Sterile Compounding of Hazardous Drugs
Session I

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Objectives

- Define a hazardous drug
- List chronic and acute effects of exposure to chemotherapy drugs
- List personal protective equipment for compounding of hazardous preparations
- Summarize requirements of primary engineering controls for hazardous compounding
- Sequence cleaning and decontamination steps for a biologic safety cabinet
- Describe proper process for priming intravenous (IV) tubing
- Explain the use of closed system drug transfer devices for hazardous compounding
Interactive Activities

POLLs

INTEGRATED LEARNING

ASSESSMENT
Agenda

- Session I (2 hour CE)
  - Chemotherapeutic Risks and Effects
  - Personal Protective Equipment
  - Primary Engineering Controls
  - Cleaning Biological Safety Cabinets
  - Priming IV Tubing
  - Closed System Transfer Devices
Hazardous Drugs

*Definition and Characteristics*
Defining Hazardous Drugs

- Hazardous drugs pose potential health risks to workers exposed to them

- May include:¹
  - Chemotherapy
  - Antiviral drugs
  - Hormone therapy
  - Some bioengineered drugs
  - Miscellaneous

- National Institute for Occupational Safety and Health (NIOSH)
  - Maintains list of antineoplastics and other hazardous drugs
  - USP <800> recognizes this list

Characteristics of Hazardous Drugs

- Hazardous drugs exhibit one or more of the following characteristics in humans and/or animals:
  - Carcinogenicity
  - Teratogenicity/Developmental Toxicity
  - Reproductive Toxicity/Fertility Impairment
  - Genotoxicity
  - Organ Toxicity at Low Doses
  - New drugs resembling existing hazardous drugs


“Controlling Occupational Exposure to Hazardous Drugs”. Available at: https://www.osha.gov/dts/osta/otm/otm_vi/otm_vi_2.html.
Institutions need to develop and maintain a list of hazardous drugs...

- May include drugs on NIOSH list
- Any additional drugs not on NIOSH list
- Must be reviewed at least annually
- Must be reviewed when a new agent or dosage form is used
How many are involved in hazardous compounding on a: 

A: Daily basis
B: Weekly basis
C: Monthly basis
D: Not at all
Chemotherapy & Exposure

Agents & Risks of Exposure
Types of Chemotherapy

- Chemotherapy encompasses chemical treatments used for conditions such as cancer

<table>
<thead>
<tr>
<th>Chemotherapy Class</th>
<th>Drug Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alkylating Agent (+ platinum drugs)</td>
<td>cisplatin, carboplatin, cyclophosphamide (Cytoxan), ifosfamide</td>
</tr>
<tr>
<td>Anti-tumor Antibiotic</td>
<td>doxorubicin (Adriamycin), bleomycin</td>
</tr>
<tr>
<td>Mitotic Inhibitor</td>
<td>paclitaxel (Taxol), docetaxel (Taxotere), vinblastine (Velban), vincristine (Oncovin)</td>
</tr>
<tr>
<td>Antimetabolite</td>
<td>cytarabine (Ara-C), 5-fluorouracil (5-FU), capecitabine (Xeloda), gemcitabine (Gemzar)</td>
</tr>
<tr>
<td>Topoisomerase Inhibitor</td>
<td>topotecan, irinotecan, etoposide</td>
</tr>
</tbody>
</table>
Which of the following are effects of exposure to chemotherapy?

A: Cancer
B: Fertility
C: Hair loss
D: Kidney damage
E: All of the above
Acute Effects of Exposure to Chemotherapy

“Occupational Exposure to Antineoplastic Agents and Other Hazardous Drugs”. Available at: http://www.cdc.gov/niosh/topics/antineoplastic/effects.html.
Chronic Effects of Exposure to Chemotherapy

“Occupational Exposure to Antineoplastic Agents and Other Hazardous Drugs”. Available at: http://www.cdc.gov/niosh/topics/antineoplastic/effects.html.
Exposure Routes

Inhalation
- Inhaling air contaminated with hazardous drug

Ingestion
- Transferring from hands into the mouth
- Transferring from hands onto food/drink

Accidental Injection
- Needle stick
- Glass/ampule cut

Dermal/Mucosal Absorption
- Touching contaminated surfaces bare skin
- Direct contact
Chemotherapy Spill

Image from: https://www.cancertutor.com/chemospill
Personal Protective Equipment

For Compounding Hazardous Preparations
Personal Protective Equipment (PPE)

- PPE has two functionalities:
  - Protect preparation from US
  - Protect US from the compounded sterile preparation (CSP)
    - Unique to hazardous compounding

- PPE must be removed prior to exiting direct compounding area

- Hands must be washed thoroughly after compounding and removing PPE
PPE Required for Sterile Compounding

- Shoe Cover
- Beard Cover
- Hair Cover
- Face Mask
- Eye Protection*
- Wash & Sanitize Hands
- Gown
- Glove
- Sanitize Gloves

*When risk for spills or splashes per USP <800> 40(3)
PPE for Hazardous Drug Preparation

• DOUBLE GLOVE
  • Always don double gloves for compounding
    • Both must be “chemotherapy gloves”
      • Meet American Society of Testing and Materials (ASTM) standard
  • Powder-free gloves
  • Outer pair for compounding
    • Remove in hood
  • Inner pair for affixing label and placing preparation in designated bag for chemotherapy
PPE for Hazardous Drug Preparation

- Gloves
  - Worn at ALL times when:
    - Compounding
    - Handling preparation
    - Handling vials
    - Handling packaging cartons
    - Unpacking shipments
    - Cleaning “hood”
    - Cleaning surface
PPE for Hazardous Drug Preparation

- **Gown**
  - Lint-Free
  - Low Permeability
  - No Seams/Closures
  - Closures in Back
  - Long Sleeves
  - Knitted, Tight Fitting Elastic Cuffs
Special Considerations

- **Gloves**
  - Change every 30 minutes
  - Change when torn, punctured, or contaminated

- **Shoe covers**
  - Don two pairs and remove outer pair prior to exiting buffer area

- **Gowns**
  - Change per manufacturer recommendations (permeability info)
  - Change every 2-3 hours if recommendations not available
  - Change immediately after splash or spill

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1 USP <800> Hazardous Drugs—Handling in Healthcare Settings, PF 40(3) [May–Jun.2013].
Handling Hazardous Drugs – When to Wear PPE

- Receiving hazardous medications from supplier
- Storage
- Transport
- Compounding (sterile and nonsterile)
- Administration
- Decontamination, cleaning, disinfecting
- Spill control

USP <800> Hazardous Drugs—Handling in Healthcare Settings, PF 40(3) [May–Jun.2013].
Primary Engineering Controls (PECs)

For Hazardous Compounding
Purpose of PEC

- Two main purposes for hazardous compounding:
  1. Protect the operator from exposure to hazardous drugs (fumes, splashes, sprays, etc.)
  2. Protect the CSP by providing quality air supply and environment

*Must be a dedicated PEC!*
No non-hazardous compounding in hazardous compounding PEC (and vice versa)
PECs for Hazardous Compounding

- ISO Class 5 environment in PEC
  - Not to exceed 3,520 particles per square meter

- PECs:
  - Laminar Airflow Workbench (LAFW)
  - Biologic Safety Cabinet (BSC)
  - Compounding Aseptic Isolator (CAI)
  - Compounding Aseptic Containment Isolator (CACI)
CACI
BSCs

Exhaust blower

HEPA filter

Sash

Air intake grilles

Workbench Surface
## BSCs

<table>
<thead>
<tr>
<th>Class</th>
<th>Characteristics</th>
<th>Protects operator?</th>
<th>Protects CSP?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class I</td>
<td>“Fume hood”</td>
<td>✔</td>
<td></td>
</tr>
<tr>
<td>Class II</td>
<td>Types A1, A2, B1, B2</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Class III</td>
<td>Attached gloves; air-tight construction</td>
<td>✔</td>
<td>✔</td>
</tr>
</tbody>
</table>
Which is used for hazardous compounding at your facility?

A: BSC  
B: CACI  
C: Horizontal laminar airflow workbench
Ideal Characteristics of PEC for Hazardous Compounding

- Unidirectional airflow
- Air intake grilles
- Sash
- Completely vented to outside air
- ISO Class 5
Ideal Choices for PECs

For compounding of hazardous preparations, the following are ideal choices:

1. Class II BSC, type B2 that is 100% vented to outside
2. CACI with unidirectional airflow that is 100% vented to outside
Cleaning the BSC

Deactivation/Decontamination, Cleaning, and Disinfecting
Operation

- Must be left “on” continuously
  - Loss of power => suspension of activities + covering
  - Restored => decontaminate + clean + disinfect + wait

- Must use a “chemo mat”
  - Inside PEC
  - Replace:
    - If spill occurs
    - Regularly during use
  - Discard at end of day

Image from: http://www.healthmark.ca/DATA/PRODUIT/61_1_1.jpg

1 USP <800> Hazardous Drugs—Handling in Healthcare Settings, PF 40(3) [May–Jun.2013].
Decontamination

- Must decontaminate dedicated workbenches used for hazardous drug preparations
  - Must occur prior to disinfection
    - Alcohol will NOT deactivate hazardous contamination
  - Follow manufacturers’ recommendations for cleaning
    - Sodium hypochlorite

- Neutralization should follow
  - Sodium thiosulfate
Disinfection

- Use sterile 70% isopropyl alcohol
- Always start near HEPA filter
- Depends on direction of laminar flow
  - Sides – Streaks should be perpendicular to airflow direction
    - Horizontal laminar flow – up and down (vertical)
    - Vertical – side to side (horizontal)
Alcohol used for compounding must be:

A: Sterile  
B: 70% or greater  
C: Any kind of alcohol  
D: Ethyl alcohol
Example

- Sodium Hypochlorite
- 1% sodium thiosulfate + 0.9% benzyl alcohol
- Sterile water rinse (to remove residue)
- Sterile 70% isopropyl alcohol
Disposable Cleaning Wipes

- 2-step process in a pair of wipes
  - 2% sodium hypochlorite
  - 1% sodium thiosulfate with 0.9% benzyl alcohol

Image from: [http://www.chemoglo.com/whatis.aspx](http://www.chemoglo.com/whatis.aspx)

### Disinfecting the BSC

<table>
<thead>
<tr>
<th>STEP 1</th>
<th>• Hood is running and has been ON for at least 5 min</th>
</tr>
</thead>
<tbody>
<tr>
<td>STEP 2</td>
<td>• Use sterile, lint-free wipes with sterile water to remove visible debris then dry</td>
</tr>
<tr>
<td>STEP 3</td>
<td>• Place sterile, lint-free wipes in a pile and saturate with sterile 70% isopropyl alcohol by pouring alcohol onto wipes and removing one from the top of pile to clean</td>
</tr>
<tr>
<td>STEP 4</td>
<td>• Clean hooks. Then wrap a sterile, lint-free wipe around IV pole and clean from one side of the hood to the other (not back and forth)</td>
</tr>
<tr>
<td>STEP 5</td>
<td>• Clean the back wall of the hood beginning at the top corner and working downward using horizontal overlapping strokes side to side</td>
</tr>
<tr>
<td>STEP 6</td>
<td>• Clean each side, starting in upper corner near HEPA filter using overlapping strokes side-to-side horizontally</td>
</tr>
<tr>
<td>STEP 7</td>
<td>• Clean the glass sash, beginning in the upper corner near HEPA filter using overlapping strokes side-to-side horizontally</td>
</tr>
<tr>
<td>Step 8</td>
<td>• Clean the workbench last beginning from back corner and working toward the front of the hood using overlapping strokes side to side</td>
</tr>
</tbody>
</table>
Cleaning Tips

- Wash hands and sanitize gloves BEFORE cleaning workbench
- Do NOT bring hands out of workbench during cleaning
- Sanitize gloves AFTER cleaning workbench
- Clean all the way to the very edge
- Do NOT place dirty wipes on clean surfaces
- Take unused gauze from the pile each time a new surface is cleaned
Work Tray¹

- Some PEC’s have work tray
  - Contamination can build up
  - Access may be difficult

- Clean monthly
  - Wear respiratory protection
    - NIOSH approved and fitted is recommended

¹ USP <800> Hazardous Drugs—Handling in Healthcare Settings, PF 40(3) [May–Jun.2013].
Preparing Chemotherapy

Priming Tubing & Closed System Transfer Devices
Priming Line

- Solutions from chemotherapy preparations will be directly administered to patient
- Nurse needs to attach line from bag to patient
- “Priming” bag is needed for hazardous compounds
  - Attaching an administration set and filling it with diluent
  - Prevents nurse from having to prime line with hazardous compound
Priming of an infusion set should be done before chemotherapy or other hazardous drug is added.
Parts of Infusion Set

- Spike
- Drip Chamber
- Roller Clamp
- Tubing
- Luer Lock Cap
### Priming Procedure

<table>
<thead>
<tr>
<th>Step</th>
<th>Instructions</th>
</tr>
</thead>
</table>
| 1    | • Close slide clamp  
      • Close roller clamp |
| 2    | • Insert spike from infusion set into spike port of bag (also known as set port) |
| 3    | • Hang bag from hook inside PEC |
| 4    | • Squeeze drip chamber on infusion set a few times to fill chamber half-way |
| 5    | • Release slide clamp |
| 6    | • Slowly release roller clamp while watching drug-free solution fill line |
| 7    | • When solution reaches 2 inches before end of tubing, close roller clamp |
After Attaching Set
LEAVE 2 INCH SPACE AT END OF TUBING
(stop flow 2 inches before it reaches the end)
Prepare for Transport

• Affix patient label
• Affix auxiliary labels
• Place preparation in dedicated transport bag
  • Bag must be for hazardous drugs
Priming IV Tubing
Closed Systems

- **Closed System**
  - “A device that does not exchange unfiltered air or contaminants with the adjacent environment” (*NIOSH*, 2004)

- **Closed System Drug-Transfer Device**
  - “A drug transfer device that mechanically inhibits the transfer of environmental contaminants into the system and the escape of hazardous drug or vapor concentrations outside the system” (*NIOSH*, 2004)
  - Decrease operator exposure and surface contamination
Does your facility use Closed System Drug-Transfer Device for hazardous compounding?

True: Yes
False: No
Systems

- ChemoLock (icumedical)
- OnGuard with Tevadaptor (B.Braun/Teva Medical)
- PhaSeal (BD)
- LifeShield ChemoClave (Hospira)
- Halo (Corvida Medical)
- Equashield (Equashield)
- Texium (CareFusion)
- Chemoprotect (Codan)
Equal?

Time & Efficiency

Effective??

Cost!!

Ease of Use (EOU)

Hosp Pharm. 2013 Mar; 48(3): 204–212. (PhaSeal)
PhaSeal ® System

Instructional Video: https://www.youtube.com/watch?v=whKZWkCPbc8

Tevadaptor™

Instructional Video: http://www.tevadaptor.com/demo.html

Equashield®

Instructional Video: https://www.youtube.com/channel/UCPknhyhfzHF2f3fApTVR5c0w
Closed System Transfer Devices
Updates in Sterile Compounding

Key Updates
USP Chapter <800>:

**April 29th:** Updated notice of intent to revise (published as *errata*)

**May 26th:** *Errata* published

**June 1st:** USP Chapter <800> becomes official
USP Chapter <797>

**July 2010:**
Revision process began

**Nov/Dec 2015:**
USP Chapter <797> published for public comment

**January 2016:**
Public commentary due

**May 2016:**
Public comments under review
TSBP

- Met February 2016
  - Discussion and passing of amendments to §291.133
    - Update requirements for sterility testing
    - Clarify requirements for temperature and humidity
    - Clarify requirements for blood labeling procedures
  - Compounding Stakeholders Meeting
    - March 1st
Board of Pharmacy Specialties

Board of Pharmacy Specialties Issues Call for Petition in Sterile Compounding Pharmacy Practice

The Board of Pharmacy Specialties (BPS), the premier post-licensure certification organization serving the pharmacy profession, has issued a call for petition in Sterile Compounding Pharmacy Practice, it was announced today. If approved, Sterile Compounding Pharmacy will be the ninth specialty offered by BPS.

Read More >>
April 13, 2016 / Press Release
Additional Resources

For Hazardous Drug Handling and Compounding
Additional Resources


- National Institute for Occupational Safety and Health (NIOSH)

- American Society of Clinical Oncology/Oncology Nursing Society.

QUESTIONS?

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THANK YOU!

We enjoyed the opportunity.