ashp Pharmacy, Practice & Policy

USP <800>: Strategies for Compliance

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Disclosures

The program chair and presenters for this continuing education activity have reported no relevant financial relationships, except:

Eric Kastango: Employee, Clinical IQ, LLC

Patricia C. Kienle:
- Employee and stockholder of Cardinal Health
- Member, Expert Compounding Committee, USP (she is an elected member of the USP Compounding Expert Committee, but is not speaking as a USP representative)

Self-Assessment Questions

- What is the key strategy to protect personnel from hazardous drug contamination?
- What does USP <797> require concerning HDs?
- How should you determine what HDs you use?
- What two types of facilities does proposed USP <800> allow for compounding of HDs?
- What agents are appropriate for decontaminating and deactivating HDs?

Learning Objectives

- Identify the key hazardous drug containment strategies in USP <800>
- List the facility requirements for receipt, storage, compounding, transport, and administration of hazardous drug required by USP <800>
- Describe the cleaning steps required to decontaminate hazardous drug areas
- Compare the requirements in USP <800> to OSHA, NIOSH, ASHP, and ONS standards and guidelines
- Develop an Action Plan to comply with USP <800> prior to the time it is enforceable

Agenda

- Patricia Kienle
  - Overview of <800>
  - How <800> compares to other documents
  - Determining your list of hazardous drugs
  - Containment strategies
  - Facility requirements
- Eric Kastango
  - Facility examples – what works and what doesn't
  - Decontamination, deactivation, and cleaning
- Action Steps to take
- Questions and Answers

Your Action Plan

- Template action plan is available as a handout on ASHP Summer Meeting site
- Complete it as we discuss the areas this morning

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Overview of Proposed USP <800> Hazardous Drugs – Handling in Healthcare Settings

Proposed USP <800>

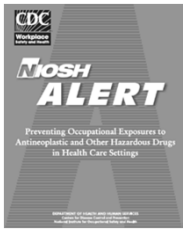
- To promote patient safety, worker safety, and environmental protection when handling hazardous drugs (HDs)
- Addresses: receipt, storage, compounding, dispensing, administration, disposal
- Applies to all healthcare personnel who handle HDs
- Applies to all entities that store, prepare, transport, or administer HDs

When did guidance about HDs first appear in the literature?

A 1985
B 1995
C 2005
D 2015

<800> Existing References

- OSHA standards
- NIOSH Alert
- ASHP Guidelines on Handling Hazardous Drugs
- ONS publications



<797> HD Requirements

- HDs prepared only under conditions that protect the healthcare worker
- Education and training
- Limited access
- Storage separate from non-hazardous drugs
- BSC or CACI
- Physically separate negative pressure room
- Use of CSTD if not in negative pressure

Proposed USP <800>

- First version – March 2014
  - Public comments received through July 2014
- Second version – December 2014
  - Public comments received through May 2015

Consistent with Other Documents

- OSHA Hazard Communication Standard
  - NIOSH – hazardous to personnel
  - EPA – hazardous to the environment
- NIOSH Alert and HD list
- ASHP Guidelines
- ONS Safe Handling of Hazardous Drugs

Defining Hazardous Drugs

Definition of Hazardous Drugs

- Drugs considered hazardous include one or more of the following characteristics
  - Carcinogenicity
  - Teratogenicity or other developmental toxicity
  - Reproductive toxicity
  - Organ toxicity at low doses
  - Genotoxicity
  - New drugs that mimic toxicity of existing drugs

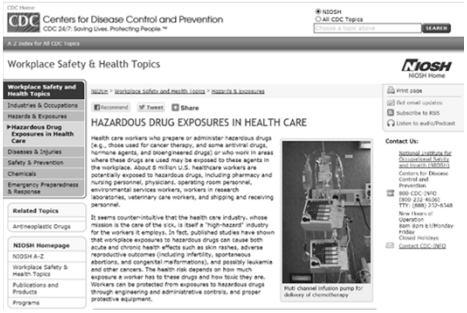
What organization compiles and updates the list of HDs?

A ASHP
B FDA
C NIOSH
D EPA

Antineoplastic and Other HDs

- NIOSH 2014 list
- Three types of HDs
  - Antineoplastic
  - Non-antineoplastic
  - Reproductive hazards only
- www.cdc.gov/niosh/docs/2014-138/pdfs/2014-138.pdf

Show Me the Science



www.cdc.gov/niosh/topics/hazdrug/

How Do You Handle HDs?

- Review the 2014 NIOSH list and determine the drugs and dosage forms your organization handles
- Proposed <800> allows two approaches
  - Treat all HDs the same
  - Perform an assessment of risk AND
    - Treat all API and all antineoplastics that require manipulation with all strategies listed in <800>
    - Develop alternative containment strategies and work practices for selected dosage forms of other non-antineoplastics and reproductive hazards only

What is the key strategy that minimizes HD contamination?

A Containment
B Education and training
C Use of isolators
D Closed system drug-transfer devices

Containment Strategies for Hazardous Drugs

Containment Strategies

- Education and training
- Personal Protective Equipment (PPE)
- Engineering Controls
- Deactivation and decontamination

Education and Training

- OSHA
- USP <795>
- USP <797>
- USP <800>
- State regulations
- Didactic
- Overseen by expert
- Monitoring

Policies and Procedures

- Requirements in regulations
- Best practices
- Manufacturers' information
- Periodic review
- Clear

How do you know if you are using the correct PPE?

A. It's what the OR uses
B. It's our GPO contract items
C. Labeled "chemo" gloves & gowns
D. I have no idea

PPE

- <797> defines PPE for sterile compounding
- Hazardous drug manipulation requires
  - Chemotherapy gloves tested to ASTM 6978
  - Impermeable gowns
  - Double booties

ENGINEERING CONTROLS

What type of PEC do you use?

A. Biological safety cabinet (BSC)
B. Compounding Isolator (CACI)
C. Something else
D. We don't use a PEC

Where is your C-PEC?

A. Positive pressure cleanroom
B. Negative pressure cleanroom
C. Normal pressure room
D. Segregated Compounding Area

Engineering Controls

- Containment Primary Engineering Control
  - Containment Ventilated Enclosure (Nonsterile)
  - Biological Safety Cabinet
  - Compounding Aseptic Containment Isolator
- Containment Secondary Engineering Control
  - The room in which your C-PEC resides
- Supplemental Engineering Control
  - Closed system drug-transfer device (CSTD)

C-PECs

- For nonsterile compounding
  - Containment ventilated enclosure (CVE) – "powder hood"
  - Externally vented or redundant HEPA filters in series
- For sterile compounding
  - Biological safety cabinet (BSC)
  - Compounding aseptic containment isolator (CACI)
  - Must be externally vented

C-SECs

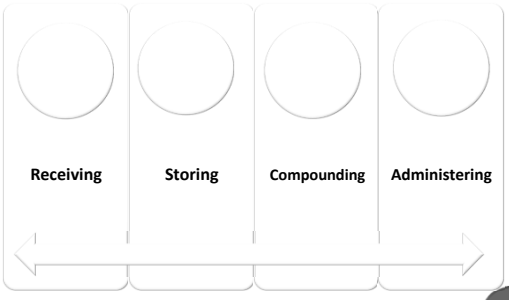
- Restricted access room (with walls)
- Externally vented
- Negative pressure
- Appropriate air changes per hour
  - Storage and/or C-SCA – 12 ACPH
  - Cleanroom – 30 ACPH

Different from USP <797>

- <797> allows C-PEC in positive pressure room
- <800> does not allow this
- When <800> becomes official, <797> will also change to NOT allow this
- Why?

CHANGE FROM <797>

Scope of <800>



Supplemental Engineering Controls

- Closed system drug-transfer device
- Mechanically prohibits the transfer of environmental contaminants into the system and the escape of HD or vapor concentrations outside the system

Photo courtesy of BD

Your Action Plan


USP <800>: Action Plan for Compliance

HD List	
PPE	Gloves Gowns Other
Nonsterile HD Compounding	
Cleanroom Suite	
Containment Segregated Compounding Area	
CSTDs	
Cleaning Procedure	Solutions Equipment
Effectiveness Testing	

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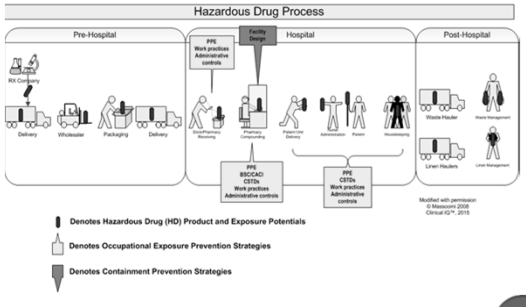
Facility Design:
What Works and What Doesn't

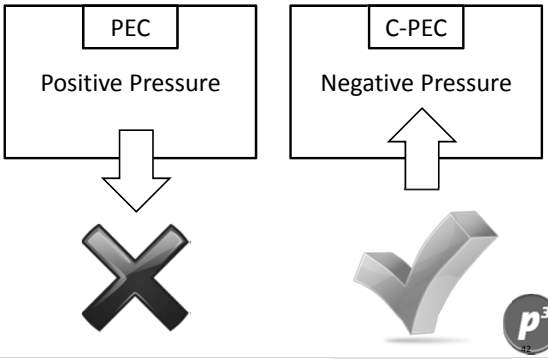
Negative-pressure rooms protect the employee in the room

A True
B False

Facility Design Strategies



Containment



Engineering Controls

Containment primary engineering control (C-PEC):

- A ventilated device designed and operated to minimize worker and environmental exposures to HDs by controlling emissions of airborne contaminants through the following:
  - The full or partial enclosure of a potential contaminant source
  - The use of airflow capture velocities to trap and remove airborne contaminants near their point of generation
  - The use of air pressure relationships that define the direction of airflow into the cabinet
  - The use of HEPA filtration on all potentially contaminated exhaust streams
- LAFW or CAI are NOT ACCEPTABLE FOR HD COMPOUNDING
- Examples of C-PECs include Class I, II, or III BSCs, CACIs, and CVE (e.g., powder hood).
- C-PECs used for nonsterile compounding do not need to have ISO Class 5 air quality, whereas C-PECs used for sterile compounding must have ISO Class 5 air quality

Engineering Controls

- **Containment secondary engineering control (C-SEC):** The C-SEC is the room in which the C-PEC is placed. It incorporates specific design and operational parameters required to contain the potential hazard within the compounding room.
- **Containment segregated compounding area (C-SCA):** A type of C-SEC with nominal requirements for airflow and room pressurization as they pertain to HD compounding.
- **Containment ventilated enclosure (CVE):** A full or partial enclosure that uses ventilation principles to capture, contain, and remove airborne contaminants through HEPA filtration and prevent their release into the work environment.

Can negative pressure rooms be too negative?

A Yes

B No

Facility Design Elements

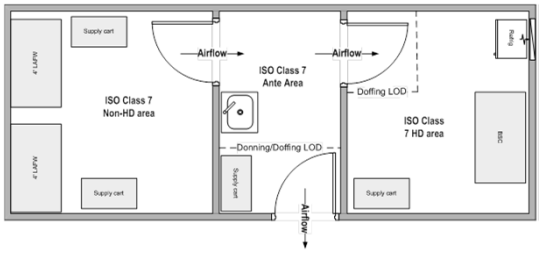
Facility Design Element	Non-sterile	Sterile
Negative Pressure	0.01" w.c. Not more than 0.03" w.c.	0.01" w.c. Not more than 0.03" w.c.
C-PEC	CVE (Powder Hood), BSC or CACI	BSC or CACI (ISO Class 5 devices)
ISO Classified Ante Area	N/A	No-*LR w/12 hr BUD Yes (ISO 7 or 8[T])
Ante Air changes per hours	N/A	At least 20 – ISO Class 8[T] At least 30 – ISO Class 7
ISO Classified Buffer Area	No	No-*LR w/12 hr BUD Yes (ISO Class 7 buffer)
Buffer Air changes per hour	12	12 for non-ISO At least 30 for ISO Class 7

* Low Risk Limited to 12 hour BUD
T: not ideal

Donning and Doffing PPE

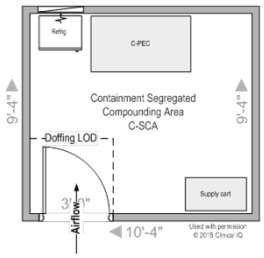
- Donning – Do on
- Doffing – Do off
- Double shoe covers
- Establish a doffing Line of Demarcation in HD room
- Remove outer most pair shoe covers prior to leaving room
- Be aware, be methodical, go slow
  - Great resource → CDC Ebola PPE Donning and Doffing Procedures

Optimal Facility Design

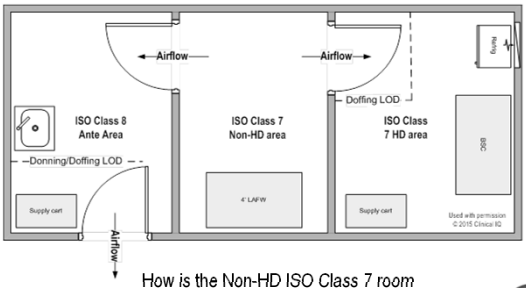


Acceptable Facility Design

- Limitations:
  - Non-sterile or Sterile Low-risk level CSPs
  - Maximum Sterile BUD: 12 hours
  - C-PEC:
    - BSC or CACI for Sterile HD or
    - Powder Hood for Non-Sterile HD

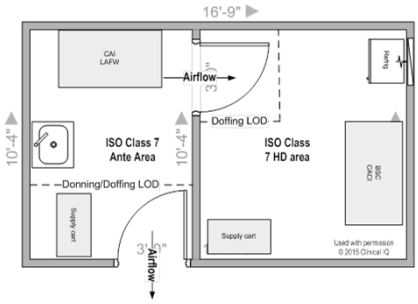


Sub-Optimal Facility Design



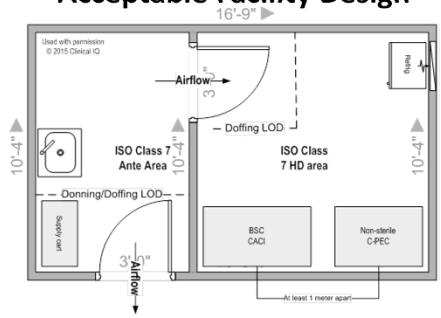
How is the Non-HD ISO Class 7 room protected from contamination?

Acceptable Facility Design



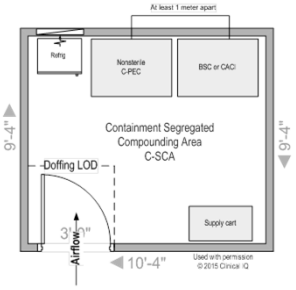
- Maximum BUD with CAI
- 12 hour BUD limitation with LAFW

Acceptable Facility Design



- No sterile compounding when particle-generating activity is performed in room

Acceptable Facility Designs



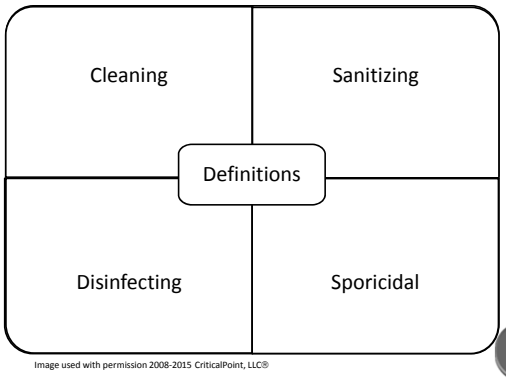
- No sterile compounding when particle-generating activity is performed in room
- BUD limited for BSC to 12 hr (Max BUD for SCA? CACI? ISO Class 7?)

Facility Design Questions

- Can I compound both sterile HD and non-HD in the same room?
  - Yes, however a separate room for sterile and nonsterile compounding is recommended
- Can I compound both sterile HD and non-HD in the same C-PEC?
  - NO, once HD used, the C-PEC is contaminated
- Can I use the same C-PEC for both sterile HD and nonsterile HD compounding?
  - YES, but must thoroughly clean hood between batches

Cleaning: Decontamination and Deactivation, Cleaning, and Disinfecting

Definitions



What do the terms "bactericidal" and "sporicidal" mean?

- EPA
  - classifies the active ingredient—that is, the ingredient that works to kill or reduce the microorganisms—as a pesticide and requires it to undergo safety and effectiveness testing prior to marketing, and the active ingredient to be identified on the label.
- Bactericidal describes a substance(s) or product that kills bacteria, generally in/on foods, inanimate surfaces, or hands.
- A "sterilizer" is an antimicrobial pesticide that destroys or eliminates all forms of microbial life in the inanimate environment, including bacterial spores. The term "sporicide" is deemed to be synonymous with "sterilizer".

Which of the following agents is NOT acceptable agent to use in the C-PEC for Sterile Compounding?

A Germicidal detergent and sterile water
B Peroxide
C Non-sterile isopropyl alcohol
D Sodium hypochlorite

Deactivation/Decontamination

- Chemical deactivation of HD residue is preferred, but no single process has been found to deactivate all currently available HDs.
- Studies have examined oxidizing agents such as potassium permanganate, peracetic acid, hydrogen peroxide, and sodium hypochlorite; vaporized hydrogen peroxide and detergents; and high- and low-pH solutions, all with varying results.

Deactivation/Decontamination

- Some potential deactivators have produced byproducts that are as hazardous as the original drug. Other deactivators have respiratory effects or result in caustic damage to surfaces.
- Note that sodium hypochlorite is corrosive to stainless steel surfaces if left untreated; therefore, sodium hypochlorite must be neutralized with sodium thiosulfate or followed by use of a germicidal detergent.

Effectiveness Testing

- Growing number of assays are available from vendors
- Surface wipe sampling now possible and should be done to document effectiveness of HD decontamination procedure
- Caveat Emptor – do your homework and understand how to sample properly

Summary Table-proposed USP GC 800

Cleaning Step	Purpose	Agents
Deactivation	Render compound inert or inactive	As listed in the HD labeling or if no specific information available, sodium hypochlorite, peracetic acid or other Environmental Protection Agency (EPA)- registered oxidizers
Decontamination	Remove inactivated residue	Sterile alcohol, sterile water, peroxide, or sodium hypochlorite (other chlorine-based products?)
Cleaning	Remove organic and inorganic material	Germicidal detergent and sterile water
Disinfection	Destroy microorganisms	Sterile alcohol or other EPA-registered disinfectant appropriate for use

What cleaning supplies do you recommend using?

- Cleaning & disinfecting agents
- Mop(s) and, if necessary, bucket(s)
- Non-shedding, non-linting wipes
  - Pre-saturated and dry
  - Polyester knit fabrics
  - Nylon fabrics
- Isolator cleaning tools
- Equipment should be dedicated!!

Which cleaning convention should be used for a sterile compounding area?

A Dirtiest to cleanest
B Cleanest to dirtiest
C Doesn't matter

What cleaning supplies do you recommend using?

Traditional buckets & mops

- Cellulose mop heads must be changed daily and rinsed thoroughly between uses (cellulose is breeding ground for microorganisms)
- No wooden handles
- Present storage issues:
  - Mops must be hung vertically to air dry
  - Bucket must be inverted (prevent standing water)
- Mop for ceiling and walls can be used for floors if it will be disposed after 1 use; if reusable: must have a mop for ceilings/walls and a separate mop for floors

What cleaning supplies do you recommend using?

- Alternatives
  - Bucket-less systems
  - Flat swivel type mops make cleaning flat surfaces such as the back surface of hoods easier
  - Disposable non-shedding mop covers can be changed frequently
  - Steam cleaners
    - Effectiveness reported at 99.9%

What are the rules for applying disinfectants?

- Perform cleaning in areas that are sufficiently ventilated to prevent accumulation of hazardous airborne drug particles, vapors and decontamination agents.
- Disinfectant dwell time is critical to work.
- Follow manufacturer's direction for solution preparation or purchased pre-mixed solutions.

What are the rules when cleaning?

- Always clean cleanest to dirtiest and top to bottom
- Use unidirectional wipes rather than circular motions
  - Slightly overlapping
  - Replace wipes or rewet mop often
- If using mop with bucket, change solution often or use two bucket system
- Be aware of the impact of all activities, including cleaning, on the cleanroom environment
  - Cleaning generates particles and compounding must not occur while cleaning

Self-Assessment Question 1

- What is the key strategy to protect personnel from contamination with hazardous drugs?

Answer: Containment

Self-Assessment Question 2

- What does USP <797> require concerning hazardous drugs?

- **Answer**:
- Prepared only under conditions that protect the worker
- Education and training
- Separate storage
- Prepared in cleanroom
- Use of CSTD if outside of negative room

Self-Assessment Question 3

- How should you determine which HDs you use?

Answer: The 2014 NIOSH list of hazardous drugs

Self-Assessment Question 4

- What two types of facilities does the proposed USP <800> allow for compounding HDs?

Answer: Either a Cleanroom or Containment Segregated Compounding Area that are under negative-pressure

Self-Assessment Question 5

- What agents are appropriate for decontaminating and deactivating HDs?

Answer: Oxidizer that is approved for use with hazardous drugs

Your Action Plan


USP <800>: Action Plan for Compliance

HD List	www.ashp.org/usp/asp/2014/08/pdfs/2014-08.pdf
PPE	Gloves Gowns Other
Nonsterile HD Compounding	
Cleanroom Suite	
Containment Segregated Compounding Area	
CSTDs	
Cleaning Procedure	Solutions Equipment
Effectiveness Testing	

Key Takeaways

- Act on your Action Plan
- Review the 2014 NIOSH list
- Design and submit facility changes if necessary
- Update your training and monitoring
- Review your PPE
- Update your policies and procedures
- Update your cleaning procedures