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

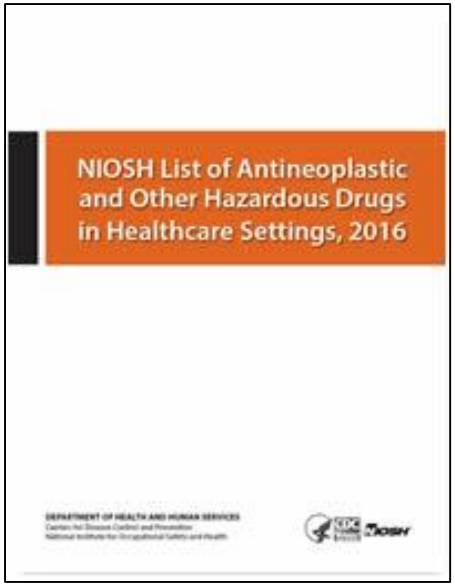
- USP has three General Chapters controlling the compounding of pharmaceutical preparations
  - Chapter 795, *Pharmaceutical Compounding-Nonsterile Preparations*
  - Chapter 797, *Pharmaceutical Compounding-Sterile Preparations*
  - Chapter 800, *Hazardous Drugs-Handling in Healthcare Settings*
- Original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

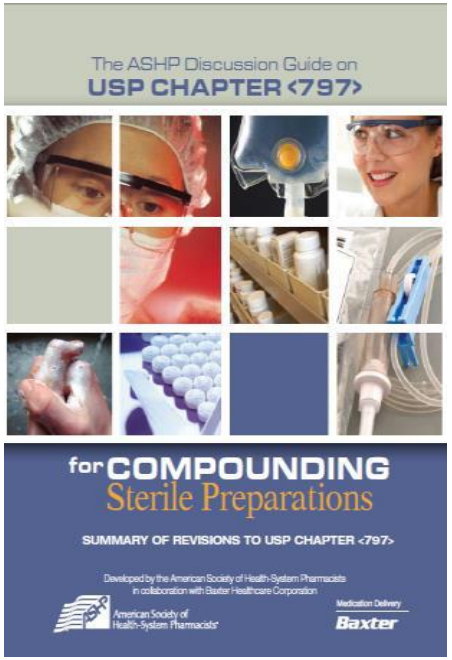
USP 800 Required PPE for Handling Hazardous Drugs

- 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



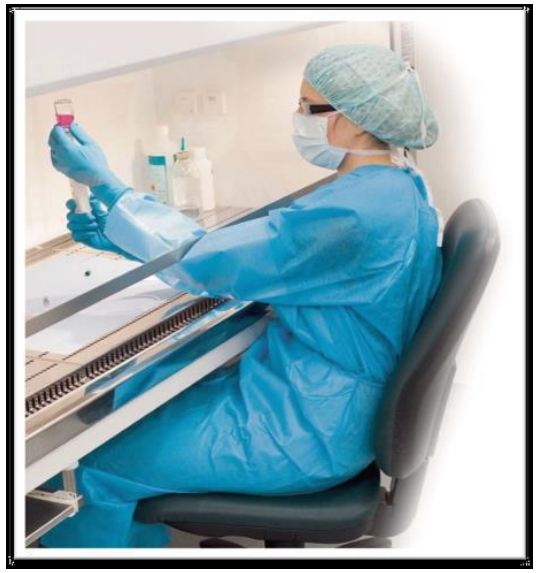
USP 797 – Sterile Drug Compounding

- 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

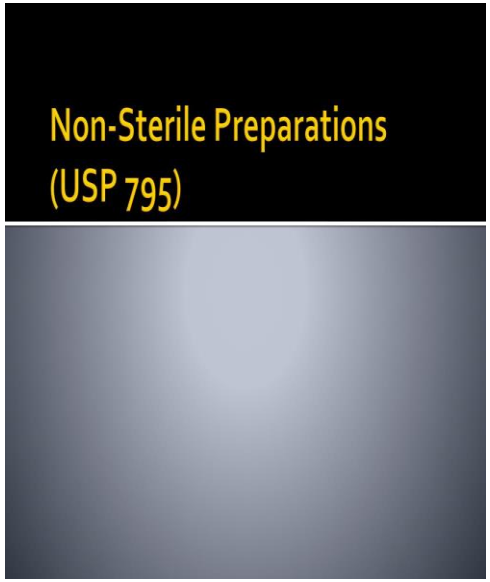
USP 797 Required PPE for Sterile Compounding

- 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

Hazard Name	Tyvek® 600	Tyvek® 800	Tychem® 2000	Tychem® 6000
Carmustine (3.3 mg/ml, 10% Ethanol)	imm.	>240	>240*	>240
Cyclophosphamide (20 mg/ml)	>240	>240	>240	
Doxorubicin HCl (2 mg/ml)	>240	>240	>240	
Etoposide (20 mg/ml, 33.2% (v/v) Ethanol)	>240	>240	>240	
Fluorouracil, 5- (50 mg/ml)	imm.	>240	>240	
Paclitaxel (6 mg/ml, 49.7% (v/v) Ethanol)	>240	>240	>240	
Thiotepa (10 mg/ml)	imm.	>240	>240*	>240*

*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 DuPont 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 µg/cm2/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

Tychem® 2000 Apron

Tychem® 6000 Apron

Tyvek® 800 Coverall

Tychem® 2000 Sleeves

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 ?