Protecting Yourself from Hazardous Drugs:
Is Your Institution following USP<800>?

Presented in partnership with the ICHP Annual Meeting

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Disclosure
Christopher A. Fausel, PharmD, MHA, BCOP has no financial relationships to disclose relating to the subject matter of this presentation.

Learning Objectives
• List criteria utilized for defining a hazardous drug
• Describe the criteria and methodology used by NIOSH to identify drugs as hazardous
• Describe potential health risks associated with exposure to hazardous drugs
• Explain strategies to employ proper use of PPE and engineering controls to protect healthcare workers from hazardous drugs
• Describe components of a surveillance program

Evolution of Recommendations
• 1990, 2006 ASHP Guidelines on Handling Hazardous Drugs
• 2004 NIOSH Safety Alert
• NIOSH LIST of Antineoplastic and Other Hazardous Drugs in Healthcare Settings – most recent update 2014 (updated every 2 years)
• USP <797>
• USP <800> Final chapter published 2/1/16 – enforceable July 1, 2018

NIOSH = National Institute for Occupational Safety and Health; PPE = personnel protective equipment.

Technician Learning Objectives
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• Describe potential health risks associated with exposure to hazardous drugs
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• Describe components of a surveillance program
Definition of a Hazardous Drug (HD)

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


NIOSH List of HDs (2014)

- Group 1: Antineoplastic Drugs
- Group 2: Non-antineoplastic Drugs deemed hazardous by meeting one or more NIOSH criteria for a hazardous drug
- Group 3: Reproductive Risks
  - Drugs that primarily pose a reproductive risk to men and women who are actively trying to conceive and women who are pregnant or breast feeding, because of excretion in breast milk

NIOSH 2014. NIOSH list of antineoplastic and other hazardous drugs in healthcare settings 2014.
By Connor TH, MacKenzie BA, DeBord DG, Trout DB, O’Callaghan JP. Cincinnati, OH US DHHS, CDC.

Listings in NIOSH Update 2014

<table>
<thead>
<tr>
<th>Table</th>
<th>Content</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Antineoplastic drugs including those with MSHG</td>
</tr>
<tr>
<td>2</td>
<td>Non-antineoplastic drugs that meet one or more of the NIOSH criteria for a HD including those with MSHG</td>
</tr>
<tr>
<td>3</td>
<td>Non-antineoplastic drugs that primarily have adverse reproductive effects</td>
</tr>
<tr>
<td>4</td>
<td>Deleted drugs from the 2004 NIOSH listing</td>
</tr>
<tr>
<td>5</td>
<td>PPE and engineering controls for HDs</td>
</tr>
</tbody>
</table>

MSHG = manufacturer’s safe handling guidelines.
NIOSH 2014. NIOSH list of antineoplastic and other hazardous drugs in healthcare settings 2014.
By Connor TH, MacKenzie BA, DeBord DG, Trout DB, O’Callaghan JP. Cincinnati, OH US DHHS, CDC.

Maintenance of HD List

- Assessment of new drugs as they enter the marketplace
- Re-categorization as new toxicologic data becomes available
- Consider investigational agents hazardous if the mechanism of action suggests HD
- Consider dosage form and whether dosage form will be altered/crushed/compounded
- All hazardous drugs should be labeled

NIOSH 2014. NIOSH list of antineoplastic and other hazardous drugs in healthcare settings 2014.
By Connor TH, MacKenzie BA, DeBord DG, Trout DB, O’Callaghan JP. Cincinnati, OH US DHHS, CDC.

HD Risk Categorization

- Assessment of risk to consider:
  - Type of HD (eg, antineoplastic, non-antineoplastic, reproductive risk only)
  - Risk of exposure
  - Packaging
  - Manipulation
- Entity must document containment strategies employed for specific dosage forms

Pharmaceutical compounding – Hazardous drugs – handling in healthcare settings (Chapter <800>).

Generating A List of Hazardous Drugs for Your Facility

- OSHA hazard communication requires employers to develop a hazard communication program appropriate for their unique workplace
- Identify all hazardous drugs that could be encountered by workers in the facility
- OSHA defines compliance as:
  - 1. Evaluation whether drugs meet criteria as a hazardous drug
  - 2. Posting a list of hazardous drugs to ensure worker safety

OSHA = Occupational Safety and Health Administration.
NIOSH 2014. NIOSH list of antineoplastic and other hazardous drugs in healthcare settings 2014.
By Connor TH, MacKenzie BA, DeBord DG, Trout DB, O’Callaghan JP. Cincinnati, OH US DHHS, CDC.
Consequences of Exposure to HDs

• Short-term:
  - Skin irritation/burning
  - GI toxicity
  - Flu-like symptoms
  - Ocular irritation

• Long-term:
  - Fertility impairment
  - Birth defects
  - Secondary cancers

Containment Strategies

• Assessment of risk to consider:
  - Type of HD (eg, antineoplastic, non-antineoplastic, reproductive risk only)
  - Risk of exposure
  - Packaging
  - Manipulation

• Entity must document containment strategies employed for specific dosage forms

Chain of Custody: Hazardous Drugs

Receipt
Storage
Compounding
Dispensing
Administration
Disposal

Pharmacy Staff Risk Points

Activity: Compounding and other manipulations
Risk Points:
- Crushing/splitting tablets or opening capsules
- Transferring oral or topical liquids between containers
- Weighing or mixing components
- Reconstituting powdered or lyophilized HDs and withdrawing or diluting injectable HDs from stock containers
- Expelling air or HDs from syringes
- Contacting HD residue present on PPE or other garments
- Cleaning activities on surfaces containing HD residue
- Maintenance activity on potentially contaminated equipment

Potential HD Exposure Risk Points

Activity: Administration
Potential Opportunity for Exposure:
- Performing certain specialized procedures (eg, intraoperative or intraperitoneal injection or bladder instillation)
- Priming an IV set

Activity: Patient Care Activities
Potential Opportunity for Exposure:
- Handling body fluids (eg, urine, feces, sweat, or vomit)
- Handling body-fluid contaminated clothing, dressing, linens, or other materials
Scope of USP Chapter <800>

- Standards apply to:
  - Areas where hazardous drugs (HDs) are compounded, stored, transported, and administered
- Health care personnel include, but are not limited to:
  - Pharmacists and pharmacy techs
  - Physicians and physician assistants
  - Nurses and home health care workers
  - Veterinarians and veterinary techs

Facilities Impacted

- Pharmacies
- Hospitals and other health care institutions
- Patient treatment clinics
- Physician practice facilities
- Veterinarian’s offices

Definitions in <800>

- Must = Compliance is mandatory effective July 1, 2018
- Should = Recommendations only – not requirements

Who Is Responsible for Compliance?

- Each institution must have a designated person who is qualified and trained to be responsible for:
  - Developing and implementing appropriate procedures
  - Overseeing entity compliance with all applicable laws, regulations and standards
  - Environmental control of compounding and storage areas

Facilities Layout

- HD handling areas must be designated with signage and restricted to authorized personnel
- Locate HD handling areas away from breakrooms/refreshment areas for staff/patients/visitors
- Designated areas must be available for:
  - Receipt and unpacking
  - Storage of HDs
  - Non-sterile HD compounding
  - Sterile HD compounding

Receipt of HDs

- Antineoplastic HDs and all HD active pharmaceutical ingredients (API) must be unpacked (removed from external shipping containers) in areas that are neutral or negative pressure relative to surrounding areas
- HD must not be unpacked from their external shipping containers in sterile compounding areas or in positive pressure areas
Storage of HDs

- HDs must be stored to prevent spillage/breakage if the container falls; no storage on the floor
  - Storage of antineoplastic HDs not in a final dosage form must be segregated from non-hazardous inventory in an externally ventilated negative pressure environment with ≥ 12 air exchanges per hour (ACPH)
  - Sterile and non-sterile HDs may be stored together
  - Refrigerated HDs must be stored in a dedicated unit in a negative pressure room with ≥ 12 ACPH
  - Reproductive risk only HD and final dosage forms of antineoplastic HDs may be stored with other inventory

Personnel Protective Equipment (PPE)

- PPE provides worker protection to reduce exposure to HDs aerosols and drug residue
- Gowns, gloves, head, hair, and shoe covers are required for compounding sterile and nonsterile HDs
- Gloves and gowns are required when administering injectable HDs
- Institutions must develop SOPs for PPE based on risk of exposure and activities performed

Use of Gloves with HD Handling

- Two pairs of gloves required for compounding and administering HDs
  - Use sterile gloves for outer pair for sterile compounding
- Gloves must meet standards set by American Society for Testing and Materials (ASTM)
- Chemotherapy gloves must be powder-free
- Inspect gloves for defects before using and do not use defective gloves
- Change gloves every 30 minutes or when torn, punctured or contaminated

Use of Gowns with HD Handling

- Gowns must be tested to resist permeability by HDs; polyethylene-coated polypropylene or other laminate materials preferred
- Gowns must close in the back and have no seams/closures to allow HDs to pass through
- Gowns changed per manufacturer’s recommendations or every 2 to 3 hours and after any spills/splashes
- Clothing, lab coats, scrubs can retain HDs

Other Recommended PPE

- Head/hair covers (including beard/moustaches) required
- Second pair of shoe covers must be donned when compounding sterile HDs; remove when exiting buffer room
- Eye and face protection must use when risk for spills/splashes
- Use NIOSH certified N95 masks for respiratory protection—for spills, cleaning activities or potential airborne exposure

Disposal of PPE

- Consider all PPE worn when handling HDs as being contaminated with trace quantities of HDs
- PPE must be placed in an appropriate waste container and disposed per regulations
- PPE used during compounding should be disposed in the proper container in the C-SEC
- Chemotherapy gloves must be discarded in an approved HD waste container inside the C-PEC or contained in a sealable bag outside the C-PEC

C-SEC = containment secondary engineering control; C-PEC = Containment Primary Engineering Control.
Engineering controls are required to prevent cross- and microbial contamination using three controls:
- **Containment primary** engineering control (C-PEC) - a ventilated device for direct handling of HDs
- **Containment secondary** engineering control (C-SEC) – the room in which the C-PEC is placed
- Supplemental engineering controls – closed-system transfer devices (CSTD)

HD Compounding and Engineering Controls

HD Compounding and Engineering Controls

• HDs must be compounded in a C-PEC (hood) in a C-SEC (buffer room)
• C-PEC shall operate continuously
• Segregate non-sterile and sterile compounding C-PECs
• Laminar airflow workbench (LAFW) or compounding aseptic isolator (CAI) must not be used for compounding HDs

Engineering Controls for Sterile HD Compounding

<table>
<thead>
<tr>
<th>Configuration</th>
<th>C-PEC</th>
<th>C-SEC</th>
</tr>
</thead>
<tbody>
<tr>
<td>ISO Class 7 buffer room with an ISO Class 7 ante-room</td>
<td>Externally vented Example: Class II BSC or CACI</td>
<td>Externally vented 30 ACPH Negative pressure between 0.01 and 0.03 inches of water column relative to the adjacent areas</td>
</tr>
<tr>
<td>Unclassifiable C-SCA</td>
<td>Externally vented Example: Class II BSC or CACI</td>
<td>Externally vented 12 ACPH Negative pressure between 0.01 and 0.03 inches of water column relative to adjacent areas</td>
</tr>
</tbody>
</table>

Recommended Configurations for Sterile HD Compounding

BSC or CACI
- Buffer ISO 7 Negative Pressure
- Area ISO 7 Positive

BSC or CACI
- Buffer ISO 7 Negative Pressure
- Area ISO 7 Positive

LAFW or CAI
- Buffer ISO 7 Negative Pressure
- Area ISO 7 Positive

Anteroom: Minimum positive pressure of 0.02 inches of water column to adjacent spaces; at least 0.01 inches of water column to HD buffer room; 30 ACPH; hand washing sink.

Environmental Quality Control – Wipe Studies

• Environmental wipe studies for HDs should be performed routinely at least every 6 months
• Surface wipe sampling should include:
  - Interior of C-PEC and equipment contained in it
  - Staging or work areas near C-PEC/pass-through
  - Areas adjacent to CPECs (e.g., nearby flooring)
  - Areas outside of buffer room and patient administration areas
• Currently no studies exists demonstrating the effectiveness of a specific number of wipe samples in determining levels of HD contamination

Supplemental Engineering Controls

• Some CSTDs shown to limit potential for generating hazardous aerosols during sterile compounding
• No universal performance standard exists by which CSTDs are evaluated for containment
• CSTD must not be used as a substitute for C-PEC when compounding
• CSTDs should be used when compounding HDs when the dosage form allows
• CSTDs must be used when administering HDs when the dosage form allows
Labeling/Packaging/Transport

- **Labeling**: HDs must be labeled as such at all times during their transport.
- **Packaging**: Compounding personnel must select and use packaging containers to maintain physical integrity, stability, and sterility during transport.
  - Packaging must protect from damage, leakage, contamination, and degradation.
- **Transport**: HDs must be transported in containers that minimize the risk of breakage/leakage.
  - Pneumatic tubes must **never** be used to transport liquid or antineoplastic HDs.

Dispensing Final Dosage Forms

- HDs not requiring further manipulation other than counting/repackaging of the final dosage form may be prepared for dispensing without further requirements for contamination except when:
  - Manufacturers recommendation state otherwise
  - Visual indicators of HD exposure exist (e.g., dust or leakage)
  - Segregate equipment used for dispensing activities for HD drugs

Compounding

- Institutions compounding HDs must be compliant with USP <795> (nonsterile) and USP <797> (sterile).
  - Use plastic-backed preparation mat on the work surface of the C-PEC; change regularly during use and following spills.
  - Disposable or clean equipment dedicated only to HD compounding.
  - Bulk containers of liquid and API HDs must be handled in C-PEC to prevent worker exposure.

Administration

- HDs must be administered safely by using protective medical devices and techniques (e.g., priming IV tubing with non-HD solution in a C-PEC).
  - Appropriate PPE to be worn when administering HDs and disposed properly thereafter.
  - CSTDs must be used for administration of antineoplastic HDs when the dosage form allows.
  - Avoid manipulating HD dosage forms (e.g., crushing tablets, opening capsules) when possible; if necessary – use appropriate PPE.

Cleaning Procedures

<table>
<thead>
<tr>
<th>Cleaning Step</th>
<th>Purpose</th>
<th>Agents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deactivation</td>
<td>Render compound inert or inactive</td>
<td>EPA-registered oxidizers (e.g., peroxide formulations, sodium hypochlorite, etc.)</td>
</tr>
<tr>
<td>Decontamination</td>
<td>Remove HD residue</td>
<td>Alcohol, water, peroxide or sodium hypochlorite or other materials validated to be effective for HD decontamination</td>
</tr>
<tr>
<td>Cleaning</td>
<td>Remove organic or inorganic material</td>
<td>Germicidal detergent</td>
</tr>
<tr>
<td>Disinfection</td>
<td>Destroy microorganisms</td>
<td>Sterile alcohol or EPA-registered disinfectant</td>
</tr>
</tbody>
</table>

Spill Control

- Train personnel about proper spill kit use.
- SOPs are required for spill prevention and clean-up procedures including use of PPE and respirators.
- Document circumstances of spill.
- Provide immediate medical evaluation to potentially exposed personnel.
  - Non-employees exposed to HD should report to designated emergency service for evaluation.
Medical Surveillance

- Institutions should develop a surveillance program for workers handling HDs
- Purpose: minimize adverse health effects in personnel potentially exposed to HDs
- Secondary prevention tool for early detection
- Program involves:
  - Assessment and documentation of symptom complaints, physical and/or laboratory findings
  - Comparison of health variables over time in populations of workers


Medical Surveillance

- Baseline assessment of worker’s health and medical history
- Estimate of workers HD exposure over time
- Monitoring of organ function at risk for toxicity from HD exposure
- Follow-up plan for acute and long-term exposure to HDs


What This Means for Pharmacy Practice

- Compliance:
  - A single published standard exists for defining requirements for HD handling
- Work Procedures:
  - Chain of custody of HDs
  - PPE
  - Cleaning methodology for HD handling areas

What This Means for Pharmacy Practice

- Facilities:
  - Updating existing buffer rooms - All HD compounding to be done in negative pressure C-SEC in externally vented C-PEC
  - Proper “de-boxing” areas for receiving HDs
- Personnel:
  - Designated person for overseeing compliance with HD handling is best suited for a trained oncology pharmacist

Conclusions

- Multiple guidelines/alert published over the course of several decades are now present in a single regulatory document
- A single standard of care will not exist for handling hazardous drugs
- Pharmacy department, infusion clinics and physician offices will be challenged to meet the physical structure requirements for engineering controls outlined in <800>

Questions?