USP <800> Keeping Patients and Practitioners Safe

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Faculty Disclosure

• Patricia C. Kienle declares no existence of a financial interest in any amount related to the content of this activity.

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Disclosure

Patricia Kienle is a member of the USP Compounding Expert Committee, but this presentation is not endorsed by or affiliated with USP.

Learning Objectives

At the conclusion of this activity, participants should be better able to:
1. Recognize how the NIOSH Hierarchy of Risk applies to <800>
2. Identify the key facility components required by <800>
3. Cite resources to assess closed system drug-transfer devices
4. State three work practices that support containment of hazardous drugs
Evidence of Health Effects

<table>
<thead>
<tr>
<th>1970s</th>
<th>Secondary malignancies identified in patients following treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1980s</td>
<td>Association between exposure to antineoplastics and adverse reproductive effects: miscarriages, congenital malformations, low birth weight and infertility</td>
</tr>
<tr>
<td>1990s</td>
<td>Link of cancer occurrence to healthcare workers exposure to antineoplastics</td>
</tr>
</tbody>
</table>

Major Elements of <800>

- List of hazardous drugs (HDs)
- Facilities
- Personnel
- Work practices

HD Standards Timeline

- OSHA Hazard Communication Standard
- USP <795> Nonsterile Preparations
- USP <797> Sterile Compounding
- NIOSH Alert

What Drugs Are Hazardous to Us?

- Carcinogen
- Reproductive toxin
- Teratogen & other developmental toxins
- Genotoxin
- Organ toxicity at low doses

New agents with similar structure or toxicity
Hazardous Materials

- EPA Haz Mat: Hazardous to the environment
- Both: Hazardous to the environment and health professionals
- NIOSH HD: Hazardous to health professionals

USP <800> Development

- Formation of USP <800> Subcommittee
- First Proposal of USP <800> Published
- Oct 2010
- Sept 2011
- Mar 2014
- Formation of USP <800> Expert Panel
- USP <800> Revised and Re-published
- Dec 2014
- Final USP <800> Published in USP39–NF34 1S
- Feb 2016
- December 2019
- USP <800> became OFFICIAL
List of Hazardous Drugs

• <800> requires use of the current NIOSH list of HDs
• Not all HDs need to be handled the same way
  • Active Pharmaceutical Ingredients (APIs) of any HD or any Table 1 antineoplastic that needs to be manipulated must follow all elements of <800>
  • Other HDs can be entity-exempt if an Assessment of Risk is done and alternative containment and/or work strategies are identified and implemented

2016 List of Hazardous Drugs

• Three tables
  • Table 1 – antineoplastics
  • Table 2 – non-antineoplastics
  • Table 3 – reproductive-only hazards
2020 Draft List of Hazardous Drugs

• Table 1
  • HD with Manufacturer’s Special Handling Instructions (MSHI)
  • “Known to be human carcinogen” listed on National Toxicology Program (NTP)
  • Group 1 (known human carcinogen) or Group 2A (probable human carcinogen) listed by International Agency for Research on Cancer (IARC)

• Table 2
  • All other HDs on the NIOSH list

Significant Changes ...

• Antineoplastics appear on both Tables
• Immunosuppressants move to Table 1
• Estrogens move to Table 1
• Hormones move to Table 2
• BCG is no longer on the list
Significant Changes ...

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Why?

... Significant Changes

- 2004 Alert (revised information) and 2016 Table 5 (personal protective equipment) move to a new document
- These guidance documents are recommended to be incorporated into your policies and practices
Your Assessment of Risk

- Must list all HDs you handle
  - Assess all?
  - Assess just the ones you use?
- List must include the drug and dosage form
- Note: this is a list of marketed hazardous drugs, not necessarily investigational agents or hazardous biologics

NIOSH Hierarchy of Controls

Most Effective

Least Effective

Elimination
  - Physically remove the hazard
Substitution
  - Replace the hazard
Engineering Controls
  - Isolate people from the hazard
Administrative Controls
  - Change the way people work
PPE
  - Protect the worker with Personal Protective Equipment

https://www.cdc.gov/niosh/topics/hierarchy/
## Handling HDs Differently

<table>
<thead>
<tr>
<th>Must follow all containment strategies and work practices listed in &lt;800&gt;</th>
<th>Eligible for an Assessment of Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active Pharmaceutical Ingredient (API)</td>
<td>NIOSH Table 1 antineoplastic HDs you only count or package</td>
</tr>
<tr>
<td>NIOSH Table 1 antineoplastic HDs that will be manipulated</td>
<td>Any non-antineoplastic NIOSH Table 1 drug/dosage form (other than API)</td>
</tr>
<tr>
<td>Other HDs you evaluate but decide to use full &lt;800&gt; requirements</td>
<td>Other NIOSH HD drug/dosage form (other than API)</td>
</tr>
</tbody>
</table>

### Differences: 2008 <797> and 2019 <800>

<table>
<thead>
<tr>
<th></th>
<th>2008 &lt;797&gt;</th>
<th>2019 &lt;800&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk Levels</td>
<td>Low-Medium-High</td>
<td></td>
</tr>
<tr>
<td>Personnel</td>
<td></td>
<td>Designated Person</td>
</tr>
<tr>
<td>Storage</td>
<td>Separate</td>
<td>API and Table 1 antineoplastics that will be manipulated must be stored in negative pressure environment</td>
</tr>
<tr>
<td>Ventilation</td>
<td>Preferred</td>
<td>Required</td>
</tr>
<tr>
<td>Hood Placement</td>
<td>Could place chemo hood in positive pressure room if only “low volume” compounded</td>
<td>Must be in negative pressure environment</td>
</tr>
</tbody>
</table>
Facility Design

• Storage
• Compounding
  • Cleanroom suite
    • Positive pressure anteroom
    • Negative pressure buffer room
  • Containment Segregated Compounding Area (C-SCA)
    • No requirement for anteroom
    • No requirement for ISO classification of room

Facilities – Storing and Compounding

Room with fixed walls separate from non-hazardous storage and compounding

Vented outside the building

C-PEC

Contains hazard

Removes hazard

Negative pressure of 0.010 to 0.030 inches to adjacent space

At least 12 air changes per hour (ACPH) (30 if buffer room)
Personal Protective Equipment (PPE)

- Gloves that meet ASTM Standard D6978
- Gowns
  - Laminate material
  - Long sleeves with closed cuff
  - No opening in the front
  - ASTM standard in draft
- Head, hair, and shoe covers
- Masks (to protect the preparation)

Additional PPE as Necessary

- Respirators
- Goggles
- Sleeve covers
CSTD Use

Closed System Drug-Transfer Devices

CSTDs required in 2008 <797> if using the “low use” exemption
CSTDs required in <800> when administering parenteral NIOSH Table 1 antineoplastics when the dosage form allows
CSTDs recommended in <800> for compounding
Other Closed Systems

- Mitosol Kit, Mobius Therapeutics: [https://mitosol.com/the-mitosol-kit/](https://mitosol.com/the-mitosol-kit/)
- Methotrexate Kit, EDGEPharma: [https://edgepharma.com/assets/Uploads/EmGYN-kit-logo-b3.jpg](https://edgepharma.com/assets/Uploads/EmGYN-kit-logo-b3.jpg)

Other Equipment

- Robots
- Mixers
- Chemo prep pads

[www.quartetrx.com](http://www.quartetrx.com)

Elements to Consider

<table>
<thead>
<tr>
<th>Follow all requirements in &lt;800&gt;</th>
<th>Consider alternative practices</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active Pharmaceutical Ingredient (API)</td>
<td>NIOSH Table 1 antineoplastic HDs you only count or package</td>
</tr>
<tr>
<td>NIOSH Table 1 antineoplastic HDs that will be manipulated</td>
<td>NIOSH non-antineoplastic Table 1 HDs</td>
</tr>
<tr>
<td>Items you decide to NOT exempt based on risk</td>
<td>NIOSH Table 2 dosage forms that present lower risk to you and your employees</td>
</tr>
</tbody>
</table>

Work Practices

- Receipt
- Unpacking
- Transporting
- Storing
- Compounding
- Delivery to patient, caregiver, nurse
- Discarding infusion containers and PPE
Receipt and Unpacking ...

• These are different processes
• Receiving
  • NIOSH Table 1 antineoplastic HDs should come from your supplier in marked totes with those HDs bagged in impervious plastic
  • Some suppliers also mark/bag other HDs

... Receipt and Unpacking ...

• Designated area for HD unpacking
  • Can be as simple as a designated counter space or use of chemo prep pad
  • Person unpacking Table 1 antineoplastic HDs should wear one pair of chemo gloves
    • Access to other PPE
    • Aware of action to take for damaged package
    • Access to spill kit
... Receipt and Unpacking ...

• NIOSH Table 1 antineoplastics that will be manipulated
  • Keep those meds in the plastic bag
  • Check in
  • Transport bag to HD storage
  • Unpack in the HD storage area

• Other HDs
  • Handle in your Assessment of Risk

... Receipt and Unpacking

• For HDs that will be co-mingled with other stock, consider
  • Separate shelf
  • Distinctive color bin
  • Shelf sticker
Consider ...

### Prepare
- Receive
- Unpack
- Transport
- Store

### Compound and Dispense
- Compound
- Dispense

### Administer
- Administer
- Discard

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... Consider ...

### Function
- Receive
- Unpack
- Transport
- Store
- Compound
- Dispense
- Administer
- Discard

### Containment
- Hood
- Negative environment
- Separate area
- Separate equipment
- PPE
- Closed system drug transfer device
- Other closed system

### Work Practice
- Distinctive bins or labels
- Enclose in chemo bag
- Decontaminate surfaces
- Limit access
... Consider

- NIOSH Table 1 antineoplastics that you manipulate prior to administering
- NIOSH Table 1 HDs you only need to count or package
- Other HDs with increased risk based on your handling practices
- Other HDs you handle
- Other hazards not on NIOSH list

Example: 5 FU, Vincristine, Gancyclovir

<table>
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<th>Required Practices</th>
</tr>
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<tbody>
<tr>
<td>Primary Engineering Control (PEC)</td>
</tr>
<tr>
<td>Secondary Engineering Control (SEC)</td>
</tr>
<tr>
<td>Supplemental Engineering Control (CSTD)</td>
</tr>
<tr>
<td>PPE</td>
</tr>
<tr>
<td>All listed work practices</td>
</tr>
</tbody>
</table>
Example: Leuprolide

**Required Practices**
Evaluate how it is manipulated prior to administration

**Consider**
Using manufacturer-supplied closed system, prepare by RN for bedside administration

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Example: Other HDs

<table>
<thead>
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<th>Practices to Consider</th>
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### Hazardous Biologics Not on NIOSH List

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### Example: Hazards Not on NIOSH List

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Recommendation: Do not include in your NIOSH HD list or policy; develop a separate policy
Disposal

- <800> refers you to applicable laws and regulations
- Your waste hauler can provide state-specific information
- Partial doses may have state-specific requirements

Spills

Place spill kits in receiving, storage, compounding, and administering areas
Be sure contents meet your needs
Assessment of Risk Resources

ASHP Assessment of Risk Toolkit, https://www.ashp.org/Pharmacy-Practice/Resource-Centers/Sterile-Compounding/USP-Chapter-800-Assessment-of-Risk-Toolkit

Joint Commission Resources, www.hazmedsafety.com

Kienle PC and Douglass K, Perform an Assessment of Risk to Comply with USP <800>, https://www.pppmag.com/article/2012/?search=assessment%20of%20risk


Resources

USP Compounding Compendium, www.usp.org

USP <800> FAQs, www.usp.org


McLeod EN, Fillis CJ, Blind JE, Practical Approach to Assess the Hazardous Exposure Potential of Investigational Drugs, AJHP, 1 May 2020
Thank You