Unpacking USP 800: 
The Hierarchy of Controls Still Rule

Potomac AIHA Technical Meeting
March 19, 2020
Presenter Background

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USP Drug Compounding Chapters

• USP has three General Chapters controlling the compounding of pharmaceutical preparations
  – Chapter 795, *Pharmaceutical Compounding-Nonsterile Preparations*
  – Chapter 797, *Pharmaceutical Compounding-Sterile Preparations*
  – Chapter 800, *Hazardous Drugs-Handling in Healthcare Settings*

• Original goal was to have all 3 aligned and official (effective) by Dec. 1, 2019 – This did not happen!

• USP 795/797 currently under revision
  – Appeals to the June 1, 2019 revisions to both chapters have been reviewed and the decision rendered to return both chapters to their respective committees for additional work
  – Official versions are dated 2014 and 2008, respectively
  – These versions remain in effect
USP 800 Implementation Status

• USP 800 was developed and finalized in 2016

• Chapter became official December 1, 2019, however, it is only informational at this time

• Regardless, it can be enforceable by FDA and State Boards of Pharmacy
  – No information that FDA is enforcing at present time
  – Unable to confirm enforcement status on MD/VA Boards of Pharmacy websites
  – Unofficial inquiries have revealed that several Boards from East Coast, Midwest and Southwest are enforcing Chapter requirements

• **USP Chapters are considered minimum standards**
USP 800 - Handling Hazardous Drugs

• Scope includes all stages of HD handling within healthcare settings
  – much broader than compounding/manipulation/dispensing and administration;
    • also covers receipt; storage; transport; patient care; cleaning; spill control; waste disposal
  – not cover suppliers or home setting

• HDs defined by NIOSH List
  – current list published 2016; proposed 2018 update
  – categories include carcinogens, teratogens, reproductive toxins, genotoxins, high potent toxins
USP 800 - Handling Hazardous Drugs

• Requires application of hierarchy of controls

• Facility Design and Engineering Control Requirements
  – Containment Primary Engineering Controls (C-PEC)
  – Containment Secondary Engineering Control (C-SEC)
    • Cleanroom Suite consisting of positive pressure ante-room with negative pressure buffer room; C-PEC is located in buffer room
  – Containment Segregated Compounding Area (C-SCA)
    • C-PEC in segregated area, but not in C-SEC; not allowed for higher risk HDs

• Cleaning
  – 3 or 4-step process – deactivation; decontamination; cleaning; disinfection (for sterile preparations)
USP 800 Required PPE for Handling Hazardous Drugs

• Dependent on role and degree of HD handling
• Compounding and administering HDs presents greatest opportunity for PPE use
  – Also cleaning, spill control and waste disposal
• HD PPE Ensemble
  – Gloves
  – Gown
  – Hair covers
  – Shoe covers
  – Eye protection
  – Face mask (sterile)
  – Respiratory protection (scenario dependent)
USP 800 Required PPE for Handling Hazardous Drugs

- **Gown requirements**
  - Disposable; laminate material; **HD permeation resistance**; no open front; long-sleeved with elastic or knit cuffs
  - **Does not have to be sterile even for sterile compounding**
- **Double gowning/gloving needed for sterile compounding**
- **Changed per manufacturer’s permeation data**
  - In absence of data, change every 2-3 hours or immediately if contacted by HD
- **Currently no recognized permeation test method for gowns**
  - Chemo gloves tested per ASTM D6978
  - Manufacturers are modifying ASTM test to apply for gowns
- **Opportunities for shoe covers and protective sleeves**

*Base selection on OSHA-required PPE hazard risk assessment*
USP 797 – Sterile Drug Compounding

• Classifies compounded sterile preparations (CSP) into microbial risk levels

• CSPs classified as low, medium or high risk

• Related requirements for facilities, personnel, finished preparations and environmental/personnel monitoring

• Requirements different between non-hazardous and hazardous drugs
USP 797 – Sterile Drug Compounding

• Facility Design and Engineering Control Requirements
  – Cleanroom Suite
    • consists of positive pressure ante-room with:
      – negative pressure buffer room for HDs
      – positive pressure buffer room for NHDs
    • handle low, medium or high risk CSPs
    • handled in a Primary Engineering Control (PEC)
      – Nonhazardous – PEC = non-containment device
      – HD – PEC = containment device
  – Segregated Compounding Area containing PEC
    • only handle low risk CSPs; no HDs
  – Ambient Air - intended only for emergency and/or immediate administration
USP 797 Required PPE for Sterile Compounding

- Dependent on whether Non-Haz or HD compounding
- Sterile PPE Ensemble
  - Sterile gloves
  - Gown (Does not have to be sterile)
  - Hair covers
  - Shoe covers
  - Eye protection
  - Face mask
  - Sterile sleeves optional
  - Double gowning/gloving for HDs
USP 795 – Nonsterile Drug Compounding

• Classifies compounded nonsterile preparations into three categories
  – Simple, Moderate or Complex

• Compounding environment suitable for intended purpose
  – Designated area; adequate space
  – Follow USP 800 for HDs

• Personnel engaged in compounding maintain good hand hygiene; wear clean clothing appropriate to type of compounding for protection of personnel and prevention of drug contamination.
  – e.g., hair nets, lab coats, gowns, gloves, face masks, aprons, etc.
  – Follow USP 800 for HDs
DuPont Offerings for Drug Compounding and Hazardous Drugs

- Hazardous Drug Permeation Test Data

<table>
<thead>
<tr>
<th>Hazard Name</th>
<th>Tyvek* 600</th>
<th>Tyvek* 800</th>
<th>Tychem* 2000</th>
<th>Tychem* 6000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carmustine (3.3 mg/ml, 10% Ethanol)</td>
<td>imm.</td>
<td>&gt;240</td>
<td>&gt;240*</td>
<td>&gt;240</td>
</tr>
<tr>
<td>Cyclophosphamide (20 mg/ml)</td>
<td>&gt;240</td>
<td>&gt;240</td>
<td>&gt;240</td>
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</tr>
<tr>
<td>Doxorubicin HCl (2 mg/ml)</td>
<td>&gt;240</td>
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<tr>
<td>Etoposide (20 mg/ml, 33.2% (v/v) Ethanol)</td>
<td>&gt;240</td>
<td>&gt;240</td>
<td>&gt;240</td>
<td></td>
</tr>
<tr>
<td>Fluorouracil, 5- (50 mg/ml)</td>
<td>imm.</td>
<td>&gt;240</td>
<td>&gt;240</td>
<td></td>
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<tr>
<td>Paclitaxel (6 mg/ml, 49.7% (v/v) Ethanol)</td>
<td>&gt;240</td>
<td>&gt;240</td>
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<tr>
<td>Thiotepa (10 mg/ml)</td>
<td>imm.</td>
<td>&gt;240</td>
<td>&gt;240*</td>
<td>&gt;240*</td>
</tr>
</tbody>
</table>

*Under the conditions of the test, an actual breakthrough time of ≤60 minutes
For further permeation test details please refer to the footnote at the end of the document

Permeation claims footnote:
The fabric permeation data was generated for Du Pont by independent testing laboratories using ASTM F739, EN369, EN 374-3, EN ISO 6529 (method A and B) or ASTM D6978 test methods. Normalized breakthrough time (the time at which the permeation rate is equal to 0.1 \( \mu \text{g/cm}^2/\text{min} \)) is reported in minutes. All liquid chemicals have been tested between approximately 20°C and 27°C unless otherwise stated. A different temperature may have significant influence on the breakthrough time; permeation rates typically increase with temperature.
DuPont Offerings for Drug Compounding and Hazardous Drugs

Tyvek® 600 Coverall

Tyvek® 800 Coverall

Tychem® 2000 Apron

Tychem® 2000 Sleeves

Tychem® 6000 Apron

Tychem® 6000 Sleeves
In Summary

• USP 800, USP 797 and USP 795 are a package of interrelated safety standards associated with compounding pharmaceutical preparations.

• USP 800 establishes “cradle to grave” control and protection guidelines for safe handling of hazardous drugs in healthcare settings.

• Enforcement of USP 800 requirements rests in the authority of FDA and State Boards of Pharmacy.

• Application of hierarchy of controls is focus of worker protections:
  – Heavy dependence on Primary and Secondary Engineering Controls.

• PPE is “Last Line of Defense”:
  – Selection of gloves and garments should be based on manufacturer’s permeation data.
? Questions ?

? Comments ?