• **Proper doffing of HD PPE is key to preventing exposure.** The order of doffing HD PPE when exiting the C-SCA or C-SEC is as follows:

1. Remove outer pair of sterile gloves (those that touched the HD CSP) inside the C-PEC
2. Remove outer shoe covers one at a time stepping over the doffing line. Discard in trace waste.
3. Remove the chemotherapy gown slowly and deliberately starting by pulling off at the shoulders slowly turning the gown inside out and being aware that the gown is not touching garb underneath the gown. Discard in yellow trace waste.
4. Remove the inner pair of gloves by carefully peeling off the first glove without touching your skin. Place that glove in the palm of the other hand. Slide finger underneath the cuff of the second glove and pull the glove off inside out making a pouch containing both gloves. Discard in yellow trace waste.
5. Exit the C-SEC and perform hand hygiene. Hand hygiene must be performed even if this is a shared anteroom and you will be garbing to go into the non-hazardous buffer room. Perform hand hygiene; don non-hazardous gown; enter buffer room; use alcohol based surgical hand rub with persistent activity and don sterile gloves.

• **If there is a potential for exposure due to splashing** which is most likely during decontamination and cleaning as well as spill cleanup, wear goggles (not safety glasses).

• **Cyclophosphamide and 5-fluorouracil are some of the drugs that have been reported to volatilize** (form a vapor or gas phase) during normal handling at room temperature. Since they are some of the most frequently prescribed HDs, it is strongly recommended that personnel who open BSCs and CACIs for daily decontamination, cleaning and disinfection or open them during the required monthly access below the deck to perform decontamination and cleaning; as well as those responsible for spill cleanup be fit-tested and properly instructed in the use of either full-
face, dual-chamber respirators or half-face, dual-chamber respirator with goggles that have been fitted with combination (particulate and vapor) filter cartridges. N95 and N100 masks are effective protection for particles but not for vapors.

**Containment Primary Engineering Controls and Containment Secondary Engineering Controls**

**Containment Primary Engineering Controls (C-PECs):**

- **By July 1, 2018, C-PECs used for the preparation of sterile antineoplastic HD CSPs must** provide ISO Class 5 unidirectional first air and be vented to the outside.

- **By July 1, 2018 Class II, Type A2, B2, Class III BSC, and CACI are all acceptable for HD sterile compounding** however, Class II Type A2 BSCs offer a simple and reliable integration with the ventilation and pressurization requirements of the C-SECs. Use of Class II Type B2 BSCs should be strongly considered if any compounding occurs of drugs known to volatilize (such as cyclophosphamide, cis-platinum and flurouracil).1

- **Don’t turn off the C-PECs.** Although all PECs are made to operate continuously, it is important that C-PECs, which are negative pressure devices are not turned off since the C-SEC in which they are placed (buffer room or C-SCA) may, at least in part, be maintaining its overall 0.01 to 0.03 inches water column negative pressure to adjacent spaces based on the function of the C-PEC.

- **Never compound HDs in an LAFW or a CAI.** These devices, especially the CAI, may “look” like they provide protection for the worker but they do not provide any worker protection. Even the use of closed system transfer devices (CSTDs) does not afford complete protection. The low volume exemption in USP 797 (low volume HD compounding can be performed inside a BSC that is inside of a positive pressure room as long as a CSTD is used) has been removed in the current USP chapter <797> revision. No safe level of exposure to antineoplastic chemotherapies has ever been established. HD compounding can occur only inside a negative pressure C-PEC.

- **BSCs must be used properly to provide protection.** It is very important that the intake grill that runs along the front and back aspects of the BSC are not be blocked by papers, boxes and as often occurs, operators arms. Do not place labels, compounding worksheets or rest arms on the BSC. If these intake grills are blocked it can cause turbulence and block the intake of HD particles and vapors, allowing them to trail up the operator’s arms and directly into the operator’s face.

- **First Air in C-PECs comes from the ceiling (top of the C-PEC) so it is vertical first air.** In vertical first air the operator’s hands are never held in a 180° (12 pm and 6 pm) angle since that would block first air from bathing the critical site. Always perform manipulations at an angle so that the critical sites receive continuous unidirectional first air.

**Containment Secondary Engineering Controls C-SECs:**

- **According to USP <800> (so by July 1, 2018), ALL types of C-SECs must be externally vented,** have fixed walls and doors that separate it from other areas, have appropriate air changes per hour (see below) and maintain a negative pressure of 0.01” to 0.03” water column negative to adjacent spaces.

- **There are 3 types of C-SECs which must meet the following criteria in addition to those listed above:**

  **Negative pressure, ISO Class 7 Buffer Room which is accessed directly from a positive pressure ISO Class 7 anteroom and both the anteroom and buffer room must maintain at least 30 ACPH from HEPA filtered air supplied from the HVAC system.**
**Negative pressure ISO Class 7 Buffer Room which is accessed directly from a positive pressure ISO Class 7 Non Hazardous Buffer Room.** The positive pressure ISO Class 7 buffer room must maintain at least 30 ACPH with at least 15 ACPH coming from HEPA filtered air supplied from the HVAC system.

*C-SCA* which is a negative pressure room that maintains an air cleanliness level worse than ISO Class 7 (it can be Non ISO classed) and maintains at least 12 ACPH.

- In the negative pressure Buffer Room that is entered through the non-hazardous buffer room, Chapter <800> requires a “doffing area” immediately inside the C-SEC and certain garbing practices to reduce the risk of introducing HD residue into the non-hazardous buffer area. Consider instituting a “doffing” area inside all C-SECs and C-SCAs as one way to reduce the risk of tracking HD residue outside the HD compounding area.

- Chapter 800 requires locations to have a working eyewash that meets local, state and federal law. Follow OSHA 29 CFR 1910.151, Medical Services and First Aid which quotes the ANSI Eyewash Standard Z351.1-2014 which says “A personal wash unit may be kept in the immediate vicinity of employees working in a potentially hazardous area. The main purpose of these units is to supply immediate flushing. With this accomplished, the injured individual should then proceed to a plumbed or self-contained eyewash and flush the eyes for the required 15-minute period.”

- Per USP 800, any antineoplastic HD drugs that require refrigeration must be stored in a dedicated refrigerator and that refrigerator is placed in a negative pressure room that has at least 12 ACPH.

- Anterooms that serve both nonhazardous and hazardous drug (HD) buffer rooms, must be ISO Class 7 and now, to meet USP 800 requirements, must have fixed walls and doors. Since the C-SEC is negative pressure, air from the anteroom will be drawn into the HD buffer room. It is imperative that the ante room air is at least as clean as the air in the HD buffer room. Therefore, cleaning in ante rooms serving negative pressure buffer rooms is as important as cleaning the buffer rooms themselves.

- Unlike non-hazardous positive pressure gradients, more negative pressure than what is required in a HD buffer room can be detrimental. Negative pressures should not exceed 0.03” water column negative. If the pressure is too negative, it results in dirty air and particles from outside the space (such as above the ceiling) being drawn into the space especially as the facility ages. Elevated particle counts and environmental hits have been in highly negative spaces.

- The HD buffer room is an ideal place to store HDs. These rooms meet the requirement for negative pressure and at least 12 ACPH. Exhaust accommodations should be installed for refrigerators to aid the sweeping away of particles generated by devices.

- Sinks for hand hygiene must be available in the anteroom and placed in such a way that it does not interfere with the C-SEC room cleanliness (at least a meter away from the entrance to the C-SEC). Sinks for C-SCAs must be placed at least a meter away from the C-PEC or immediately outside the C-SCA.

**Decontamination, Cleaning and Disinfection in Hazardous Drug Sterile Compounding Environments**

- Those who perform cleaning to HD areas must don HD garb as though they were compounding. Remember HD PPE must be worn regardless of whether a BSC or a CACI is used to compound HDs to protect the compounding and cleaning staff from contamination that exists in the HD compounding area. Anyone who performs cleaning duties must employ full HD PPE which in addition to regular nonhazardous garb, includes back closing HD gowns which have demonstrated the ability to shed...
liquids, gloves that have been tested to ASTM standard D6978-05 (2013) as well as double booties. HD garb (outer gloves, HD gown and outer booties) must be doffed (taken off) before leaving the HD buffer area preferably in a designated doffing area inside the HD buffer area.

- **Chapter 800 requires the use of double shoe covers** where the outer pair is taken off prior to leaving the C-SEC to reduce tracking HD contamination outside the C-SEC. CriticalPoint performed some ad-hoc testing and strongly recommends that that outer pair of shoe covers be water-resistant or water-proof rather than standard shoe covers. The testing found that very small amounts of fluorescent HD surrogate powder spread on the C-SEC floor to simulate HD residue, penetrated through two pairs of standard shoe covers whereas the water-resistant shoe covers prevented contamination from getting through to the inner shoe covers by the used during testing.

- **Cleaning supplies and equipment used in the HD area may not be used in the non-hazardous areas.** By using ready-to-use agents (do not require dilution with water) for decontamination and cleaning, use of buckets and sinks can be avoided. Cleaning supplies can be stored in the C-SEC.

- **Do not spray cleaning agents inside C-PECs or C-SECs.** Spraying further spreads any HD residues in the area. Use presaturated wipes (whether commercial presaturated or presaturated by personnel and transferred into the C-PEC) wetted with different decontamination agent, cleaning agent and disinfecting agent. Some of the chemicals or products used for decontamination can also be irritating when sprayed, creating an aerosol. Pouring the products on wipers, mop heads or mop covers minimizes the potential for irritation. Another strategy is to place low-linting wipes, mop heads and covers into a large zip lock bags containing the chemical agents to be used. The zip lock can be closed to contain the wetted cleaning supplies. Use another zip lock in which to discard used wetted wipes or covers.

- **Daily decontamination/deactivation of HD residues should occur before performing daily cleaning in the C-PEC.** Deactivate/decontaminate HD residues with 2% sodium hypochlorite, or other appropriate, EPA registered oxidizing products based upon the safety data sheets of the HDs. Daily cleaning inside a C-PEC is a three-step procedure:
  1. Decontamination and deactivation with appropriate oxidizing agent
  2. Cleaning with proper prepared (diluted) germicidal detergent/sporicidal agent
  3. Disinfection with sterile 70% isopropyl alcohol. If the 2% sodium hypochlorite is followed by application of the cleaning agent, then deactivation of the bleach with sodium thiosulfate is not necessary.

- **The deck of the C-PEC should also be decontaminated between different types of HDs.** This same surface must also be disinfected between all batches with sterile 70% IPA. Therefore, if you are compounding two different patient-specific preparations of doxorubicin, you must only disinfect with sterile 70% IPA between batches. However, if you are switching to compound a different agent, such as cyclophosphamide, you must first decontaminate the deck or compounding surface of the C-PEC (including use of a new disposable prep pad) and follow that with sterile 70% IPA to disinfect the surface.

- **It is acceptable (and necessary) to open the front cover of a CACI or view screen of the BSC to perform decontamination/deactivation and cleaning under certain circumstances.** At least monthly the area underneath the deck of the CACI/BSC must be decontaminated, cleaned and disinfected. In order to access this area, the C-PEC must be opened. Additionally, the C-PEC may be opened daily to facilitate more efficient and thorough daily cleaning (that choice is up to you). When the C-PEC is opened, CriticalPoint recommends the following:
• Compounding may not be occurring in any room where cleaning is taking place

• Personnel in the area must be wearing full HD PPE

• Though any HD particles and volatiles would have been exhausted, it is possible that during the first step of the process (decontamination/deactivation), that HD residue may become volatile. Therefore, when any C-PEC is opened, personnel MUST wear a fit-tested, full-face, dual-chamber respirator fitted with combination multi-gas/P100 canisters (protect against both particulates and vapors).

• N-95 and N-100 masks only protect against particles.

• Chapter 800 requires the area beneath the deck to be decontaminated and cleaned monthly, but weekly may be a more desirable frequency (depending on the observed state under the deck) as well as after any significant spill event inside the C-PEC.

• It is strongly recommended that weekly decontamination of the floor and high touch areas in the HD buffer area. Based on wipe studies, it is clear that the floor inside the C-SEC as well as high-touch areas are routinely contaminated with HD residue. Because the goal is to achieve 100% containment of HD residue within the C-SEC, CriticalPoint recommends decontamination of the HD buffer area floor and high touch areas at least weekly. The thinking is that between this measure, proper donning and doffing of HD PPE as well as proper decontamination of final CSPs before leaving the PEC, the spread of HD residue can be drastically reduced.

• PeridoxRTU® requires two applications if it is used as both a decontamination agent and a sporicidal agent. This sporicidal agent has also been validated to inactivate 5-fluorouracil, cyclophosphamide, ifosfamide, methotrexate and paclitaxel when applied as directed by the manufacturer. This product can be used weekly in HD buffer areas to both deactivate and decontaminate HD residue however it must be applied twice and the second application allowed to dwell for 3 minutes to be an effective sporicidal agent before the application of sIPA.

References


Simplifi 797® quality assurance and CriticalPoint™ training help ensure compliance with USP <797> and USP <800> standards. For more information, visit www.pharmacyonesource.com or call 800.654.8395