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Learning Objectives

- Recognize the classification of a hazardous drug per USP <800>
- Describe containment required for compounding in USP <800>
- Recognize how to apply an Assessment of Risk to utilize alternative work practices

History of Hazardous Drugs (HD)

- Concern over exposure to hazardous drugs (HDs) is not new!
  - 1986 – first OSHA guidelines for cytotoxic drugs
  - 1990 – ASHP technical assistance bulletin on handling cytotoxic and hazardous drugs
  - 2004 - NIOSH Alert - Preventing Occupational Exposures to Antineoplastic and Other Hazardous Drugs in Health Care Settings
  - 2008 – USP Chapter <797> included sterile hazardous drug guidance
  - March 2014 – USP Chapter <800> draft released
  - February 2016 – final version of Chapter <800> released
  - December 1, 2019 – “Effective Date” for <800> Hazardous Drugs – Handling in Healthcare Settings
Why Care? - Industry Evidence

- 1999: Pharmacists, techs, & nurses handling HDs
  - 40% higher risk of stillbirths and spontaneous abortions
- 2010: Healthcare Worker Study (including pharmacy)
  - Chromosome 5&7 abnormalities
  - Breast and prostate cancer both linked to C-5
- 2014: Pharmacy student dies of fentanyl overdose at a compounding pharmacy
  - After only four days on the job
- 2014: Evaluation of manufacturing practices finds drug residue on external packaging of containers of 5-FU and cisplatin

Why Care? – External Factors

- HD protection is growing as a regulatory requirement
  - State Boards of Pharmacy
    - Maine and Vermont – pending rules or to be incorporated by reference with <795> and <797>*
    - New Hampshire, Massachusetts, Connecticut, Rhode Island have specific regulation*
  - FDA
  - OSHA – Controlling Occupational Exposure to Hazardous Drugs
  - Growing interest in waste-streams
  - Liability?

* From USP 800 By State – updated May 2019. Joint effort from NCPA, APhA, and NASPA.

What is a Hazardous Drug?

- NIOSH HDs are:
  - Carcinogenic
  - Teratogenic
  - Reproductive toxicity
- NIOSH Classification:
  - Group 1 (Table 1) - Antineoplastics
  - Group 2 (Table 2) - Other drugs that nonetheless meet NIOSH criteria
  - Group 3 (Table 3) - Substances mainly posing reproductive risk

Chapter <800> covers:

- List of HDs
- Areas where exposure may occur
- Personnel responsibilities
- Facility and engineering controls
- Environmental quality and control
- Personal Protective Equipment (PPE)
- Hazard Communication Program
- Personal training
- Receiving HDs
- Labeling, packaging, transport, disposal
- Dispensing final dosage forms
- Compounding
- Administering
- Deactivation, decontamination, cleaning, disinfecting
- Spill control
- Documentation and SOPs
- Medical Surveillance

Containment Requirements

- What qualifies?
- What are the environmental requirements?
- Engineering controls?
- Additional equipment?

What requires containment?

- NIOSH-list drugs that must follow <800>’s containment requirements:
  - HD API
  - Antineoplastics requiring further manipulation
- NIOSH-list drugs that do not have to follow containment requirements if an assessment of risk is performed and implemented:
  - Final dosage forms of compounded HD preparations
  - Conventionally manufactured HD products that require no further manipulation than counting or repackaging
  - Non-antineoplastic HD dosage forms on the NIOSH list
Containment looks like...

C-PEC: Containment Primary Engineering Control
- Examples:
  - Class I or II BSC
  - CVE
  - CAD
- C-PEC for sterile compounding must be externally vented
- C-PEC for nonsterile compounding may be externally vented or go through redundant HEPA filtration

C-SEC: Containment Secondary Engineering Control
- Negative 0.01-0.03 inch water column relative to adjacent areas
- Externally vented
- Physically separated from other preparation areas
- Meets Air Changes per Hour requirements

Compounding Environment - Nonsterile

- Dedicated room for HD compounding
- Negative pressure -0.01 to 0.03 inches water
- 12 ACH
- Unclassified air
- Externally vented

Compounding Environment - Nonsterile

Smooth, seamless, and impervious surfaces:
- Avoid particle board
- Floor laid seamlessly
- Epoxy drywall or other wall material
- Impervious ceiling tiles and lighting fixtures
- Must be able to withstand decontamination with sodium hypochlorite solution

Class I BSC for Nonsterile Compounding

- Protect the operator from HD exposure
- Do not protect HDs from exposure to the compounder

Class I BSC – Externally Vented

Image is used with permission of AirClean Systems
Class I BSC – Redundant HEPA Filtration

Sterile HD Compounding — Category 1

Remember — Category 2 BUDs are limited to:
- 12 hours room temperature
- 24 hours refrigerated

Sterile HD Compounding – Category 2

Remember — Category 2 BUDs are limited to:
- 12 hours room temperature
- 24 hours refrigerated

The Shared Anteroom

Anteroom:
- ISO 7
- >30 ACH
- >0.02 inches water column
- At least 1 meter from negative buffer door

The Shared Anteroom

Class I internally-vented BSC:
- Not for BUDs
- For non-NIOSH-listed drugs:
  - Fentanyl
  - Prednisone
  - Methylprednisolone
The Buffer Room

- ISO 7
- 30 ACH
- Negative 0.01-0.03 inch water column
- Doffing Area and Line of Demarcation
- Pass-through
  - Sealed doors

Sterile HD Buffer Room

- Smooth, seamless, and impervious surfaces
- Avoid particle board
- Floor laid seamlessly
- Epoxy drywall or other wall material
- Coved moldings
- Impervious ceiling tiles and lighting fixtures
- Must be able to withstand decontamination using sodium hypochlorite solution
  - Can ruin stainless steel when not inactivated

Class II BSC Types

Type A1:
- 75 ft./min. inflow velocity
- Exhaust into lab or canopy:
  - Into lab would be non-compliant
- 70% of the air recirculated/30% exhausted
- Have positive-pressure exhaust ducts — NOT SUITABLE FOR HDs

Type A2:
- 100 ft./min. inflow velocity
- Exhaust to outside via direct duct connection
- 30% of the air recirculated/70% exhausted
- Suitable for minute quantities of volatile drugs

Type B1:
- 100 ft./min. inflow velocity
- Exhaust to outside via direct duct connection
- 30% of the air recirculated/70% exhausted
- Suitable for volatile drugs

Type B2:
- 100 ft./min. inflow velocity
- Exhaust to outside via direct duct connection
- 100% of the air is exhausted
- Suitable for volatile drugs

Assessment of Risk

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Class II BSC Types

Type B1:
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- Exhaust to outside via direct duct connection
- 30% of the air recirculated/70% exhausted
- Suitable for volatile drugs

Type B2:
- 100 ft./min. inflow velocity
- Exhaust to outside via direct duct connection
- 100% of the air is exhausted
- Suitable for volatile drugs
Assessment of Risk

- Assessment of Risk must include the following:
  - Type of HD
  - Dosage form
  - Risk of exposure
  - Packaging
  - Manipulation

Assessment of Risk – Ganciclovir

<table>
<thead>
<tr>
<th>Drug</th>
<th>Ganciclovir for Injection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of HD</td>
<td>NIOSH Group 2 – Non-anthoeplastic</td>
</tr>
<tr>
<td>Dosage Form</td>
<td>Powder for Reconstitution</td>
</tr>
<tr>
<td>Packaging</td>
<td>Glass Vial</td>
</tr>
<tr>
<td>Manipulation</td>
<td>Reconstituting closed manufacturer container</td>
</tr>
<tr>
<td>Withdrawn via syringe, injected into piggyback</td>
<td></td>
</tr>
<tr>
<td>Alternative Containment Strategies And/or Work Practices</td>
<td>Compounding may take place in a LAFW in a positive-pressure buffer area</td>
</tr>
<tr>
<td>HD PPE is to be worn, CSTD to be used during reconstitution and transfer</td>
<td></td>
</tr>
<tr>
<td>After compounding, DCA is decontaminated and disinfected per facility protocol</td>
<td></td>
</tr>
</tbody>
</table>

Assessment of Risk Tips

- Don't overthink it!
- Remember to do each drug and dosage for separately
- Suggestion – create a template (text document, spreadsheet)
- Utilize your hazardous drug list to guide the AOR process
- Industry 'norms' have yet to emerge, this will happen in time

Audience Poll

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**Questions?**

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