USP 800: Beyond the Basics

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Disclosures

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 1st – USP <800> becomes enforceable

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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

NIOSH HD list

- 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

USP 800 HD List

- 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

HOPA
Hematology/Oncology Pharmacy Association

Approved/Effective Date:	
Approved by:	
Annual Review by:	
Date Reviewed:	

ASSESSMENT OF RISK FORM

TO BE COMPLETED FOR ANY DRUG BEING CONSIDERED FOR CONTAINMENT STRATEGIES THAT DIFFER FROM FULL NIOSH RECOMMENDATIONS, AS DEFINED IN USP GENERAL CHAPTER <800> HAZARDOUS DRUGS-HANDLING IN HEALTHCARE SETTINGS.

Drug Name		
Dosage Form	☐ Tablet / Capsule ☐ Oral Liquid (commercial) ☐ Compounded liquid	☐ Pre-filled syringe ☐ Solution/powder for injection ☐ Other:
NIOSH Category:	☐ Table 1: Antineoplastic Drugs that only require packaging or counting ☐ Table 2: Non-antineoplastic Drugs ☐ Table 3: Reproductive Toxin Drugs	
Description of Packaging	☐ Final dosage form, ready for dispensing directly to patient (*i.e., unit dose, unit-of-use*) ☐ Bottle of [tablet/capsule/liquid] to be repackaged ☐ Other:	
Description of Required Manipulation	☐ None (product available in ready-to-dispense package) ☐ Repackaging only (e.g. counting; transfer container) ☐ Other:	
Risk of Exposure	☐ Skin contact ☐ Ingestion ☐ Inhalation ☐ Injection ☐ Other (specify):	
Alternative Containment Strategies and/or Work Practice	**[Engineering Control** *(i.e., BSC, containment isolators, CSTDs, temporary designated prep. area)*]	
	[Administrative Control *(i.e., educational materials, acknowledgement form, training)*]	
	[PPE Strategies *(i.e., gloves, gowns, booties, head cover, face shield, eye protection, respirators)*]	
Recommendation	☐ Follow all containment requirements (as per USP<800>) ☐ Follow alternative containment strategies documented above	

AoR = assessment of risk; API = active pharmaceutical ingredient; CSTD = closed system drug-transfer device; HD = hazardous drug; MSHG = Manufacturer Suggested Safe Handling Guideline; NIOSH = National Institute for Occupational Safety and Health; PPE = personal protective equipment; USP = U.S. Pharmacopeia

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

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HD List

MEDICATION NAME	Dosage For	Antineoplastic (Anticancer)	Hazardou	NIOSH HZD Category	commonly crushed or manipulated solids
Abacavir	tablet, oral solution		X	2	
Abemaciclib	tablet	X	X	1A	
Abiraterone	tablet	X	X	1	

Supplemental Information	MNF handling guideline	Storage/Tra	BSC (y	Pharmacy PPE	Nursing ac
FDA Pregancy 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					

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)

HD Spills

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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/Decontamination

- 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

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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 Monitoring of HDs

- 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							
Wipe	Location	Department	Paclitaxel Concentration ng/ft^2 (ng/cm^2)	5-FU Concentration ng/ft^2 (ng/cm^2)	Cyclophosphamide Concentration ng/ft^2 (ng/cm^2)	Doxorubicin Concentration ng/ft^2 (ng/cm^2)	Irinotecan Concentration ng/ft^2 (ng/cm^2)
1		Nursing	ND	ND	ND	ND	ND
2		Nursing	ND	ND	ND	ND	ND
3		Pharmacy	ND	ND	ND	ND	ND
4		Pharmacy	ND	ND	ND	ND	ND
5		Pharmacy	38.44 (0.04)	ND	ND	ND	ND
6		Pharmacy	ND	1172.64 (1.26)	82.65 (0.09)	ND	ND

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

References

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