USP 800: Beyond the Basics

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November 9, 2019
I do not have any commercial interest, financial relationships, or conflicts of interest to disclose in regards to the content of this presentation.
Objectives

- Explain the process of creating a hazardous drug list
- Understand the requirements for hazardous drug disposal and spill management
- Discuss the key components of USP 800 that impact nursing practice
Hazardous Drugs (HD) Handling Timeline

• 1983 - ASHP published its first guidance on hazardous drugs (HDs)

• 2004 - National Institute for Occupational Safety and Health (NIOSH) Alert: Preventing Occupational Exposure to Antineoplastic and Other Hazardous Drugs in Health Care Settings issued

• 2006 - ASHP Guidelines on Handling HD’s created to harmonize with NIOSH

• 2008 - USP <797> revised and established many of the NIOSH recommendations as enforceable requirements

• 2016 - USP <800> Hazardous Drugs—Handling in Healthcare Settings published, 2019, December 1\textsuperscript{st} – USP <800> becomes enforceable
Exposure Risk

• Healthcare workers may be exposed to HDs at many points
  – Manufacturing
  – Distribution
  – Receipt
  – Storage
  – Transport
  – Compounding
  – Administration
  – Waste handling
  – Care of treated patients
Exposure Risk

• Study from 1999 at multiple cancer centers showed surface contamination with antineoplastic HDs in both compounding and infusion areas
• Measurable amounts of chemotherapy (cyclophosphamide, ifosfamide, and fluorouracil) were detected in 75% of the pharmacy wipe samples and 65% of the infusion area wipe samples
• A NIOSH-sponsored study published in 2010 looked at HD contamination and other risk points from the 1999 study
  – Found 75% of the pharmacy wipe samples and 43% of the infusion wipe samples
• Multiple other international studies showing similar results
Routes of Exposure

- Inhalation
- Dermal absorption
  - Skin contact with contaminated surfaces is the primary route
- Accidental injection
- Ingestion
In 2014 NIOSH started producing their list in the current format with three groups:

- Group 1: Antineoplastic drugs
- Group 2: Non-antineoplastic drugs
- Group 3: Reproductive risk
In 2016, USP Chapter 800 adopted the NIOSH HD list as the list of antineoplastic and other HDs that an organization should review.

- This list may be modified to include only the drugs that they handle and must be reviewed at least every 12 months.

When new agents or dosage forms are used by an organization it should be reviewed against the list.
Assessment of Risk

- Determination of risk
- Requires review of
  - Available dosage forms
  - Packaging
  - Manipulation requirements
  - Risk of Exposure
  - PPE
  - Containment strategies
<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Divalproex</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dosage Form</strong></td>
<td></td>
</tr>
<tr>
<td>☑ Tablet / Capsule</td>
<td>☑ Solution/powder for injection</td>
</tr>
<tr>
<td>☑ Oral Liquid (commercial)</td>
<td>☑ Other:</td>
</tr>
<tr>
<td>☐ Compounded liquid</td>
<td></td>
</tr>
<tr>
<td><strong>NIOSH Category:</strong></td>
<td></td>
</tr>
<tr>
<td>☑ Table 1: Antineoplastic Drugs that only require packaging or counting</td>
<td></td>
</tr>
<tr>
<td>☑ Table 2: Non-antineoplastic Drugs</td>
<td></td>
</tr>
<tr>
<td>☐ Table 3: Reproductive Toxin Drugs</td>
<td></td>
</tr>
<tr>
<td><strong>Description of Packaging</strong></td>
<td></td>
</tr>
<tr>
<td>☑ Final dosage form, ready for dispensing directly to patient (i.e., unit dose, unit-of-use)</td>
<td></td>
</tr>
<tr>
<td>☑ Bottle of [tablet/capsule/liquid] to be repackaged</td>
<td></td>
</tr>
<tr>
<td>☐ Other:</td>
<td></td>
</tr>
<tr>
<td><strong>Description of Required Manipulation</strong></td>
<td></td>
</tr>
<tr>
<td>☑ None (product available in ready-to-dispense package)</td>
<td></td>
</tr>
<tr>
<td>☑ Repackaging only (e.g. counting; transfer container)</td>
<td></td>
</tr>
<tr>
<td>☐ Other:</td>
<td></td>
</tr>
<tr>
<td><strong>Risk of Exposure</strong></td>
<td></td>
</tr>
<tr>
<td>☑ Skin contact</td>
<td>Exposure risk minimal, risk is associated with ingestion not due to routine handling</td>
</tr>
<tr>
<td>☐ Ingestion</td>
<td></td>
</tr>
<tr>
<td>☐ Inhalation</td>
<td></td>
</tr>
<tr>
<td>☐ Injection</td>
<td></td>
</tr>
<tr>
<td>☐ Other (specify):</td>
<td></td>
</tr>
<tr>
<td><strong>Alternative Containment Strategies and/or Work Practice</strong></td>
<td></td>
</tr>
<tr>
<td>[<strong>Engineering Control</strong> (i.e., BSC, containment isolators, CSTDs, temporary designated prep. area)]</td>
<td></td>
</tr>
<tr>
<td>[<strong>Administrative Control</strong> (i.e., educational materials, acknowledgement form, training)]</td>
<td></td>
</tr>
<tr>
<td>Hazardous Drug Acknowledgement of Risk Form</td>
<td></td>
</tr>
<tr>
<td><strong>PPE Strategies</strong> (i.e., gloves, gowns, booties, head cover, face shield, eye protection, respirators)]</td>
<td></td>
</tr>
<tr>
<td>Chemotherapy Gloves only for any handling</td>
<td></td>
</tr>
<tr>
<td>MEDICATION NAME</td>
<td>Dosage Form</td>
</tr>
<tr>
<td>-----------------</td>
<td>-------------</td>
</tr>
<tr>
<td>Abacavir</td>
<td>tablet, oral solution</td>
</tr>
<tr>
<td>Abemaciclib</td>
<td>tablet</td>
</tr>
<tr>
<td>Abiraterone</td>
<td>tablet</td>
</tr>
</tbody>
</table>

**Supplemental Information**

- FDA Pregnancy Category C; malignant tumors observed in male and female mice and rats, genotoxic in invivo micronucleus test
- Women who are pregnant or may be pregnant should not handle without protection (e.g., gloves); FDA Pregnancy Category X

**MNF handling guideline**

**Storage/Transport**

**BSC (y/n)**

**Pharmacy PPE**

**Nursing area**
HD Spills

• Facility dependent processes
• Response teams may include EVS, Security and Pharmacy
• Nurse response vs. Spill Team response
  – Determine what a large spill vs. small spill
    • Entity specific
    • MCI: Large Spills (> 50cc) Small Spills (less than or equal to 50cc)
Spill Cleanup

- Personnel must assess the size and scope of the spill
- Obtain a spill kit and don PPE
- Once fully garbed, contain spill using spill kit.
  - Carefully remove any broken glass fragments and place them in a puncture resistant container.
  - Absorb liquids with spill pads from spill kit.
- Spill cleanup should proceed progressively from areas of lesser to greater contamination.
  - Completely remove and place all contaminated material in the HD waste disposal bags.
Spill Cleanup

- Apply a Deactivating/Decontaminating agent liberally to all exposed areas for appropriate dwell time and wipe away all remaining residue.
- Rinse the area several times with a cleaning agent and place all materials used for containment and cleanup in disposal bags. Seal bags and place them in the appropriate final container for disposal as hazardous waste.
- Carefully remove all PPE using the inner gloves.
  - Place all disposable PPE into disposal bags. Seal bags and place them into the appropriate final container.
  - Remove inner gloves, contain in a small, sealable bag, and then place into the appropriate final container for disposal as hazardous waste.
- Wash hands thoroughly with soap and water.
• **Deactivation**: making hazardous substance inert
• **Decontamination**: transfer of hazardous drug residue from contaminated area to a disposable material
  – Decontamination occurs by inactivating, neutralizing, or physically removing HD residue from non-disposable surfaces (e.g. Hoods) and transferring it to absorbent, disposable materials (e.g., wipes) appropriate to the area being cleaned
• Often used interchangeably
• Deactivating a HD is preferred
  – No single process has been found to deactivate all currently available HDs from different surface materials
Deactivation/Decontamination

- All areas where HDs are handled and all reusable equipment and devices must be deactivated/decontaminated
- Don’t use sprays
  - Decontamination/deactivation agents should be applied through the use of wipes wetted with appropriate solution and not delivered as a spray to avoid aerosolizing and/or spreading HD residue
HD Administration

- Only individuals trained in the administration of HDs should do so.
- Nurses who administer HDs and care for patients receiving chemotherapy should meet the requirements of Oncology Nursing Society (ONS).
- Other Considerations
  - MUST use closed system transfer devices for administration when drug allows.
  - Limit access for hazardous administration areas to patients receiving therapy and essential personnel.
    - Eating, drinking, applying makeup, and the presence of foodstuffs should be avoided in patient care areas while HDs are administered.
  - Minimize environmental contamination.
Closed System Transfer Devices

Required for administration
Closed System Transfer Devices

- USP Chapter 800 describes an additional layer of protection
  - Containment supplemental engineering control
    - Closed System Transfer Devices (CSTD’s)
  - A drug transfer device that mechanically prohibits the transfer of environmental contaminants into the system and the escape of HD or vapor concentrations outside the system
- Initial CSTD developed in Europe
  - Compared to surface contamination of similar work areas reported in the literature, the closed system was more effective than the BSC in reducing contamination during preparation
Closed System Transfer Devices

- NIOSH originally defined the CSTD in 2004
  - Did not specify design or performance criteria
- A number of devices marketed as CSTDs have appeared since 2004
  - These devices are designated by the FDA as Class II medical devices
  - Not requiring premarket approval
  - “FDA clears” the new device
- Although some CSTDs have been shown in peer-reviewed studies to limit the potential of generating aerosols and reduce HD contamination in the workplace
  - No surrogate or marker HD has been shown to be superior in measuring CSTD effectiveness or has been universally adopted
Personal Protective Equipment (PPE)

- PPE provides worker protection to reduce exposure to HD and residues
- Disposable PPE must not be re-used
- USP Chapter 800 addresses PPE
  - Receiving
  - Compounding
  - Administration
  - Spill management
PPE Removal

• PPE used for handling HD should be considered contaminated and disposed of as hazardous
  – Administration
  – Patient care
  – Discard patient waste
  – Compounding
  – Disposing
  – HD spill cleanup
  – Receiving
• Removal of HD gown
  – Done cautiously to avoid transferring contamination
  – Turn the gown inside out, fold it tightly, and discard
Gloves

• USP Chapter 800 requires that chemotherapy gloves meet ASTM 6978 standards
  – This standard tests gloves for resistance to permeation to a group of HDs selected for characteristics of toxicity, diluent, and ability to permeate standard gloving material
Hazardous Waste Disposal

• Processes differ amongst institutions
  – All hazardous waste disposed of in one bin (BLACK)
  – Separate bins (Trace and Bulk) hazardous waste
    • Reminder! Include chemo gowns
Environmental Monitoring of HDs

- Surface wipe sampling of healthcare settings for HD contamination is advocated as a means of environmental quality and control.
- Determine a benchmark of contamination and then to monitor the effectiveness of safe handling programs.
- No acceptable levels of HD surface contamination have been determined by any regulatory agency.
• Environmental wipe sampling for HD surface residue should be performed routinely

• Surface wipe sampling should include
  – Interior of the hoods and equipment contained within
  – Pass-through chambers
  – Surfaces in staging or work areas near the hood
  – Areas adjacent to hoods (e.g., floors, staging, and dispensing area)
  – Areas immediately outside the cleanroom
  – Patient administration areas
Environmental Monitoring of HDs

• Multiple Manufacturers on the market
  – Often performed in conjunction with implementation of CSTD’s to show effectiveness
• There are no certifying agencies for vendors of wipe sampling kits
  – There is no standard for acceptable limits for HD surface contamination
Environmental Monitoring of HDs

- Surface wipe sampling
  - Method of choice
  - Provides a way to determine the efficacy of HD work practices and cleaning methods
  - As dermal uptake is the most likely route of occupational exposure surface wipe sampling can be a useful tool
  - Can be used for most classes of drugs
- Surface wipe sampling of healthcare settings for HD contamination is advocated as a means of environmental quality and control
- Determine a benchmark of contamination and then to monitor the effectiveness of safe handling programs
Considerations

- Frequency
- Locations
- Medications to test
- Number of samples
- Shipping requirements
- Spill management

- Staff training
- Documentation methods
- Impact of results
  - Baseline
  - Retesting
- Financial impact
## Table 1: Results from the March 26, 2019 Wipe Study in ng/ft\(^2\) and ng/cm\(^2\)

<table>
<thead>
<tr>
<th>Wipe</th>
<th>Location</th>
<th>Department</th>
<th>Paclitaxel Concentration ng/ft(^2) (ng/cm(^2))</th>
<th>5-FU Concentration ng/ft(^2) (ng/cm(^2))</th>
<th>Cyclophosphamide Concentration ng/ft(^2) (ng/cm(^2))</th>
<th>Doxorubicin Concentration ng/ft(^2) (ng/cm(^2))</th>
<th>Irinotecan Concentration ng/ft(^2) (ng/cm(^2))</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td>Nursing</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td>Nursing</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td>Pharmacy</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>4</td>
<td></td>
<td>Pharmacy</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>5</td>
<td></td>
<td>Pharmacy</td>
<td><strong>38.44 (0.04)</strong></td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>6</td>
<td></td>
<td>Pharmacy</td>
<td>ND</td>
<td>1172.84 (1.28)</td>
<td><strong>82.65 (0.09)</strong></td>
<td>ND</td>
<td>ND</td>
</tr>
</tbody>
</table>
Environmental Monitoring of HDs

- Identifying the root cause
- Implementing change
  - Redesign workflow
  - Ensure proper personal protective equipment
  - Provide additional staff training on cleaning procedures
  - Establish additional decontamination procedures
Medical Surveillance

• Medical surveillance is part of a comprehensive exposure control program
• Purpose is to minimize adverse effects in personnel
• Involve assessment and documentation of
  – symptom complaints
  – physical findings
  – laboratory values
Medical Surveillance

• Key elements of program
  – Confidentiality
  – Identification of workers with potential risk of exposure
  – Initial baseline assessment (pre-placement) of a worker's health status and medical history.
    • medical and reproductive history
    • work history to assess exposure to HDs
    • physical examination
    • laboratory testing
  – Monitoring of employee health prospectively through periodic surveillance
  – Monitoring of the data to identify prevention failure leading to health effects
Follow Up Actions

- Perform a post-exposure examination tailored to the type of exposure
- Verify that all engineering controls are in proper operating condition
- Confirmation that employee complied with existing policies. (eg. PPE)
- Develop and document a plan of action that will prevent additional exposure of workers
Follow Up Actions

• Provide follow-up medical survey to demonstrate that the plan implemented is effective
• Ensure that any exposed worker receives confidential notification of any adverse health effect.
• Offer alternative duty or temporary reassignment as appropriate
• Provide ongoing medical surveillance of all workers at risk for exposure to HDs to determine whether the plan implemented is effective