Disclosures

- Recommendation to the audience to review nationally accepted guidelines, FDA approvals, and peer reviewed studies for clarification of information presented.
“…Recommendations support ..maintaining product sterility while providing for the safety of the personnel involved in preparing and administering chemotherapy”
Hazardous Drug Compounding USP <800>

First Release
March 2014

Comment Due Date
July 31, 2014

Second Release
December 2014

Comment Due Date
May 31, 2015

Approved
February 1, 2016

Official Compliance Date
July 1, 2018

Polling Question

How compliant is your site with USP <800>? 

A. Meets or exceeds USP <800>  
B. Meets most of USP <800>  
C. Meets some of USP <800>  
D. Planning to formally address USP <800>  
E. No plans for compliance
Las Vegas – Some health systems pharmacies do not effectively protect their staff from exposure to cytotoxic agents, according to survey findings presented at the ASHP 2016 Midyear Clinical Meeting.

The survey of almost 900 facilities found that roughly two-thirds of workers handling hazardous drugs complied with U.S. Pharmacopeial (USP) Chapter <800> requirements.

Source: Pharmacy Practice News: February 7, 2017
Hospital Compliance ...36%
Educating Administration

Five pharmacy regulations health execs must keep on their radars in 2017

March 19, 2017         By Kenneth Maxik

1. USP <797> Pharmaceutical Compounding – Sterile Compounds
2. USP <800> Hazardous Drug - Handling in Healthcare Settings
3. MM.09.01.01 Antibiotic Stewardship Standard
4. 503A & 503B Compounding
5. 340B Mega-Guidance Withdrawn
What’s Inside the Final Chapter?
Road Map to Safety

- Introduction and scope
- List of Hazardous Drugs
- Types of exposure
- Responsibilities of handling HDs
- Facilities and engineering controls
- Environmental quality and control

- Personal protective equipment
- Hazard communication program
- Personnel training
- Receiving
- Labeling, packaging, transport & disposal
- Dispensing final dosage forms

- Compounding
- Administering
- Deactivating, decontaminating, cleaning, & disinfecting
- Spill Control
- Documentation and standard operating procedures (SOPs)
- Medical surveillance
Source: Massoomi, Firouzan
What is Missing?

Mutagenicity in Urine of Nurses Handling Cytostatic Drugs

Lancet 1979; June 9: 1(8128):1250-1

What is Missing?

Issues and Risks Associated with Handling Antineoplastic Drugs


Structures and processes of care in ambulatory oncology settings and nurse-reported exposure to chemotherapy

BMJ Qual Saf published online August 16, 2011

Bladder Cancer in a 39-Year-Old Female Pharmacist

JNCI 1993;85:1089-90

Association of antineoplastic drug handling with acute adverse effects in pharmacy personnel

AJHP 1993; June 9: 1(8128):1250-1

Cancer morbidity among Danish female pharmacy technicians

Scand J Work Environ Health 1994;20:22-6

Mutation Frequency in Nurses and Pharmacists Working with Cytotoxic Drugs

AUST NZ J Med 1984;14(6):831-4

Occupational Exposure to Antineoplastic Agents and Self-Reported Infertility Among Nurses and Pharmacists

Introduction & Scope

“This chapter describes practice and quality standards for handling hazardous drugs (HDs) to promote patient safety, worker safety, and environmental protection. “

- Pharmacists, pharmacy technicians, nurses, physicians, physician assistants, home healthcare workers, vets, and vet technicians
- Not listed: Manufacturers; Wholesale personnel; Researchers; Family
- **Must** incorporate into Occupational Safety Plan

# List of Hazardous Drugs

**Must have a list** (USP, TJC, NIOSH)

**Type of HD:**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Route</th>
<th>Class</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adotrastizumab</td>
<td>IV</td>
<td>Antineoplastic</td>
</tr>
<tr>
<td>Arsenic trioxide</td>
<td>IV</td>
<td>Antineoplastic</td>
</tr>
<tr>
<td>Azacitidine</td>
<td>IV/SQ</td>
<td>Antineoplastic</td>
</tr>
<tr>
<td>Bacillus Calmette-Guerin (BCG)</td>
<td>Intravesical/Intradermal</td>
<td>Vaccine</td>
</tr>
<tr>
<td>Belinostat</td>
<td>IV</td>
<td>Antineoplastic</td>
</tr>
<tr>
<td>Bendamustine</td>
<td>IV</td>
<td>Antineoplastic</td>
</tr>
<tr>
<td>Bleomycin</td>
<td>IV</td>
<td>Antineoplastic</td>
</tr>
<tr>
<td>Bortezomib</td>
<td>IV/SQ</td>
<td>Antineoplastic</td>
</tr>
<tr>
<td>Brentuximab</td>
<td>IV</td>
<td>Antineoplastic</td>
</tr>
<tr>
<td>Busulfan</td>
<td>IV</td>
<td>Antineoplastic</td>
</tr>
</tbody>
</table>

Facilities & Engineering Controls

Designated areas **must** be available for HDs:

- Receipt & unpacking
- Storage
- Non-sterile compounding
- Sterile compounding

Photos: Firouzan Massoomi, Pharm.D, FASHP
Receipt & Storage

Receipt
• HDs **must** be unpacked in a designated area
  – Neutral/Negative pressure

Storage
• **Must** be stored in manner to prevent spillage/breakage
• HDs requiring manipulation stored separately
  – Externally vented, Negative pressure,
  – 12 air changes per hour (ACPH)
Compounding

Containment Primary Engineering Controls (C-PEC)

• **Low volume exemption is no longer acceptable**

• **Biological Safety Cabinet**
  – Class II BSC types A2, B1, or **B2**

• **Containment Aseptic Compounding Isolator (CACI)**
  – USP <797> = **RABS** (Restricted Access barrier system)
  – MUST be in a negative pressure room

• **Must** follow UPS <795> for non-sterile compounding and USP <797> for sterile compounding
Compounding

Containment Secondary Engineering Controls (C-SEC)

- **C-SEC** = The Room
- Externally vented
- Physically separated
- Negative Pressure
  - 0.01 and -0.03 Inches Water Column
- Eyewash Station Available
  - Bottles **NOT** Acceptable
Containment Segregated Compounding Area (C-SCA)

- C-PEC is placed in an unclassified C-SCA with fixed walls
  - No ISO 7 or HEPA system for room
- Negative pressure 0.01 and 0.03 inches of water
- Minimum of 12 ACPH
- C-SCA (room) must be externally vented
- Sink must be placed at least 1 meter from C-PEC (hood)
  - may be either inside the C-SCA
- Only low- and medium-risk HD CSPs
  - Dating segregated compounding area is 12 hours max
Compounding

Supplemental Engineering Controls

Closed System Transfer Devices CSTDs

Pharmacy Compounding: **Should**

Nursing Administration: **Must**
<table>
<thead>
<tr>
<th>Device</th>
<th>Manufacturer</th>
<th>FDA Cleared</th>
<th>ONB</th>
<th>Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>BD Phaseal™ System</td>
<td>Becton Dickenson and Company; Carmel Pharma, Inc. (original)</td>
<td>1998</td>
<td>*</td>
<td>Containment</td>
</tr>
<tr>
<td>Spiros®</td>
<td>ICU Medical, Inc.</td>
<td>2005</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Texium™ with SmartSite™</td>
<td>Becton Dickinson and Company; CareFusion, Inc. (original)</td>
<td>2006</td>
<td></td>
<td>Air Cleaning</td>
</tr>
<tr>
<td>OnGuard® with Tevadaptor®</td>
<td>B. Braun Medical Inc. (U.S. distributor) TEVA Medical, Ltd. (manufacturer)</td>
<td>2006</td>
<td>*</td>
<td>Air Cleaning</td>
</tr>
<tr>
<td>ChemoClave®</td>
<td>ICU Medical, Inc.</td>
<td>2006</td>
<td></td>
<td>Containment &amp; Air Cleaning</td>
</tr>
<tr>
<td>ChemoLock®</td>
<td>ICU Medical, Inc.</td>
<td>2013</td>
<td>*</td>
<td>Containment &amp; Air Cleaning</td>
</tr>
<tr>
<td>ChemoSafety</td>
<td>Becton, Dickinson and Company; CareFusion, Inc. (original)</td>
<td>2013</td>
<td></td>
<td>Containment &amp; Air Cleaning</td>
</tr>
<tr>
<td>EquaShield II®</td>
<td>Equashield, LLC</td>
<td>2014</td>
<td>*</td>
<td>Containment</td>
</tr>
<tr>
<td>Halo®</td>
<td>Corvida Medical</td>
<td>2015</td>
<td>*</td>
<td>Containment</td>
</tr>
</tbody>
</table>
Polling Question

Has your site implemented a CSTD?

A. Yes, on the pharmacy side only
B. Yes, on the nursing side only
C. Yes, both pharmacy and nursing sides
D. Planning to implement prior to July 1, 2018
E. No plans for compliance
Pharmacy’s CSTD Adoption by Facility Size (in number of beds)

- CSTD implementation will continue at pace as adoption rates are projected to break 80% of health systems in the next few years.

- Projected adoptions
- CSTDs in Use

State of Pharmacy Compounding. Pharm Purch Prod. 2016; 4: S1-45
USMP/MG1/16-0084 10/16
Who Regulates the CSTDs?

- FDA for clearance and 510K process
- FDA for ONB designation as a CSTD
- NIOSH recommending body for best practices
  - CDC and OSHA
- NO Regulatory Oversight
- CSTD defined as part of 2004 NIOSH Alert

“A drug transfer device that mechanically prohibits the transfer of environmental contaminants into the system and the escape of hazardous drug or vapor outside the system”

Nothing in and Nothing Out!
CSTD Timeline

- **1998** First FDA approved CSTD
- **2004** NIOSH Defines CSTSD
- **2015** NIOSH publishes or comment NIOSH Alcohol Vapor protocol
- **2016** NIOSH creates new Vapor test with new substrates based on feedback
  - Substrates mimic hazardous drugs
  - Comment period through June 2017
- **2016** NIOSH Town Hall Meeting CSTD Testing Protocol
- **Present:** NO standardized tests for CSTDs

Proposed Surrogates for NIOSH Test

This information is distributed solely for the purpose of pre-dissemination peer review under applicable information quality guidelines. It has not been formally disseminated by the NIOSH. It does not represent and should not be construed to represent any agency determination or policy.

<table>
<thead>
<tr>
<th>Compound</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dimethyl sulfoxide</td>
</tr>
<tr>
<td>Trimethyl phosphate</td>
</tr>
<tr>
<td>Tetramethylurea</td>
</tr>
<tr>
<td>Triacetin</td>
</tr>
<tr>
<td>Propylene glycol</td>
</tr>
<tr>
<td>Tetraethylurea</td>
</tr>
<tr>
<td>Triethyl phosphate</td>
</tr>
<tr>
<td>2-Phenoxyethanol</td>
</tr>
<tr>
<td>Tripropyl phosphate</td>
</tr>
</tbody>
</table>

Source: [https://www.cdc.gov/niosh/docket/review/docket288a/pdfs/aperformancetestprotocolforclosedsystemtransferdevices.pdf](https://www.cdc.gov/niosh/docket/review/docket288a/pdfs/aperformancetestprotocolforclosedsystemtransferdevices.pdf)
Updated NIOSH Protocol

- Two positive control samples, each where one droplet of propylene glycol was placed in the chamber, produced measurable results.
- Pilot test runs were completed in accordance with the proposed protocol. Results shown below.

<table>
<thead>
<tr>
<th>Positive Control ng/sample</th>
<th>CSTD w/air filtration during draw</th>
<th>CSTD w/air filtration during draw</th>
<th>CSTD w/air cleanser during push into vial</th>
<th>CSTD w/air cleanser during push into vial</th>
</tr>
</thead>
<tbody>
<tr>
<td>3000 ng/sample</td>
<td>BDL</td>
<td>BDL</td>
<td>BDL</td>
<td>BDL</td>
</tr>
<tr>
<td>2300 ng/sample</td>
<td>BDL</td>
<td>BDL</td>
<td>BDL</td>
<td>BDL</td>
</tr>
</tbody>
</table>

BDL ‘Below Detectable Limit’
- Results show a universal protocol can used to test vented and barrier technologies
## Opening the CSTD

### Do they really contain vapors?

<table>
<thead>
<tr>
<th>Phaseal</th>
<th>Vialshield</th>
<th>Chemolock</th>
<th>Equashield</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1" alt="Phaseal" /></td>
<td><img src="image2" alt="Vialshield" /></td>
<td><img src="image3" alt="Chemolock" /></td>
<td><img src="image4" alt="Equashield" /></td>
</tr>
<tr>
<td><img src="image5" alt="Phaseal" /></td>
<td><img src="image6" alt="Vialshield" /></td>
<td><img src="image7" alt="Chemolock" /></td>
<td><img src="image8" alt="Equashield" /></td>
</tr>
<tr>
<td><img src="image9" alt="Phaseal" /></td>
<td><img src="image10" alt="Vialshield" /></td>
<td><img src="image11" alt="Chemolock" /></td>
<td><img src="image12" alt="Equashield" /></td>
</tr>
<tr>
<td><img src="image13" alt="Phaseal" /></td>
<td><img src="image14" alt="Vialshield" /></td>
<td><img src="image15" alt="Chemolock" /></td>
<td><img src="image16" alt="Equashield" /></td>
</tr>
</tbody>
</table>

### Marker: Cyclophosphamide

The images above demonstrate the process of opening the CSTD for various vialshields and chemolocks, with cyclophosphamide as the marker. Each step in the process is visually represented to ensure a clear understanding of the procedure.
## Containment Confirmed

**Cyclophosphamide Concentration ng/ft\(^2\)**

<table>
<thead>
<tr>
<th>CSTD</th>
<th>Control</th>
<th>Outside</th>
<th>Inside</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phaseal</td>
<td>ND/ND</td>
<td>ND/ND</td>
<td>652.04/720.99</td>
</tr>
<tr>
<td>Vialshield</td>
<td>ND/ND</td>
<td>ND/ND</td>
<td>ND/ND</td>
</tr>
<tr>
<td>ICU</td>
<td>ND/ND</td>
<td>ND/ND</td>
<td>&gt;2000/&gt;2000</td>
</tr>
<tr>
<td>Equishield</td>
<td>ND/ND</td>
<td>ND/ND</td>
<td>105.61/89.72</td>
</tr>
</tbody>
</table>

| Negative Control | ND/ND |
| Positive Control | >2000/>2000 |

Source: Fred Massoomi, Pharm.D.; Presented at the ASHP MCM New Orleans, LA 2015
Submitted to NIOSH by: Fred Massoomi, Pharm.D., FASHP
The way it was. Maybe still is.
Visualizing Dry Connections

Fluorescein 0.05%

Litmus with Lemon Juice

Spivey S, Jorgenson J. Contamination Comparison of Transfer Devices Intended for Handling Hazardous Drugs. Study presented at ONS Congress, April, 2007, Las Vegas, NV.
Thoughts On The NIOSH Tests

- Can we just agree that CSTDs are better than a needle and syringe?

- Once a test is decided upon where is FDA?

- How does the consumer interpret results?
  - Especially conflicting results

- Most tests published are outdated

- Strive for no human manipulation with HDs

Submitted to NIOSH by: Fred Massoomi, Pharm.D., FASHP
Considerations in CSTD Selection

Key CSTD Features

1. Containment

2. User interface

3. Device interface

4. Integration

5. Workflow

6. Repetitive strain reduction

7. Pre-bonded components

Source: Massoomi. Pharmacy Purchasing Products 2015; February S1-S12
Non-Sterile Compounding

• **Must** follow USP <795>

• C-PEC not required for final dosage
  – Counting
  – Repackaging

• C-PEC required for some manipulations
  – Cutting, crushing
  – Containment Ventilated Enclosure

Photo Courtesy of Firouzan Massoomi, Pharm.D, FASHP
Environmental Quality & Control

Recommended ‘Routinely’ = initially then every 6 months

Verify cost for testing supplies

Photo Courtesy of Firouzan Massoomi, Pharm.D, FASHP
Personal Protective Equipment

- Head covers
- Beard covers
- Eye protection for spill protection
- Face mask – limited safety
- Powered air-purifying respirator - for spills

Disposable Gowns
- Polyethylene or laminate
- Close in the back

- Don 2 pairs prior to entry
- Remove outer when leaving
- Anti-skid
Compliance with the Basics

241 nurses and 183 pharmacy practitioners who compounded hazardous drugs in the seven days prior to the survey

<table>
<thead>
<tr>
<th>Compounding Practice Assessment</th>
<th>Nursing</th>
<th>Pharmacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lack of safe handling procedures</td>
<td>20%</td>
<td>11%</td>
</tr>
<tr>
<td>Not wearing 1 pair of gloves</td>
<td>8%</td>
<td>10%</td>
</tr>
<tr>
<td>Not wearing 2 pairs of gloves</td>
<td>85%</td>
<td>47%</td>
</tr>
<tr>
<td>Not always using a CSTD</td>
<td>75%</td>
<td>53%</td>
</tr>
<tr>
<td>Not always using a BSC/CACI</td>
<td>9%</td>
<td>15%</td>
</tr>
<tr>
<td>Lack of medical surveillance</td>
<td>61%</td>
<td>45%</td>
</tr>
<tr>
<td>Reported skin contact with HD</td>
<td>11%</td>
<td>4%</td>
</tr>
</tbody>
</table>

Defect Visualizing the Concerns

Source; E. Kastango
Source; S. Eisenberg
Source; F. Massoomi
Personnel & Training

• **Must** have a designated specialist

• All personnel who handle HDs **must** be trained based on their job functions

• **Must** be assessed every 12 months

• **Must** be trained on new HDs and equipment

• **Must** document competencies
Labeling, Packaging, Transport & Disposal

• Labeling
  – Precaution clearly labeled

• Packaging
  – Protect against damage, leakage, contamination, and degradation

• Transport
  – Transport containers
  – **Must Not** transport via pneumatic tubes any liquid HDs

Photos: Firouzan Massoomi, Pharm.D, FASHP
Deactivation, Decontaminating, Cleaning & Disinfecting

Deactivation
2% Sodium Hypochlorite solution

Cleaning
Tri or Quadra-valent detergent

Decontamination
- Physical wiping of surface
- Peroxide RTU (ready-to-use)

Disinfecting
- Sterile Isopropyl Alcohol 70%
- UV-C light
Spill Control

- **Must** have proper training for spill management
- **Must** have spill kits readily available
- Spill materials disposed of as hazardous wastes
- **SOPs must** address size of spills

Photos: Firouzan Masoomi, Pharm.D, FASHP
Segregated HD Linen

Source: Uline S-12986Y

Source: F.Massoomi
Medical Surveillance

Plan should be consistent with Human Resource’s Plan

Identify folks at risk of HD exposure

Quantify handling risk

Medical Assessment on hire and routinely

Develop exit interview assessment strategy

Direct Contact with HD or Wastes

Direct Contact with Patient on HD

Indirect HD Contact or HD Patient Contact

No Contact by Position with HD or Patients on HD

No Contact Allowed: Pregnancy, Breast Feeding, Attempt at Pregnancy

Quantify handling risk

Plan should be consistent with Human Resource’s Plan

Identify folks at risk of HD exposure

Develop exit interview assessment strategy

Medical Assessment on hire and routinely

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No Contact Allowed: Pregnancy, Breast Feeding, Attempt at Pregnancy

Direct Contact with HD or Wastes

Direct Contact with Patient on HD

Indirect HD Contact or HD Patient Contact

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USP <800>’s Implications to Nursing Practices

• Section 1: Identified as at risk healthcare provider
• Section 2: Knowledge of institution’s hazardous drug list
• Section 3: Competent Personnel
• Section 5.3.1 Non-sterile Compounding
• Section 7: Personal Protective Equipment (PPE)
• Section 14: Hazardous Drug Administration
• Section 16: Spill Control
• Section 17: Documentation and Standard Operating Procedures
• Section 18: Medical Surveillance
USP <800> Section 14 Administering

- Administered safely using protective devices & techniques
  - Needless systems
  - Closed System Transfer Devices
  - Spiking or priming IV tubing with non-HD solution
  - Crushing tablets in a plastic pouch
- Appropriate PPE must be donned and doffed
  - Disposed as hazardous waste
- Proper waste disposal of equipment used to administer Hazardous Drugs
- CSTD MUST be used for Hazardous Drug administration
  - CAUTION on when systems need to open for administration
- ANY manipulation or sterile and non-sterile formulation require PPE
  - Includes crushing
Exposure of family members to antineoplastic drugs via excreta of treated cancer patients

Journal of Oncology Pharmacy Practice

- 42 Urine samples were collected from the three patients and their family members; ALL samples were positive for cyclophosphamide and 5-FU

- Cyclophosphamide detected levels of **0.03–7.34 ng/cm²** in 8 of the 12 wipe samples from the homes

- Measured contamination of the home setting and exposure of family members
Hazardous Drug Consideration

Monster Robots on the US market

Micro-Robot on the US market
Surveying Bodies for Hazardous Drug Handling

- State Boards of Pharmacy
- FDA: Food and Drug Administration
- CMS: Centers for Medicare/Medicaid Services
- OSHA: Occupational Safety & Health Administration
- TJC: The Joint Commission
- DNV Healthcare
- HFAP: AOA’s Healthcare Facilities Accreditation Program
- ACHC: Accreditation Commission for Healthcare
- AAASC/FASA: Ambulatory Surgical Centers
Medication Compounding Providers

First customer certified in February 2017.