Safe Handling of Hazardous Drugs and USP <800> in the Healthcare Industry

October 23, 2018

Presented by:
Bernard Fontaine, CIH, CSP, FAIHA
Objectives

• List the acute and chronic health effects of occupational exposure to hazardous drugs.

• Recognize the challenges associated with implementing the practice and quality standards published by the USP in Chapter <800> that address all aspects of hazardous drug handling activities in healthcare settings.

• Evaluate their current workplace to identify gaps in compliance with hazardous drug handling procedures.
## Historical Perspective on Hazardous Drugs

<table>
<thead>
<tr>
<th>Decade</th>
<th>Events</th>
</tr>
</thead>
<tbody>
<tr>
<td>1949</td>
<td>Nitrogen Mustard approved by Food &amp; Drug Administration</td>
</tr>
<tr>
<td>1970s</td>
<td>Chemotherapy agents linked to secondary leukemia &amp; cancer</td>
</tr>
<tr>
<td></td>
<td>Published data: risks of occupational chemotherapy exposure</td>
</tr>
<tr>
<td>1980s</td>
<td>Occupational Safety &amp; Health Administration Guidelines</td>
</tr>
<tr>
<td></td>
<td>Oncology Nursing Society (ONS) Guidelines</td>
</tr>
<tr>
<td></td>
<td>American Society of Hospital Pharmacists (ASHP) Guidelines</td>
</tr>
<tr>
<td>1990s</td>
<td>First published data about surface contamination</td>
</tr>
<tr>
<td>2000s</td>
<td>National Institute for Occupational Safety &amp; Health Alert</td>
</tr>
<tr>
<td>2019</td>
<td>USP General Chapter &lt;800&gt; (Official December 1, 2019)</td>
</tr>
</tbody>
</table>
NIOSH Definition of Hazardous Drugs

- Carcinogenicity
- Teratogenicity or other developmental toxicity
- Reproductive toxicity
- Organ toxicity at low doses
- Genotoxicity
- Structure and toxicity profiles of new drugs that mimic existing drugs determined
Hazardous Drug Safety Overview

• In the United States, OSHA and NIOSH identified worker exposure to HDs as a problem of increasing health concern

• Preparation, administration, manufacturing, disposal of hazardous medications may expose thousands of workers
• Table 1: Cytotoxic antineoplastic drugs

• Table 2: Non-antineoplastic meets one or more of the NIOSH criteria for a hazardous drug

• Table 3: Drugs that pose a reproductive risk to men and women who are actively trying to conceive and women who are either pregnant or breastfeeding
Hazards of Occupational Exposure

Chronic Effects

- Cancer
- Developmental or reproductive toxicity
- Genotoxicity: Changes to chromosomes 5 or 7
- Harm to organs:
  - Liver and Kidney

Acute Effects

- Nausea
- Rashes
- Hair loss
- Hearing loss
- Cardiac symptoms
- Hematopoietic effects
- Or NONE
Healthcare Workers At-Risk

About 8 million U.S. healthcare workers are potentially exposed to hazardous drugs, including:

pharmacy and nursing personnel, physicians and physician’s assistants, operating room personnel and surgical assistants, environmental services workers, workers in research labs, veterinarians, veterinary care workers, shipping and receiving
Pharmaceutical Workers At-Risk

• Workers also may be exposed included those in drug manufacture and sterile compounding of HDs

• Best practices using USP <800> Hazardous Drugs - Handling in Healthcare Settings and USP <797> Pharmaceutical Compounding
Genotoxic Biomarkers of Exposure

• Chromosomal aberrations: 17-study meta-analysis
  • CAs in exposed HCWs much higher than controls
    (Roussel, Witt, Shaw, & Connor, 2017)

• Micronuclei (MN): 24-study meta-analysis
  • Confirmed association occupational exposure and
    MN frequency (Villarini, et al., 2016)

• Sister Chromatid exchanges (SCE): 6-study review
  • Exposed workers positive for SCE
    (Suspiro & Prista, 2011)
## Hazardous Drugs - Carcinogens

<table>
<thead>
<tr>
<th>Known Carcinogens</th>
<th>Probable Carcinogens</th>
<th>Possible Carcinogens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arsenic trioxide</td>
<td>Tamoxifen</td>
<td>Azacitidine</td>
</tr>
<tr>
<td>Azothiaprime</td>
<td>Thiotepa</td>
<td>Carmustine</td>
</tr>
<tr>
<td>Busulfan</td>
<td>Treosulfan</td>
<td>Cisplatin</td>
</tr>
<tr>
<td>Chlorambucil</td>
<td>MOPP*</td>
<td>Doxorubicin</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>ECB*</td>
<td>Lomustine</td>
</tr>
<tr>
<td>Etoposide</td>
<td></td>
<td>Nitrogen Mustard</td>
</tr>
<tr>
<td>Melphalan</td>
<td></td>
<td>Procarbazine</td>
</tr>
<tr>
<td>Semustine</td>
<td></td>
<td>Teniposide</td>
</tr>
</tbody>
</table>

*Combination regimens

Hazardous Drugs - Carcinogens

• Non-melanoma skin cancer
  [1.5-fold increase, pharmacy techs]
  (Hansen & Olsen, 1994)

• Excess leukemia [OR = 1.9, nurses]
  (Blair, et al., 2001);[MOR = 2.3, nurses & pharmacists]
  (Petralia, et al., 1999)

• Overall increased occurrence of cancer
  [OR = 3.27, nurses] (Martin, 2005)

OR = Odds Ratio; MOR = Mortality Odds Ratio
## Reproductive Issues

<table>
<thead>
<tr>
<th>Adverse Effect</th>
<th>Magnitude</th>
</tr>
</thead>
<tbody>
<tr>
<td>Longer time to conceive</td>
<td>$\text{OR} = 0.8$</td>
</tr>
<tr>
<td>Infertility</td>
<td>$\text{OR} = 1.42$</td>
</tr>
<tr>
<td>Spontaneous abortion</td>
<td>2 - 3.5 - fold increase</td>
</tr>
<tr>
<td>Premature labor</td>
<td>$\text{OR} = 2.98$</td>
</tr>
<tr>
<td>Pre-term birth</td>
<td>$\text{OR} = 5.56$</td>
</tr>
<tr>
<td>Learning disabilities in offspring</td>
<td>$\text{OR} = 2.56$</td>
</tr>
</tbody>
</table>

$\text{OR} =$ Odds Ratio

Fransman, 2007; Lawson, 2012; Martin, 2005
Reproductive Issues

• Personnel of reproductive capability must confirm in writing that they understand the risks of handling HDs (USP, 2017, p. 8)

• Professional organizations and NIOSH propose employees who are pregnant or actively attempting to conceive be given the option of alternative work that doesn’t involve HD handling
Routes of Exposure

• Dermal absorption:
  • Direct drug contact
  • Contact with contaminated surfaces
  • Contact contaminated body fluids

• Injection:
  • Sharps
  • Breakage

• Ingestion via surface contaminated:
  • Food, gum
  • Hand-to-mouth transfer
  • Inhalation:
    • Aerosols
    • Vapors

• Inhalation of drug aerosol – dust or droplets
Exposure: Drug Preparation

- Unpacking / stocking hazardous drugs
- Handling drug vials
- Breaking open ampoules
- Reconstituting / mixing drugs
- Expelling air or HDs from syringes
- Transferring drugs between containers
- Needle sticks
- Crushing oral forms
- Contacting HD residue present on PPE or other garments
Exposure: Drug Administration

- Injected drugs
  - Aerosols from purging air
  - Needle-sticks
- Intravenous infusions
  - Spiking drug-filled bag
  - Leaks from prime tubing
  - Loose connections
  - Needle-sticks
  - “Un-spiking”
- Intracavitary drugs
  - Poor fitting connections
  - Splashing
- Oral drugs
  - Broken tablets / capsules
  - Crushing tablets / opening capsules
  - Spilling liquid forms
Exposure: Drug Disposal

- Handling contaminated materials
- Used IV equipment
- Drug residue
- Used personal protective equipment
- Collection and transport of drug waste from administration site to disposal site
- Reaching into waste containers
- Using wrong containers
- Over-full containers
Exposure: Contaminated Excretions

- Variable HD excretion: hours to days (48 hours average)
- Handling body fluids of HD patients
- Urinals / urine
- Bedpans / stool
- Emesis basins / emesis
- Sweat (?) and flushing toilets
- Linen contaminated with bodily fluids
- Cross-contamination of building surfaces
## Environmental Contamination

<table>
<thead>
<tr>
<th>Area</th>
<th>Positive Wipe Samples (N=438)</th>
<th>Most Contaminated Surfaces</th>
</tr>
</thead>
<tbody>
<tr>
<td>HD Delivery</td>
<td>8% (5/60)</td>
<td>Elevator button</td>
</tr>
<tr>
<td>HD Preparation</td>
<td>61% (87/144)</td>
<td>Pens</td>
</tr>
<tr>
<td>HD Transport</td>
<td>33% (12/36)</td>
<td>Bin for pick-up</td>
</tr>
<tr>
<td>AD Administration</td>
<td>28% (54/192)</td>
<td>IV pumps</td>
</tr>
<tr>
<td>HD Waste</td>
<td>17% (1/6)</td>
<td>Elevator button</td>
</tr>
</tbody>
</table>
NIOSH Survey Self-Reported Practices

• Failure to wear nonabsorbent gown with closed front and tight cuffs (42%)
• Intravenous tubing primed with antineoplastic drug by respondent (6%) or pharmacy (12%)
• Contaminated clothing taken home (12%)
• Spill/leak administering antineoplastic drug (12%)
• Failure to wear gloves (12%)
• Lack of hazard awareness training (4%)
Objectives of Drug Safety Plan

- Evaluate workplace to assess all health and safety hazards and risk
- Environmental wipe sampling to determine the level of workplace contamination by antineoplastic agents
- Regularly review the inventory of hazardous drugs, equipment, and work practices
- Conduct regular training with all potentially exposed workers
- Implement a program for safely handling hazardous drugs at work and review program annually
Objectives of Drug Safety Plan

• Establish procedures and provide training for handling hazardous drugs safely, cleaning up spills, and using respirators and PPE properly

• Establish work practices related to both drug manipulation techniques and to general hygiene practices - not permitting eating or drinking in areas where drugs are handled (pharmacy or clinic)

• Wash face and hands before eating, drinking, smoking or applying makeup
Objectives of Drug Safety Plan

- Develop workplace procedures for using and maintaining all equipment that functions to reduce exposure - ventilated biosafety cabinets, closed system drug-transfer devices, needleless systems, and PPE.
Medical Surveillance

- Pre-placement medical exams with a medical, family, and occupational history
- Periodic medical examinations
- Post-exposure examinations
- Exit examinations
- Exposure-health outcome linkage
- Reproductive issues
Medical Surveillance: Lab Tests

- Most valued test in a laboratory assessment is a Complete Blood Count (CBC) with differential.

- Other lab testing (liver function, blood urea nitrogen, creatinine, and urine dipstick for blood)

- Tests conducted at the discretion of the physician, as a function of the medical, family, and occupational history, or formal medical surveillance with well-defined goals
Medical Surveillance: Lab Tests

• Measure of genetic effects (i.e., chromosomal aberrations, micronuclei, or other genotoxic markers) are not recommended in routine exams
Medical Surveillance: Periodic

- Medical, reproductive, and exposure history should be updated every 1-3 years.
- Interval between exams depends on the opportunity for exposure, the duration and intensity of exposure, and (possibly) the age of the worker.
Medical Surveillance: Periodic

• Worker's health and exposure history may influence the decision of the occupational medicine physician

• Physical exam and laboratory tests follow the format outlined in the pre-placement examination
Medical Surveillance: Post Exposure

• Post-exposure evaluations are tailored to the type of short-term or acute exposure (e.g., spills or needle sticks from syringes with HDs)
• Physical exam focuses on exposed body parts, as well as other organ systems commonly affected (i.e., for a spill, the skin and mucous membranes of the affected area; for aerosolized HDs, the respiratory system)
• Treatment and lab tests follow as indicated and should be guided by emergency protocols
Recordkeeping

- Employee exposure records, including workplace monitoring, biological monitoring, and SDSs, as well as employee medical records related to HDs.

- Records regarding HD handling shall be kept, transferred, and made available for at least 30 years, and medical records shall be kept for the duration of employment plus 30 years.

- Training records should be created, and include the following information:
  - Dates, contents or summary of the training sessions;
  - Names and qualifications of persons conducting training;
  - Names and job titles of persons attending the training.
USP Standards

• Chapter <800> builds on the standards established by other compounding chapters
• <795> Pharmaceutical Compounding – Nonsterile Preparations
• <797> Pharmaceutical Compounding – Sterile Preparations
• Adds the element of containment of hazardous drugs
Elements of USP <800> Cradle to Grave

- Facilities
- PPE
- Hazard Communication
- Transport & Disposal
- Compounding
- Administration
- Cleaning
- Medical Surveillance
Facility Design

Containment Primary Engineering Control (C-PEC)

- Nonsterile
  - Containment Ventilated Enclosure (CVE)
  - Class I Biological Safety Cabinet (BSC)
- Sterile
  - Class II Biological Safety Cabinet (BSC)
  - Compounding Aseptic Containment Isolator (CACI)
Compounding Sterile and Non-Sterile HDs

• Considerations
  • Preparation mat (not required)
  • Dedicated equipment
  • Bulk containers, handle APIs and HD powder in C-PEC (crushing powders, opening capsules, weighing powders)
  • Sink and eye wash

• Avoid
  • Unauthorized access
  • Rough textures (e.g. corrugated cardboard)
  • External shipping containers
The **MUST** Standards

- Maintain HD list
- Label all HDs
- Designate individual responsible for oversight
- Designate areas for receipt, unpacking, storage, compounding
- Use engineering controls for compounding
- Provide/ use appropriate PPE
- Follow all packaging/ transport/ disposal standards
The **MUST** Standards

- Use CSTDs for administering antineoplastic HDs
- Develop policies & procedures for all aspects of HD handling
- Establish a Hazard Communication Plan
- Provide job-specific personnel training
- Decontaminate equipment/ environment
- Prevent/ manage HD spills
Governing Initiatives

• State Laws in United States
  • Washington (2011)
  • California (2013)
  • North Carolina (2014)

• Non-legislative state-level actions
  • Michigan
  • Maryland
  • New Jersey
Other Politics

• Most professional associations agree on HD standards – but not all
  • Physician’s society in US
  • Nurses’ association in UK

• Local struggles
  • Non-hospital health care facilities

• Question of enforcement
  • Accreditation in some states falls under medical board vs. pharmacy board
Be Real: Identify the Barriers

• Knowledge deficit (risks/ precautions)
• Psychosocial (worker/ peer attitudes)
• Financial (increased cost/ “cost shift”)
• Practical (storing protective equipment)
• Environmental (safety climate)
• Situational (time constraints)
Knowledge as a Barrier: Only Chemotherapy…..?

1. Antineoplastic drugs $N = 115$ (53%)
2. Non-antineoplastic drugs $N = 53$ (24%)
3. Reproductive effects $N = 49$ (23%)

*Over 1,000 commercially available drugs; 12 billion doses/yr.

Affected Healthcare Settings:

<table>
<thead>
<tr>
<th>Any hospital unit</th>
<th>Intensive care</th>
</tr>
</thead>
<tbody>
<tr>
<td>Operating room</td>
<td>Interventional radiology</td>
</tr>
<tr>
<td>Hemodialysis</td>
<td>Skilled nursing facilities</td>
</tr>
</tbody>
</table>

NIOSH, 2016

AIHA New England Local Section
Safe Handling is *NOT* Intuitive

- It’s prescriptive
- Requires different thought processes
- Most *oncology* staff are knowledgeable
- Most other staff are not
- Requires specific education and training
- Recognize risks
- Know precautions
Psychosocial Barriers

• Belief that exposure is rare
  • “I’ve been doing this for 30 years and never had a problem”
  • I’ve never had a chemo spill

• Attitudes toward PPE
  • Makes it harder to get the job done
  • Too much trouble/ time/ “waste”

• Attitudes of peers
  • Others around me don’t use PPE
  • People would think I am overly cautious
Financial Barrier: Construction

- Room with fixed walls separated from non-hazardous storage and compounding
- Vented outside the building
- Negative pressure of 0.01 to 0.03" to adjacent space
- At least 12 air changes per hour
Financial Barrier: Equipment & Safety Monitoring

- Personal Protective Equipment
  - Gloves meeting ASTM D6978
  - Gowns - polyethylene-coated polypropylene or other laminate materials
- Closed system drug-transfer devices (CSTDs)
- Environmental wipe samples
- Medical surveillance program
Practical Barriers

• Adequately trained personnel
  • “Designated person who is qualified and trained to be responsible” (USP, 2017, p. 3)

• Space for storage of drugs/ equipment
  • HD separate storage
  • CSTDs
  • PPE

• Record keeping
  • Training, competency
  • Medical surveillance
Workplace Safety Climate

• “Culture” refers to principles, norms, values, beliefs, and assumptions related to safety
• “Climate” is how culture is experienced by workers
  • Workers’ perceptions about commitment to safety (positive, neutral, or negative)
• Climate and culture affect protective behaviors
Situational Barriers

- Industry: expected work pace affects safety
- Workers cite time pressure as reason for not using PPE across occupations
  - Chemical workers
  - Factory workers using hearing protection devices
  - Healthcare workers handling HDs
- Nurse: patient ratio predicts worker safety
Speak the Right Language

• Health care organizations understand:
  • **Standards**
    • Expectation; basis for comparison, reference point against which something is evaluated
  • **Quality improvement**
    • Systematic work to make something better
    • Designed to ‘raise the bar’

National Quality Forum [NQF], 2018
Improving Hazardous Drug Safety

- Safety equipment and qualified personnel for safety
- USP standards policies & procedures
- HD safety

Structure → Process → Outcome

Time

Donabedian, 2003
Structure

- Policies and procedures for HD safety exist; compliance is expected
- Equipment and supplies for safety available
- Safe behavior is reinforced; feedback provided to workers
- Management supports safety programs
- Education and training is provided

DeJoy, 1995; 2000; Gershon, 2007; Moore, 2005
Interprofessional Team

- Pharmacy*
- Physicians/Nursing*
- Administration
- Purchasing / Products Committee
- Human Resources
- Safety Committee
- Industrial Hygiene
- Environmental Services
- Employee Health
- Quality Department*
Job-Specific Education, Training and Competency

- Classroom instruction
- Supervised practice with a preceptor
- Measurement of knowledge
- Validation of competency
Gap Analysis

- **Current state** → **Future state**
- Steps
  - Review results of baseline assessment
  - List areas of non-compliance

*Share the data*
# Readiness Survey

## 4. Responsibilities of Personnel Handling HDs

<table>
<thead>
<tr>
<th>#</th>
<th>Item</th>
<th>Present</th>
<th>Absent</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Entity designates a person to oversee compliance</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.</td>
<td>Designated person is qualified and trained</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.</td>
<td>Designated person monitors compliance, maintains reports of testing/sampling</td>
<td></td>
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</tbody>
</table>

**Additional Notes:**

https://www.readyfor800.com/download-ready-800-checklist/
## Readiness Survey

### 8. Hazard Communication Program

<table>
<thead>
<tr>
<th>#</th>
<th>Item</th>
<th>Present</th>
<th>Absent</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>a.</td>
<td>Written plan in place</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>b.</td>
<td>All HD containers are labeled with a hazard warning</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>c.</td>
<td>SDS onsite for each hazardous chemical</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>d.</td>
<td>SDSs accessible to personnel in all locations and at all times</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>e.</td>
<td>Personnel receive initial and updated information and training</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>f.</td>
<td>Personnel of reproductive capability confirm understanding of risks in writing</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

https://www.readyfor800.com/download-ready-800-checklist/
# Action Plan

<table>
<thead>
<tr>
<th>Specific Requirement</th>
<th>Action Steps</th>
<th>Target Date</th>
<th>Responsible Person</th>
<th>Resources Needed</th>
</tr>
</thead>
</table>
| 1. Designate a person to oversee USP<800> compliance | • Develop position description  
• Request applicants  
• Identify training/education needs  
• Identify education source | September 2018 | John Smith | XX Committee  
Fees: Education/training |
| 2. Personnel of reproductive capability confirm understanding of risk in writing | • Develop policy  
• Develop form  
• Develop training/education plan  
• Implement policy | December 2018 | Susan Jones | Employee Health  
XX Committee |

“If you don’t know where you are going, any road can take you there.” Lewis Carroll, *Alice in Wonderland*
Questions?