USP <800>: What you need to know

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Disclosure and Conflict of Interest

• Alison Smith declares no conflicts of interest, real or apparent, and no financial interests in any company, product, or service mentioned in this program, including grants, employment, gifts, stock holdings and honoraria.
Pharmacist Objectives

At the conclusion of this program, the pharmacist will be able to:

1. Define “hazardous drug” and use the NIOSH list to identify hazardous drugs in their practice setting

2. Apply USP <800> facility design requirements to various pharmacy practice settings

3. Create an action plan for USP <800> compliant practices, policies and procedures
At the conclusion of this program, the technician will be able to:

1. Define “hazardous drug” and use the NIOSH list to identify hazardous drugs in their practice setting

2. Describe the facility and engineering controls that protect workers from exposure to hazardous drugs

3. Identify USP <800> compliant practices applicable to their work environment
USP <800> standards apply to which of the following practice settings?

a) Hospital / Infusion Pharmacies Only
b) All Pharmacy Practice Settings
c) Hospitals only
d) All health care personnel or entities that handle hazardous drugs
Pre-Test Questions

The most recent version of the NIOSH List of Antineoplastic and Other Hazardous Drugs in Healthcare Settings was published in

a) 2016  
b) 2014  
c) 2010  
d) 2004
Pre-Test Questions

Which of the following characteristics is NOT listed in the NIOSH or ASHP definition of a hazardous drug?

a) Genotoxicity
b) Hypersensitivity
c) Teratogenicity
d) Carcinogenicity
Which of the following is NOT a USP <800> requirement?

a) Separate storage for hazardous drugs including a separate refrigerator
b) The use of closed system transfer devices during compounding of hazardous drugs
c) A positive pressure clean room for sterile compounding
d) Gowns and gloves shown to be resist permeability to hazardous drugs
Hazardous Drugs

• Guidelines vs. Recommendations
• Definitions
• NIOSH List
• USP <800> Compliant HD List
• Risk Assessments
• Examples
# History of Hazardous Drug Guidelines & Recommendations

<table>
<thead>
<tr>
<th>Decade</th>
<th>National Institutes of Health (NIH)</th>
<th>American Society of Health System Pharmacists (ASHP)</th>
<th>Occupational Safety and Health Administration (OSHA)</th>
<th>National Institute of Occupational Safety and Health (NIOSH)</th>
<th>United States Pharmacopeia (USP)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000s</td>
<td></td>
<td><em>ASHP guidelines</em> on handling hazardous drugs (2006)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Recommendations & Guidelines**

**Requirements**

- **Alert:** Preventing Occupational Exposures to Antineoplastic and Other Hazardous Drugs in Health Care Settings (2004)
  - USP <797> published (2004)
  - USP 797 updated (2008)
  - USP <800> published (2016)
  - USP <800> effective (2018)
Recommendations for the safe handling of injectable antineoplastic drug products

PF Zimmerman, RK Larsen, EW Barkley and JF Gallelli

Abstract

Routes through which health-care workers may be exposed to injectable antineoplastic drug products are reviewed, and recommendations developed by the National Institutes of Health for the safe handling of such products are presented. Routes of exposure are primarily through inhalation of the aerosolized drug product and by direct skin contact. The potential risks from repeated contact with injectable antineoplastic drug products can be controlled by the use of specific containment equipment and certain work techniques. It is recommended that all procedure involved in the preparation of injectable antineoplastics be performed in a Class II laminar flow biological safety cabinet.

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HAZARDOUS DRUGS—HANDLING IN HEALTHCARE SETTINGS

1. INTRODUCTION AND SCOPE

This chapter describes practice and quality standards for handling hazardous drugs (HDs) to promote patient safety, worker safety, and environmental protection. Handling HDs includes, but is not limited to, the receipt, storage, compounding, dispensing, administration, and disposal of sterile and nonsterile products and preparations.

This chapter applies to all healthcare personnel who handle HD preparations and all entities that store, prepare, transport, or administer HDs (e.g., pharmacies, hospitals and other health care institutions, patient treatment clinics, physicians’ practice facilities, or veterinarians’ offices). Personnel who may potentially be exposed to HDs include, but are not limited to: pharmacists, pharmacy technicians, nurses, physicians, physician assistants, home healthcare workers, veterinarians, and veterinary technicians.

Entities that handle HDs must incorporate the standards in this chapter into their occupational safety plan. The entity’s health and safety management system must, at a minimum, include:

- A list of HDs

USP: U.S. Pharmacopeial Convention

• Not a government entity
  – A scientific nonprofit organization

• Sets standards for the identity, strength, quality, and purity of medicines, food ingredients, and dietary supplements

• USP Council of Experts and Expert Committees developing and revise standards

• Standards are enforceable by the FDA

• State Boards of Pharmacy may adopt USP compounding standards into their regulations

NEW $2.3 MILLION WORKPLACE INTERVENTION AIDS TO REDUCE EXPOSURE RISK FOR ONCOLOGY NURSES

Submitted on Sep 4, 2014

The study is designed to promote safety at chemotherapy infusion sites.

ANN ARBOR, Mich. - Researchers at the University of Michigan School of Nursing and Comprehensive Cancer Center have received a $2.3 million grant to study oncology nurses' exposure to hazardous drugs, including identifying ways to reduce exposure.

“There are significant acute and long-term side effects from hazardous drug exposures in oncology settings, but not enough evidence-based, risk-reduction efforts to protect health care workers,” says Christopher Friese, PhD, RN, AOCN®, FAAN, University of Michigan School of Nursing assistant professor and member of U-M’s Comprehensive Cancer Center and Institute for Healthcare Policy and Innovation.

Dr. Friese aims to lower the risk through a new study called DEFENS: Drug Exposure Feedback and Education for Nurses’ Safety. The four-year study, with funding from the National Institute for Occupational Safety and Health (NIOSH), will examine

Table C1. Platinum-containing chemotherapy drugs in surface wipe samples collected in September 2009 and November 2010

<table>
<thead>
<tr>
<th>Location</th>
<th>Description</th>
<th>Results ng/100 cm²</th>
</tr>
</thead>
<tbody>
<tr>
<td>November 2010</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.4</td>
<td>NS</td>
<td>12</td>
</tr>
<tr>
<td>3.3</td>
<td>(0.48)</td>
<td>NS</td>
</tr>
<tr>
<td>5.7</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>5.9</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>2.9</td>
<td>(0.77)</td>
<td>NS</td>
</tr>
<tr>
<td>2.1</td>
<td>NS</td>
<td>ND</td>
</tr>
<tr>
<td>5.9</td>
<td>NS</td>
<td>ND</td>
</tr>
<tr>
<td>0.97</td>
<td>(0.77)</td>
<td>ND</td>
</tr>
<tr>
<td>13</td>
<td>(0.57)</td>
<td>ND</td>
</tr>
<tr>
<td>1.4</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Estimated 100 cm² sampling area
†September 2009: LOD = 0.7 ng platinum/sample and LOQ = 9.8 ng platinum/sample
‡November 2010: LOD = 0.3 ng platinum/sample and LOQ = 0.84 ng platinum/sample
( ) Sample results in parentheses were between the LOD and the LOQ, meaning that they have more uncertainty associated with them.
ND = not detected (below the LOD)
NS = location was not sampled
Exposure to Hazardous Drugs can Occur During…
# Hazardous Drug (HD) Definition

<table>
<thead>
<tr>
<th>ASHP 1990 Criteria</th>
<th>NIOSH 2004 Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carcinogenicity in animal models, in the patient population, or both as reported</td>
<td>Carcinogenicity</td>
</tr>
<tr>
<td>by the International Agency for Research on Cancer</td>
<td></td>
</tr>
<tr>
<td>Teratogenicity in animal studies or in treated patients</td>
<td>Teratogenicity or developmental toxicity</td>
</tr>
<tr>
<td>Fertility impairment in animal studies or in treated patients</td>
<td>Reproductive toxicity</td>
</tr>
<tr>
<td>Evidence of serious organ or other toxicity at low doses in animal models or</td>
<td>Organ toxicity at low doses</td>
</tr>
<tr>
<td>treated patients</td>
<td></td>
</tr>
<tr>
<td>Genotoxicity (i.e., mutagenicity and clastogenicity in short-term test systems)</td>
<td>Genotoxicity</td>
</tr>
<tr>
<td></td>
<td>Structure and toxicity profile of new drugs that mimic existing drugs determined</td>
</tr>
<tr>
<td></td>
<td>hazardous by the above criteria</td>
</tr>
</tbody>
</table>

- ASHP (American Society of Health System Pharmacists). Guidelines on handling hazardous drugs.
- Am J Health Syst Pharm 2006; 63: 1172—1193
USP <800> Requirement: Create a Hazardous Drugs List

• Each entity must maintain a list of hazardous drugs that the entity handles

• Drugs included on the entity’s list of hazardous drugs must be handled according to the requirements in USP Chapter <800>

• Before trying to apply USP <800> standards you need to identify your hazardous drugs! This will help you design appropriate facilities / workflows / policies

Creating a USP <800> Compliant HD List

- Must use the NIOSH List of Antineoplastic and Other Hazardous Drugs as a basis for your Hazardous Drug List
  - 2016 NIOSH List Published September 13, 2016
  - Available at: https://www.cdc.gov/niosh/docs/2016-161/
  - Contains FDA approved drugs through December 2013

- 3 Tables of Hazardous Drugs
  - Table 1: AHFS classified antineoplastic drugs
  - Table 2: Meet one or more NIOSH criteria for a hazardous drug
  - Table 3: Reproductive risk only

NIOSH list of Antineoplastic and Other Hazardous Drugs in Healthcare Settings, 2016. Available at https://www.cdc.gov/niosh/docs/2016-161/
Accessed 12.31.16
NIOSH List FYIs

- Pre-amble contains useful information on how NIOSH determines whether a medication is Hazardous
- Tables 1 & 2 also list whether the drug has Manufacturer Safe Handling Guidance (MSHG) listed in the prescribing information
  - Typically section 16 of the package insert
- All tables include both parenteral and oral medications (if available as both oral and parenteral, may only be listed once)
- Drugs are classified as antineoplastic agents by the American Hospital Formulary Service (AHFS) [http://ahfs.ashp.org/drug-assignments.aspx](http://ahfs.ashp.org/drug-assignments.aspx)
  - Can see new drug classifications on this website

USP <800> says…

- All antineoplastics that *require manipulation* and are included on the NIOSH list **must** be on the entity’s list

- All active pharmaceutical ingredients (APIs) included on the NIOSH list and handled by the entity must be on the entity’s list

- If Manufacturer Safe Handling Guidance, include on entity’s list

- Other agents on the NIOSH list
  - Perform risk assessment and document other containment strategies or work practices necessary to reduce exposure
  - If no risk assessment performed, must handle as hazardous and according to USP 800 requirements

- Must use NIOSH criteria to assess new drugs that enter the market place after most recent NIOSH list update (2014 – now)

Create your Facility HD List

- NIOSH List Agents with Manufacturer Safe Handling Guidance (MSHG)
- NIOSH List Table 1 agents requiring manipulation (i.e. compounding)
- Investigational agents lacking information to determine hazardous nature
- HD Active Pharmaceutical Ingredients (APIs)
- New medications post NIOSH list that meet HD criteria and:
  1. Are APIs
  2. Are antineoplastic agents requiring manipulation
  3. Have MSHG
Perform Risk Assessment

NIOSH List Table 2-3 agents

NIOSH List Table 1 agents that do not require manipulation (i.e. final dosage forms)

New medications post NIOSH list that meet HD criteria but are not APIs or antineoplastics requiring manipulation

Add to Facility HD List

Document Alternative Safe Handling

USP <800> Risk Assessments

• Consider the following during an Assessment of Risk
  – Type of HD (e.g. antineoplastic, non-antineoplastic, reproductive risk only)
  – Dosage Form
  – Risk of Exposure
  – Packaging
  – Manipulation

• If an assessment of risk approach is taken, must document what alternative containment strategies and/or work practices are being employed to minimize occupational exposure

• Review risk assessments every 12 months and document review
Two Paths to Compliance

All NIOSH List Agents Must Follow USP <800> Requirements
Final Dosage Forms

• Hazardous Drugs that only require counting or repackaging of final dosage forms *may be prepared for dispensing without any further requirements for containment*
  – unless required by the manufacturer (MSHG)
  – or if visual indicators of HD exposure hazard are present (i.e. dust / leakage)

• Counting / repackaging of HDs should be done carefully
  – Use clean equipment dedicated for use with HDs
  – Decontaminate equipment after each use
  – Do not place HD tablets / capsules in automated counting machines

• Healthcare personnel should avoid crushing tablets or opening capsules of HDs
  – If manipulation is required, must wear PPE and use a plastic pouch to contain any dust or particles

### NIOSH List Table 1 Agents Requiring Manipulation

<table>
<thead>
<tr>
<th>Agents</th>
<th>Cytosine</th>
<th>Idarubicin</th>
<th>Pertuzumab</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ado-Trastuzumab</td>
<td>Cyclophosphamide</td>
<td>Idarubicin</td>
<td>Pertuzumab</td>
</tr>
<tr>
<td>Amsacrine</td>
<td>Cytarabine</td>
<td>Ifosfamide</td>
<td>Pralaxtrexate</td>
</tr>
<tr>
<td>Arsenic Trioxide</td>
<td>Cytarabine Liposomal</td>
<td>Irinotecan</td>
<td>Romidepsin</td>
</tr>
<tr>
<td>Azacitidine</td>
<td>Dacarbazine</td>
<td>Irinotecan (Liposomal)</td>
<td>Streptozocin</td>
</tr>
<tr>
<td>Bacillus Calmette Guerin</td>
<td>Dactinomycin</td>
<td>Ixabepilone</td>
<td>Temozolomide</td>
</tr>
<tr>
<td>Belinostat</td>
<td>Daunorubicin</td>
<td>Mechlorethamine</td>
<td>Temsirolimus</td>
</tr>
<tr>
<td>Bendamustine</td>
<td>Decitabine</td>
<td>Melphalan</td>
<td>Teniposide</td>
</tr>
<tr>
<td>Bleomycin</td>
<td>Docetaxel</td>
<td>Methotrexate</td>
<td>Thiopeta</td>
</tr>
<tr>
<td>Bortezomib</td>
<td>Doxorubicin</td>
<td>Methotrexate</td>
<td>Topotecan</td>
</tr>
<tr>
<td>Brentuximab Vedotin</td>
<td>Doxorubicin Liposomal</td>
<td>Mitomycin</td>
<td>Valrubicin</td>
</tr>
<tr>
<td>Busulfan</td>
<td>Epirubicin</td>
<td>Mitoxantrone</td>
<td>Vinblastine</td>
</tr>
<tr>
<td>Cabazitaxel</td>
<td>Eribulin</td>
<td>Nab-Paclitaxel</td>
<td>Vincristine</td>
</tr>
<tr>
<td>Carboplatin</td>
<td>Etoposide</td>
<td>Nelarabine</td>
<td>Vinorelbine</td>
</tr>
<tr>
<td>Carfilzomib</td>
<td>Floxuridine</td>
<td>Omacetaxin</td>
<td>Ziv-aflibercept</td>
</tr>
<tr>
<td>Carmustine</td>
<td>Fludarabine</td>
<td>Oxaliplatin</td>
<td>Talimogene laherparepvec</td>
</tr>
<tr>
<td>Cisplatin</td>
<td>Fluorouracil</td>
<td>Paclitaxel</td>
<td>Trabectedin</td>
</tr>
<tr>
<td>Cladribine</td>
<td>Gemcitabine</td>
<td>Pemetrexed</td>
<td></td>
</tr>
<tr>
<td>Clofarabine</td>
<td>Gemtuzumab ozogamicin</td>
<td>Pentostatin</td>
<td></td>
</tr>
</tbody>
</table>

**Note** – Majority of Monoclonal Antibodies are not Hazardous

NIOSH list of Antineoplastic and Other Hazardous Drugs in Healthcare Settings, 2016. Available at [https://www.cdc.gov/niosh/docs/2016-161/](https://www.cdc.gov/niosh/docs/2016-161/)  
Accessed 12.31.16
<table>
<thead>
<tr>
<th>Drug</th>
<th>AHFS Classification</th>
<th>MSHG?</th>
<th>Reason for Listing on NIOSH List</th>
<th>Facility HD List</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anastrazole (Arimidex)</td>
<td>10:00 antineoplastic agents</td>
<td>No</td>
<td>FDA Pregnancy Category X</td>
<td>Perform Risk Assessment</td>
</tr>
<tr>
<td>Capecitabine (Xeloda)</td>
<td>10:00 antineoplastic agents</td>
<td>Yes</td>
<td>Metabolized to 5-fluorouracil; FDA Pregnancy Category D</td>
<td>Add to HD List due to MSHG</td>
</tr>
<tr>
<td>Imatinib (Gleevec)</td>
<td>10:00 antineoplastic agents</td>
<td>Yes</td>
<td>FDA Pregnancy Category D</td>
<td>Add to HD List due to MSHG</td>
</tr>
<tr>
<td>Letrozole (Femara)</td>
<td>10:00 antineoplastic agents</td>
<td>No</td>
<td>FDA pregnancy Category X</td>
<td>Perform Risk Assessment</td>
</tr>
<tr>
<td>Megestrol (Megace)</td>
<td>10:00 antineoplastic agents</td>
<td>No</td>
<td>Nursing should be discontinued if megestrol is required. Women at risk of pregnancy should avoid exposure; FDA Pregnancy Category X</td>
<td>Perform Risk Assessment</td>
</tr>
</tbody>
</table>

## Risk Assessments

<table>
<thead>
<tr>
<th>Drug</th>
<th>Hazardous Risk</th>
<th>Dosage Form</th>
<th>Risk of Exposure</th>
<th>Packaging / Manipulation</th>
<th>Alternative Safe Handling</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anastrazole (Table 1)</td>
<td>Reproductive (pregnancy category X)</td>
<td>Film Coated Tablets</td>
<td>May occur during counting</td>
<td>30 or 90 count vials or unit dose</td>
<td>Dispense in original container and do not repackage</td>
</tr>
<tr>
<td>Megestrol (Table 1)</td>
<td>Reproductive (pregnancy category X)</td>
<td>Tablets / Suspension Tablets scored for splitting</td>
<td>May occur during counting and repackaging</td>
<td>Must count Often must pour suspension May split tablets</td>
<td>Reproductive age staff do not handle Separate counting tray cleaned before &amp; after Wear gloves</td>
</tr>
<tr>
<td>Cyclosporine (Table 2)</td>
<td>IARC Group 1 carcinogen; FDA Pregnancy Category C</td>
<td>Oral, IV, Oral Solution</td>
<td>During sterile compounding Pouring of oral solution May occur during counting</td>
<td>Sterile compounding for IV doses Must count Often must pour suspension</td>
<td>Use of CSTDs during sterile compounding Priming IV line with saline Additional PPE</td>
</tr>
</tbody>
</table>

Possible Strategy for HD List

- Divide Hazardous Drugs into Risk Levels and define requirements for each risk level

| Risk Level 1 | HD | • Antineoplastic Agents requiring sterile compounding |
| Risk Level 2 | HD | • Non-antineoplastic Agents requiring sterile compounding |
| Risk Level 3 | HD | • Final dosage forms with possible administration risks |
| Risk Level 4 | HD | • Final dosage forms: oral tablets and capsules |
USP <800> Requirements

- Designated Person
- Facility and Engineering Controls
- Environmental Wipe Sampling
- Closed System Transfer Devices (CSTDs)
- Personal Protective Equipment (PPE)
- Deactivating, Decontaminating, Cleaning and Disinfecting
- Personnel Training
- Medical Surveillance
- SOPs
USP <800> Requirement: Designated Person

• Each entity must designate a person responsible for overseeing compliance with USP <800>

• Responsibilities would include
  – Implementing procedures
  – Assessing competency of personnel
  – Ensuring environmental control of storage and compounding areas
  – Monitoring facility reports of testing / sampling performed

### USP <800> Requirement: Facility & Engineering Controls

<table>
<thead>
<tr>
<th>Hazardous Drug Activity</th>
<th>Non-Sterile Compounding</th>
<th>Sterile Compounding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Receipt</td>
<td>• Receipt and unpacking must occur in a neutral or negative pressure area</td>
<td></td>
</tr>
<tr>
<td>Storage</td>
<td>• HDs and APIs requiring manipulation <strong>must be stored separately</strong> from non hazardous medications (separate refrigerator) in an externally ventilated, negative-pressure room with at least 12 air changes per hour (ACPH)</td>
<td>• Non-antineoplastic, reproductive risk only drugs and final dosage forms of antineoplastic HDs may be stored with other inventory if permitted by entity policy</td>
</tr>
</tbody>
</table>

### USP <800> Requirement: Facility & Engineering Controls

<table>
<thead>
<tr>
<th>Hazardous Drug Activity</th>
<th>Non-Sterile Compounding</th>
<th>Sterile Compounding</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Compounding</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• In a C-PEC located in a C-SEC</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• C-PEC must be</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Externally vented (preferred) or have a redundant HEPA filter</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• C-SEC must</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Be externally vented</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Be physically separate</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Have 12 ACPH</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Have a negative pressure of 0.01 – 0.03 inches of water column relative to adjacent areas</td>
<td></td>
</tr>
</tbody>
</table>

|                         | • In a C-PEC located in a C-SEC |
|                         | • C-PEC must                 |
|                         | • Be externally vented       |
|                         | • Provide an ISO Class 5 or better environment |
|                         | • C-SEC can be either an     |
|                         | • An externally vented, negative pressure ISO Class 7 buffer room/ante room with 30 ACPH or |
|                         | • A negative pressure containment segregated compounding area that is externally vented with 12 ACPH |

**C-PEC** = containment primary engineering control  
**C-SEC** = containment secondary engineering control
USP <800> Optimal Facility Design for Non-Sterile Compounding

Containment Primary Engineering Control (i.e. Biological Safety Cabinet)

Negative pressure 0.01 – 0.03”

Containment Secondary Engineering Control (Buffer Room)

Room Air: 12 Air Exchanges per Hour (ACPH)

USP <800> Optimal Facility Design for Sterile Compounding

Negative Buffer Rm - ISO 7 Hazardous Compounding

Ante ISO 7

Positive Buffer Rm - ISO 7 Non-Hazardous Compounding

BSC

Negative pressure 0.01 – 0.03”

Room Air: 30 Air Exchanges per Hour (ACPH)

Positive pressure

LAFH

## Types of Containment Primary Engineering Controls (C-PECs)

<table>
<thead>
<tr>
<th>Type of C-PEC</th>
<th>Protection</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Personnel</td>
</tr>
<tr>
<td>Containment Ventilated Enclosure</td>
<td>Yes</td>
</tr>
<tr>
<td>Class I Biological Safety Cabinet</td>
<td>Yes</td>
</tr>
<tr>
<td>Class II Biological Safety Cabinet</td>
<td>Yes</td>
</tr>
<tr>
<td>Class III Biological Safety Cabinet</td>
<td>Yes</td>
</tr>
<tr>
<td><em>(Total Containment Cabinets, gas tight, used for working with carcinogens, diseases etc.)</em></td>
<td></td>
</tr>
</tbody>
</table>

### Class II BSCs

<table>
<thead>
<tr>
<th>Class II BSCs</th>
<th>Protection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class II A1 / A2</td>
<td>70% of air is recirculated 30% of air is exhausted</td>
</tr>
<tr>
<td>Class II B1</td>
<td>40% of air is recirculated 60% of air is exhausted</td>
</tr>
<tr>
<td>Class II B2</td>
<td>0% of air is recirculated 100% of air is exhausted</td>
</tr>
</tbody>
</table>


Containment Primary Engineering Controls (C-PECs)

- Which C-PECs are allowed for **non-sterile compounding** of Hazardous Drugs according to USP 800?

Photos from left to right

Containment Primary Engineering Controls (C-PECs)

- Which C-PECs are allowed for *sterile compounding* of Hazardous Drugs according to USP 800?

Photos from left to right

6. [https://www.nuaire.com/labgard-nu-430-class-ii-type-b2-biosafety-cabinet](https://www.nuaire.com/labgard-nu-430-class-ii-type-b2-biosafety-cabinet)

Must be externally vented!
Non-Sterile and Sterile Compounding

• Ideally separate rooms with separate primary engineering controls for sterile and non sterile compounding

• Allowed to compound non-sterile medications in sterile compounding rooms and C-PEC IF room can maintain ISO 7 classification during the non-sterile compounding activity

• If the C-PECs used for sterile and nonsterile compounding are placed in the same room, they must be placed at least 1 meter apart and particle-generating activity must not be performed when sterile compounding is in process

Layout with Negative Pressure Hazardous Drug Storage Room
Non Hazardous Ante Room
Non Hazardous Clean Room
Hazardous Ante Room
Hazardous Clean Room
USP <800> Requirement: Closed System Transfer Devices & Environmental Sampling

- Closed system transfer devices *should* be used for compounding HDs when the dosage form allows.

- Closed system transfer devices *must* be used when administering antineoplastic HDs.

- Environmental wipe sampling for HD surface residue:
  - Every 6 months
  - Include areas where contamination from HDs likely
  - If measurable contamination found → identify, document and contain contamination then repeat wipe test.

Closed-System Transfer Devices (CSTDs)

- Offer an additional level of protection during compounding / administration

- No certainty that all CSTDs will perform adequately

- Which Closed-System Transfer Device is recommended by USP <800>?  
  
  No universal performance standards to evaluate CSTDs – users should do their own evaluation

Closed-System Transfer Devices (CSTDs)

1. Texium™
2. PhaSeal™
3. ChemoClave®
4. EquaShield®
5. OnGuard®

USP <800> Requirement: Personal Protective Equipment (PPE)

<table>
<thead>
<tr>
<th>PPE</th>
<th>Sterile Compounding</th>
<th>Non-Sterile Compounding</th>
<th>Cleaning</th>
<th>Unpacking Orders</th>
<th>Administering</th>
<th>Cleaning up Spills</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gowns</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
<td>Per institutional SOPs</td>
</tr>
<tr>
<td>Head / Hair Covers</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
<td>Per institutional SOPs</td>
</tr>
<tr>
<td>Shoe Covers</td>
<td>2 pairs</td>
<td>2 pairs</td>
<td></td>
<td></td>
<td></td>
<td>Per institutional SOPs</td>
</tr>
<tr>
<td>Chemotherapy gloves</td>
<td>2 pairs (outer must be sterile)</td>
<td>2 pairs</td>
<td>2 pairs</td>
<td>✓</td>
<td>2 pairs</td>
<td>Per institutional SOPs</td>
</tr>
<tr>
<td>Eye / Face Protection</td>
<td>Per institutional SOPs</td>
<td></td>
<td>If splashing likely</td>
<td>Per institutional SOPs</td>
<td>Per institutional SOPs</td>
<td></td>
</tr>
<tr>
<td>Respiratory Protection</td>
<td>Per institutional SOPs</td>
<td></td>
<td>Yes when cleaning under surface of C-PEC</td>
<td>Yes if HDs not contained in plastic</td>
<td>Yes when spills to large for a spill kit</td>
<td></td>
</tr>
</tbody>
</table>

- Institutional SOPs for PPE must be designed based on risk of exposure, types of activities performed, and an assessment of risk

Chemotherapy Gloves

- When chemotherapy gloves are required they must meet American Society for Testing and Materials (ASTM) standard D6978
- Chemotherapy gloves **should** be worn for handling all HDs including non-antineoplastics
- Should be powder free
- For sterile compounding, outer glove must be sterile
- Change gloves every 30 minutes unless otherwise recommended by manufacturer’s documentation

Gowns, Head, Hair, Shoe & Sleeve Covers

• Gowns
  – Must be disposable
  – Must be shown to resist permeability by HDs
  – Must close at the back, be long sleeved and have closed cuffs that are elastic or knit
  – Change per manufacturer’s recommendations or every 2-3 hours & always after a spill / splash

• Head, Hair, Shoe & Sleeve Covers
  – When compounding, second pair of shoe covers must be donned before entering the C-SEC and taken off when exiting

• PPE worn when handling hazardous drugs should be disposed of as hazardous drug waste
Eye / Face / Respiratory Protection

• Eye and Face Protection
  – Must be worn when there is a risk for spills or splashes of HDs (i.e. working in a surgical suite, cleaning a spill)
  – Googles
  – Face shields
  – Full-facepiece respirator

• Respiratory Protection
  – A fit tested NIOSH-certified N95 mask provides protection from airborne particles
    • Sufficient for “most activities requiring respiratory protection”
  – An elastomeric half-mask with a multi-gas cartridge and P100 filter
    • When unpacking HD orders not contained in plastic
  – A full-facepiece, chemical cartridge-type respirator or powered air-purifying respirator (PAPR) should be worn when there is a risk of exposure such as
    • Cleaning up spills
    • Deactivating, decontaminating and cleaning underneath the work surface of a C-PEC
    • There is known or suspected airborne exposure to powders / vapors
**USP <800> Requirement: Deactivating, Decontaminating, Cleaning and Disinfecting**

- **All areas** where hazardous drugs are handled and all reusable equipment must be deactivated, decontaminated, and cleaned
  - Sterile compounding areas and devices must be subsequently disinfected

<table>
<thead>
<tr>
<th>Cleaning Step</th>
<th>Purpose</th>
<th>Example Agents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deactivation</td>
<td>Render compound inert / inactive</td>
<td>EPA registered oxidizers (peroxide formulations, sodium hypochlorite)</td>
</tr>
<tr>
<td>Decontamination</td>
<td>Remove HD residue</td>
<td>Alcohol, water, peroxide, sodium hypochlorite</td>
</tr>
<tr>
<td>Cleaning</td>
<td>Remove organic and inorganic material</td>
<td>Germicidal detergent</td>
</tr>
<tr>
<td>Disinfection</td>
<td>Destroy Microorganisms</td>
<td>EPA registered disinfectant, sterile alcohol</td>
</tr>
</tbody>
</table>
USP <800> Requirement: Personnel Training

• All personnel who handle hazardous drugs must be trained and pass competency before they handle HDs and every 12 months

• Training / competency assessment must be documented and must include
  – An overview of the entity’s HD list
  – Review of the entity’s HD SOPs
  – Proper use of PPE
  – Proper use of equipment and devices (engineering controls)
  – Response to known or suspected HD exposure
  – Spill management
  – Proper disposal of HDs and trace-contaminated materials
USP <800> Requirement: Medical Surveillance

• Healthcare workers who handle HDs should be enrolled in a medical surveillance program
• Baseline and after HD exposure
• Assess
  – Labs
  – Medical history
  – Work history (previous hazardous drug exposure)
  – Estimated amount of HD handling
  – Symptoms that arise post handling of HDs

USP <800> Requirement: SOPs

- Entity must maintain SOPs for the safe handling of HDs for all situations
- Must be reviewed annually by the designated person

<table>
<thead>
<tr>
<th>USP &lt;800&gt; Required SOPs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hazard Communication Program</td>
</tr>
<tr>
<td>Designation of HD Areas</td>
</tr>
<tr>
<td>Storage</td>
</tr>
<tr>
<td>Use and Maintenance of Proper Engineering Controls</td>
</tr>
<tr>
<td>Deactivation, Decontamination, Cleaning and Disinfection</td>
</tr>
<tr>
<td>Transport</td>
</tr>
<tr>
<td>Environmental Monitoring (including wipe sampling)</td>
</tr>
<tr>
<td>Spill Control</td>
</tr>
<tr>
<td>Occupational Safety Program</td>
</tr>
<tr>
<td>Receipt</td>
</tr>
<tr>
<td>Compounding</td>
</tr>
<tr>
<td>Hand Hygiene, use of PPE based on activity (receipt, transport, compounding, administration, spill, disposal etc.)</td>
</tr>
<tr>
<td>Dispensing</td>
</tr>
<tr>
<td>Administering</td>
</tr>
<tr>
<td>Disposal</td>
</tr>
<tr>
<td>Medical Surveillance</td>
</tr>
</tbody>
</table>

This presentation was not an all inclusive summary of USP <800> Requirements
References

A new FDA approved monoclonal antibody comes to market for lung cancer. You review applicable literature and determine that the medication is not carcinogenic, does not produce developmental or reproductive toxicity and has no end organ toxicity or genotoxicity. You review section 16 of the product package insert and it does not list manufacturer safe handling guidance. The most likely safe handling for this medication at your institution would be

A. Add it to your institution’s hazardous drug list and treat it according to USP <800> requirements
B. Perform a risk assessment and determine what other safe handling requirements may be necessary
C. Do not add it to the hazardous drug list or perform a risk assessment
D. Do not add it to formulary
The medication does not meet any hazardous drug criteria as outlined by NIOSH so is unlikely to be considered a hazardous drug by NIOSH and therefore would not be subject to USP <800> requirements.
My institution prepares both sterile and non-sterile compounds with hazardous drugs. My facilities should be set up as follows (select ALL correct answers)

A. Separate refrigerators for hazardous and non-hazardous medications
B. A positive pressure room for unpacking hazardous medications
C. An externally vented, negative pressure ISO class 7 clean room for sterile compounding
D. Non-sterile compounds are prepared in the ISO class 7 negative pressure clean room because we’ve verified the room maintains ISO class 7 during non-sterile compounding
• USP <800> requires separate refrigerators for hazardous and non-hazardous medications
• A neutral or negative pressure room is required for unpacking hazardous medications
• The ISO class 7 clean room must be negative pressure for sterile compounding of hazardous drugs
• Ideally non-sterile compounding would be performed in a separate, negative pressure room; however, USP <800> allows non-sterile compounding in a sterile compounding ISO 7 clean room as long as the clean room is able to maintain ISO 7 conditions during compounding
Post Test: Question #3

For sterile compounding of hazardous medications, the following is true

A. 2 pairs of gloves are required
B. Chemotherapy rated gloves are required (compliant with ASTM standard D6978)
C. The outer gloves must be sterile
D. All of the above
USP <800> lists PPE requirements for various activities including sterile and non-sterile compounding, receiving, administering, and cleaning.

2 pairs of chemotherapy rated gloves are required for handling all hazardous drugs most hazardous drugs handling activities.
All of the following are required by USP <800> except

A. A hazardous drugs list
B. Training for all staff that handles hazardous drugs
C. Environmental wipe sampling monthly
D. Use of closed system transfer devices
E. A medical surveillance program
Question 4 Justification

• USP <800> requires environmental wipe sampling every 6 months to detect areas contaminated with hazardous drugs

• All other answers are required as a part of USP <800> compliance
Take Home Points

USP <800> is effective July 1, 2018!!!
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