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Environment Matters:
Ensuring Safety in Hazardous Drug Compounding Areas

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DISCLOSURE

Liz Vogel, faculty for this CE activity, has no relevant conflicts of interest within the past 24 months to disclose for this presentation.

There are no relevant financial relationships within the past 24 months to disclose for the following planners of this CE activity:

- Taryn Newsome, CPhT
- Tahsin Imam, PharmD
- Daisy Doan, PharmD

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OBJECTIVES

After completion of this program, pharmacist and pharmacy technician learners will be able to:

1. Summarize United States Pharmacopeia (USP) <800> and its importance in hazardous drug compounding.
2. Outline the different kinds of engineering controls (primary, secondary, and supplementary) and their roles in keeping compounding personnel safe.
3. Describe proper cleaning and environmental monitoring procedures, per USP <797> and USP <800>.
4. Identify the differences in hazardous drug compounding areas in comparison to non-hazardous compounding areas.

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What Makes a Drug Hazardous?

The National Institute for Occupational Safety and Health (NIOSH) defines a drug to be hazardous if it exhibits one or more of the following characteristics in humans or animals

- Carcinogenicity
- Teratogenicity
- Developmental toxicity
- Reproductive toxicity
- Organ toxicity at low doses
- Genotoxicity
- Structure and toxicity profiles of new drugs that mimic existing hazardous drugs

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Distinctive Medical. 18GBL_4.jpg (400x400) (distinctivemedical.com). Accessed: 8/16/2024.

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Hazardous Drug Examples

1. Drugs used for cancer treatment (chemotherapy)
2. Antiviral drugs
3. Hormones
4. Some bio-engineered drugs
5. Other miscellaneous drugs

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Hazardous Drugs Can…

- Bind or damage DNA
- Interfere with cell growth or with DNA synthesis
- Disrupt the function of both healthy and diseased cells
  - Results in toxic side effects for treated patients and their offspring
- Cause adverse effects on healthcare workers
  - The primary characteristic of concern is reproductive-related

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United States Pharmacopeia (USP) <800> Hazardous Drugs-Handling in Healthcare Settings

- This applies to all healthcare personnel who handle hazardous preparations and all entities that store, prepare, transport, or administer hazardous drugs (HD)
  - Includes pharmacies, hospitals, patient treatment clinics, physician practice facilities, or veterinarian offices
- Describes practice and quality standards for handling HDs to promote patient safety, worker safety, and environmental protection
- Handling includes but is not limited to"
  - Receipt
  - Storage
  - Compounding
  - Dispensing
  - Administration
  - Disposal

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USP <800> and Compounding

1. Personnel involved in compounding hazardous drugs must be compliant with the appropriate USP standards for compounding found in USP <795> and USP <797>
2. Compounding must be done using proper engineering controls (primary, secondary, and supplemental)
3. Disposable or clean equipment for compounding must be dedicated for use with hazardous drugs (HDs)
4. Active pharmaceutical ingredients or other hazardous drugs must be handled in a containment primary engineering (C-PEC) to protect against occupational exposure, especially during particle-generating activities

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QUESTION 1

True or False: USP <800> only applies to pharmacy personnel who compound hazardous drugs.

a. True
b. False

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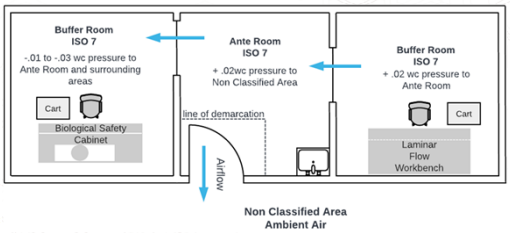
Cleanroom Layout



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Engineering Controls

- Required to protect compounded sterile preparations from cross-contamination and microbial contamination for sterile products during all phases of compounding
- Divided into 3 categories
  - Primary
  - Secondary
  - Supplementary- includes closed system transfer devices (CSTDs) or adjunct controls to offer additional levels of protection

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Primary Engineering Controls

- Containment Primary Engineering Control (C-PEC)
  - Biological Safety Cabinet (BSC)
  - Compounding Aseptic Containment Isolator (CACI)
- Ventilated device designed to minimize worker and environmental hazardous drug exposure when directly handling HDs
- Used to manipulate sterile hazardous drugs
- Provide an ISO Class 5 or better air quality
  - <3520/ m^3 particulate matter in air
- Located in an ISO Class 7 buffer room, with an ISO Class 7 anteroom (in this case)

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Area Scientific. https://areascientific.com/wp-content/uploads/2021/08/BioChemGARD.jpg. Accessed 8/16/2024

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Secondary Engineering Controls

- "Buffer room"
- ISO Class 7 air quality
  - <352,000/m^3 particulate matter in the air
- Physically separate from other preparation areas
- Negative pressure between 0.01 and 0.03 in of water column
- Fixed walls
- At least 30 air changes for an hour
- Attached to positive pressure ISO Class 7 ante room (in this case)

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Design with Ma. https://designwithma.com/wp-content/uploads/2022/06/USP800System-widePharmacyUpgrades-OhioHealth-3.jpg. Accessed 8/16/2024

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ISO Class 7 Ante Room

1. Fixed walls
2. Provides inward air migration of equal cleanliness air into the negative pressure buffer room to contain any airborne hazardous drug
3. Hand-washing sink placed 1 meter from the entrance to buffer room to avoid contamination migration
4. Hazardous drug preparations prepared in an ISO Class 7 buffer room AND ISO Class 7 ante room may be used beyond use dates described in USP <797> based on
   - CSP category
   - Sterility testing
   - Storage temperature

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Supplementary Engineering Controls

Closed System Transfer Devices (CSTD)

- Drug transfer device that mechanically prohibits the transfer of environmental contaminants into the system and the escape of the hazardous drug or vapor concentrations outside the system
- Limit the potential of generating aerosols during compounding
- CSTDs generally follow one of two design concepts, using either a physical barrier or an air-cleaning technology to prevent the escape of hazardous drugs into the work environment
- Examples include Equashield©, PhaSeal©, ChemoClave©, and Onguard©
- CSTDs should always be used when compounding hazardous drugs when the dosage form allows
- CSTDs are NOT to be used as a substitute for a C-PEC when compounding

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BD. https://www.bd.com/assets/images/us-products/hazardous-drug-safety/body-components/phaseal-optima_hotspot_20220328B.png. Accessed 8/16/2024

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QUESTION 2

True or False: Compounding and manipulation of a hazardous medication should occur in a POSITIVE pressure room.

a. True
b. False

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Room Certification and Recertification

1. Must be done prior to compounding any Category 1 or 2 compounded sterile products using current Controlled Environment Testing Association (CETA) certification guide for Sterile Compounding Facilities
2. Certification of all classified areas including the primary engineering control must be performed initially
3. Recertification must be performed at least every 6 months or if there are changes to the area such as redesign, construction, replacement or relocation of a PEC, or alteration in the configuration of the room that could affect airflow or air quality
4. Records must be reviewed by the designated person(s)
5. A corrective action plan must be implemented and documented in response to any out-of-range results

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CETA™ Controlled Environment Testing Association

Controlled Environment Testing Association. ah-logo.png (387x160) (mambercdata.net). Access 8/16/2024

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Microbiological Air and Surface Sampling

- Provides information on the environmental quality of the compounding area
- Identifies environmental quality trends, potential routes of contamination, and allows for implementation of corrective actions to minimize the risk of CSP contamination
- Performed initially for sterile compounding facilities to establish baseline level of environmental quality
- After initial sampling, surface sampling is performed monthly or as described in site's standard operating procedure (SOP)
- After initial sampling, air sampling is performed every 6 months or as described in site's standard operating procedure

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Microbiological Air and Surface Sampling SOP

Must include:

- Diagram of sampling locations
- Procedures for collecting samples
- Frequency of sampling
- Size of samples (surface area or volume of air)
- Time of day of sampling in relation to activities of the compounding area
- Action levels that will trigger corrective action

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Sampling Locations

- Viable Air Sampling (done at least every 6 months)
  - ISO Class 5 PEC
  - ISO Class 7 room during dynamic operating conditions
- Microbiological Surface Sampling
  - Interior of the ISO Class 5 PEC
  - Equipment contained in PEC
  - Staging or work area(s) near the PEC
  - Frequently touched surfaces

When conducted, surface sampling must be performed at the end of the compounding activity or shift, but before the area has been cleaned and disinfected

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Environmental Wipe Sampling

- Performed to detect hazardous drug residue on surfaces
- SHOULD be performed routinely (initially as a benchmark and at least every 6 months, or more often as needed)
- Surface wipe sampling locations include:
  - Interior of the C-PEC and equipment contained in it
  - Pass-thru chambers
  - Surfaces in staging or work areas near C-PEC
  - Areas adjacent to C-PECs
  - Areas immediately outside the HD buffer room
  - Patient administration areas

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Cleaning

- All areas where hazardous drugs are handled, as well as all reuseable equipment and devices must be deactivated, decontaminated, and cleaned. Additionally, all sterile compounding areas and devices must be subsequently disinfected.
  - All sterile compounding cleaning must comply with USP <797>
  - All entities should establish written procedures for decontamination, deactivation, cleaning and disinfecting
- All personnel performing these activities must wear appropriate PPE resistant to the cleaning agents used, including two pairs of chemotherapy rated gloves and impermeable disposable gowns.
- Eye protection or face shields must be used if splashing is likely
- If warranted, respiratory protection must be used

*PPE, personal protective equipment

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Grayline Medical. C20_MEQT-PSME0001_300x300_png_1bdb5d31-2b64-4a05-89e3-2c3fe5091ba4_300x300.png (300×300) (graylinemedical.com). Accessed 8/16/2024

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Cleaning Steps

- Deactivating-rendering a compound as inert or inactive
  - EPA-registered oxidizer
- Decontamination-remove hazardous drug residue
  - May include alcohol, water, peroxide, or sodium hypochlorite
- Cleaning-Removal of organic and inorganic material
  - Germicidal detergent
- Disinfection (for sterile manipulations)-destroy microorganisms
  - EPA-registered disinfectant and/or sterile alcohol as appropriate for use

*EPA, Environmental Protection Agency

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Fisher Scientific. PS-840IR.jpg-650.jpg (650×385) (fishersci.com). Accessed 8/16/2024

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End of Day Cleaning

- C-PEC
  - Complete full clean (deactivate, decontaminate, clean, and disinfect)
- High touch surfaces within buffer room
  - Clean and disinfect counters, pass-thru, laptops, door handles, chairs
- Floor
  - Clean
  - Mop, beginning at the point farthest from the door and work your way out of the room (cleanest to dirtiest)

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Monthly Cleaning

- Performed using a sporicidal agent
- At a minimum done monthly (as well as weekly in the negative pressure buffer room) or in accordance with the sterile compounding facility's standard operating procedures
- Includes all items within the classified areas
  - C-PEC, PEC (including outside)
  - Equipment inside PECs
  - Removable work tray of PEC
  - Pass-thrus
  - Work surface(s) outside the PEC
  - Walls, doors, and door frames
  - Ceilings
  - Storage shelving
  - Bins and items inside
  - Equipment outside PECs

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Fischer Scientific. OPHS.mb912kqsucPFPw474C474 (240×330) (bing.com). Accessed 8/16/2024

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QUESTION 3

At a minimum, how often does microbial surface sampling and viable air sampling need to be performed within classified areas?

a. Monthly
b. Monthly and at baseline
c. Whenever personnel have time
d. Monthly, at baseline, and according to site's standard operating procedures (SOP)

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What's the Difference??
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Microsoft Stock Photos

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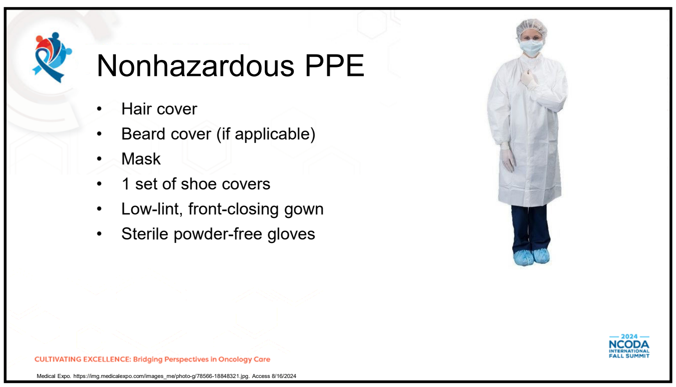
Nonhazardous PPE
• Hair cover
• Beard cover (if applicable)
• Mask
• 1 set of shoe covers
• Low-lint, front-closing gown
• Sterile powder-free gloves
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Medical Expo. https://img.medicalexpo.com/images_me/photo-g/78566-18848321.jpg. Access 8/16/2024

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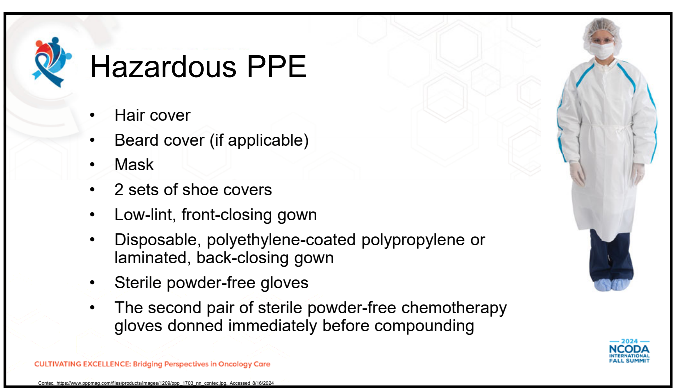
Hazardous PPE
• Hair cover
• Beard cover (if applicable)
• Mask
• 2 sets of shoe covers
• Low-lint, front-closing gown
• Disposable, polyethylene-coated polypropylene or laminated, back-closing gown
• Sterile powder-free gloves
• The second pair of sterile powder-free chemotherapy gloves donned immediately before compounding
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Contec. https://www.pppmag.com/files/products/images/1209/ppp_1703_nn_contec.jpg. Accessed 8/16/2024

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QUESTION 4

True or False: Additional sterile garb and PPE may be needed when compounding, preparing, and handling hazardous medications.

a. True
b. False

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SUMMARY

Nonhazardous Drug Compounding Area

- Compounding occurs in a laminar airflow workbench (LAFW) that provides unidirectional air and designed to only protect the direct compounding area/compounded sterile preparation NOT workers
- Positive pressure ISO Class 7 or 8 buffer room
- Use of needles and ampules in compounding
- Sporicidal agents used in monthly cleaning

Hazardous Drug Compounding Area

- Compounding occurs in a containment primary engineering control (C-PEC) to protect workers
- Negative pressure ISO Class 7 buffer room
- Use of supplementary engineering controls including closed system transfer devices
- Use of cleaning supplies including sporicidal agents for daily, weekly, and monthly cleaning
- Use of additional PPE

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QUESTION & ANSWERS

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Ensuring Safety in Hazardous Drug Compounding Areas

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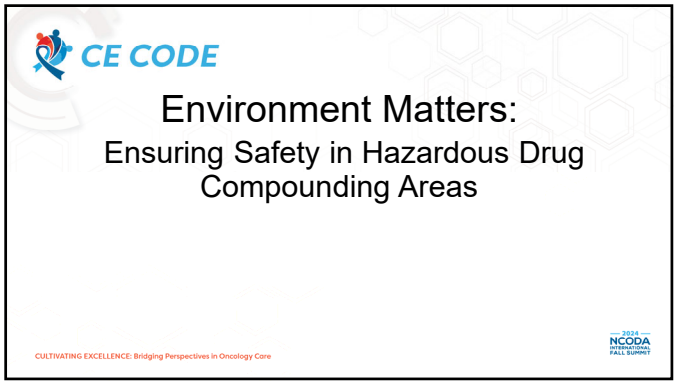
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