Summary of the Proposed USP <797> Chapter
Comment Period ends 11/30/2018

Presented by

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The proposed revision to USP <797> is open for comment. The comment period for this revision ends on November 30, 2018. Final document published June 1, 2019. Official on December 1, 2019

Proposed USP <797> July 2018 distinguishes two categories of CSPs, Cat 1 & Cat 2. There is no formal definition of Category 1 and 2, only requirements for the two categories.

- Category (1) classification allows for compounding outside of a clean room. Beyond Use Dating (BUD) is limited to 12 hour non-refrigerated / 24 hour refrigerated.

- Category (2) classification requires compounding to occur within an ISO Class 7 clean room or the usage of an Isolator (new definition under proposed <797>). Category (2) classification allows for a longer BUD of 6 day non-refrigerated / 12 day refrigerated.
Introduction

This presentation breaks down the Proposed USP <797> document into 7 distinct segments for easier understanding and reference.

- Segment 1 - Buildings and Facilities
- Segment 2 - Primary Engineering Controls (PEC)
- Segment 3 - Beyond Use Dating (BUD)
- Segment 4 - Personnel
- Segment 5 - Air and Surface Quality Standards
- Segment 6 - Cleaning and Decontamination
- Segment 7 - Omissions
Segment 1- Buildings and Facilities

Buildings and Facilities
Segment 1- Buildings and Facilities

- The PEC must be located in an SEC, which may be either a cleanroom suite (buffer room with ante-room) or an SCA.

- Cleanroom suite is an ISO-classified ante-room separated from the surrounding unclassified areas by fixed walls and doors. ISO classifications are ISO 7 and ISO 8.
Segment 1- Buildings and Facilities

- **Cleanroom - ISO 7**
  - Controls must minimize the flow of lower-quality air into the more controlled areas.
  - Air supply introduced through HEPA filters in ceiling of the buffer and ante-rooms.
  - Returns must be low on the wall unless a visual smoke study demonstrates dilution of particles and sweeping out of particles from the entire room.
  - The classified rooms **must be** equipped with a pressure-differential monitoring system.
  - The ante-room **must have** a line of demarcation separating clean from the dirty side.
  - The temperature and humidity **must be** monitored in the cleanroom suite each day.
  - Seals and sweeps **should not** be installed at doors between buffer and ante-rooms.
  - Access doors **should be** hands-free.
  - Tacky surfaces **must not** be used in ISO- classified areas.
  - ***New Free-standing humidifiers/dehumidifiers and air conditioners **must not** be used.***
Segment 1- Buildings and Facilities

- **Segregated Compounding Area (SCA)**
  - PEC may be located within an unclassified area, without an ante-room or buffer room.
  - Only Category 1 CSPs can be compounded in an SCA.
  - SCA must be located away from: Unsealed windows; Doors that connect to outdoors
  - Traffic flow: must not be located adjacent to environmental control challenges (e.g., restrooms, warehouses, or food preparation areas) and a visible perimeter must establish the boundaries of the SCA.
Segment 1- Buildings and Facilities

- **Monitoring and Sampling**
  - Nonviable airborne monitoring
    - Category (1) and (2) - every 6 months
  - Temperature and Humidity
    - Monitoring devices must be verified for accuracy every 12 months.
    - Temperature and humidity must be monitored in cleanroom suite daily.
Pressure Differentials

- Cleanroom suite, a minimum differential positive pressure of 0.02-inch water column is required between each ISO classified area (e.g., between the buffer room and ante-room)
- The pressure differential between the ante-room and the unclassified area must not be less than 0.02-inch water column.
- No pressure differential is required between the SCA and the surrounding area.
Segment 1- Buildings and Facilities

***New in Proposed 797

Water source - Cleanroom

- Sinks should enable hands-free use with a closed system
- In a cleanroom suite, sink may be placed either inside or outside of the ante-room.
- The buffer room must not contain sink(s), eyewash(es), shower(s), or floor drain(s).
- The ante-room must not contain floor drain(s).
- If installed, sprinkler systems should be recessed and covered, must be easily cleanable.

Water Source - SCA

- Sink must be accessible but located at least 1 meter away from the PEC.
- The sink must not be located inside the perimeter of the SCA.
Segment 1- Buildings and Facilities

***New in Proposed 797

- **Soap**
  - Non-refillable container to minimize the risk of extrinsic contamination.
Primary Engineering Controls (PEC)
Segment 2 Primary Engineering Controls (PEC)

- **Primary Engineering Control (PEC)**
  - Must be certified to ISO Class 5 or better conditions during dynamic operating conditions
  - Must be designed to prevent contamination during compounding of CSPs.
  - Unidirectional airflow must be maintained in the PEC.
  - HEPA-filtered air must be supplied at a velocity sufficient to sweep particles away from critical sites and maintain unidirectional airflow during operations.
Different Types of PEC’s

- **Isolator** - provides isolation from the surrounding area and maintains ISO Class 5 air quality during dynamic operating conditions. A CAI or CACI is not an Isolator. An isolator comprises of four elements (see ISO 14644-7).

- **Restricted Access Barrier System (RABS)** - New Term replaces CAI/CACI. A RABS is an enclosure that provides HEPA-filtered ISO Class 5 unidirectional air. It allows for the ingress and/or egress of materials through defined openings that have been designed and validated to preclude the transfer of contamination, and that generally are not to be opened during compounding operations.

- **Class II Biological Safety Cabinet (BSC)** - A Class II BSC is a ventilated cabinet with an open front and inward and downward unidirectional HEPA-filtered air.

- **LAFW** - An open front airflow system that provides an ISO Class 5 or better environment for sterile compounding. The LAFW provides unidirectional airflow.

- **If a robotic enclosure is used as the PEC, a dynamic smoke visualization test must be performed initially and every 6 months. No indication of type of SEC required**
Segment 2 Primary Engineering Controls (PEC)

- **Environmental Placement of the primary engineering control (PEC)**
  - Category (1) - Placement within a classified area is not required
  - Category (2) - Placement within a classified area is required
Segment 2 Primary Engineering Controls (PEC)

Minimum Requirements for Placement of PEC for Compounding Non-HD CSP

- **Category (1)**
  - LAFW - Unclassified SCA
  - IVLFZ - NA
  - BSC - Unclassified SCA
  - RABS - Unclassified SCA
  - Isolator - Unclassified SCA

- **Category (2)**
  - LAFW - ISO Class 7 positive pressure buffer room with ISO Class 8 positive pressure ante-room
  - IVLFZ - ISO Class 7 positive pressure buffer room with ISO Class 8 positive pressure ante-room
  - BSC - ISO Class 7 positive pressure buffer room with ISO Class 8 positive pressure ante-room
  - RABS - ISO Class 7 positive pressure buffer room with ISO Class 8 positive pressure ante-room
  - Isolator - Environment 8 positive pressure room
Segment 3 - Beyond Use Dating (BUD)

Beyond Use Dating (BUD)
Segment 3 - Beyond Use Dating (BUD)

- **Category (1) CSP’s**
  - Beyond Use Dating (BUD): ≤12 hours room temperature and/or ≤24 hours refrigerated
Segment 3 - Beyond Use Dating (BUD)

- **Category (2) CSPs - Preparation Characteristics**
  - Aseptically prepared CSPs
    - Room Temp (20c - 25c)
      - Sterility Test Passed: NO (1 day) / YES (4 days)
    - Refrigerated Temp (2c - 8c)
      - Sterility Test Passed: NO (4 days) / YES (9 days)
    - Freeze Temp (-25c - -10c)
      - Sterility Test Passed: NO (45 days) / YES (45 days)
Segment 3 - Beyond Use Dating (BUD)

- **Category (2) CSPs - Preparation Characteristics**
  - Terminally Sterilized CSP
    - Room Temp (20c - 25c)
      - Sterility Test Passed: NO (14 day) / YES (30 days)
    - Refrigerated Temp (2c - 8c)
      - Sterility Test Passed: NO (28 days) / YES (60 days)
    - Freeze Temp (-25c - -10c)
      - Sterility Test Passed: NO (45 days) / YES (90 days)
Segment 4 - Personnel

Personnel
Segment 4 - Personnel

- **Category (1) and (2) Personnel Qualifications - Every 6 Months:**
  - Visual observation of hand hygiene and garbing
  - Gloved fingertip and thumb sampling
  - Media fill testing
  - Requalification
Compounding personnel must successfully complete gloved fingertip and thumb sampling every 6 months after completing the media-fill test.

- Successful completion of initial gloved fingertip and thumb sampling is defined as zero colony-forming units (cfu).
- Successful completion of subsequent gloved fingertip and thumb sampling after media-fill testing is defined as ≤3 cfu.
Segment 4 - Personnel

**Garbing Requirements**

- The order of garbing must be determined by the facility and documented in the facility’s SOP.
- Donning and doffing garb must not occur in the ante-room or the SCA at the same time.
- All compounding personnel must be visually observed every 6 months.
**Segment 4 - Personnel**

***New in Proposed 797***

The minimum garbing requirements for preparing CSPs include:

- Non-cotton, low-lint garment with sleeves fit snugly around the wrists and neck
- Low-lint, disposable covers for shoes
- Low-lint, disposable covers for head that cover the ears and forehead
- Face mask
- Low-lint, disposable covers for all facial hair
- Sterile gloves
- Garb must be discarded upon exiting the compounding area
Segment 4 - Personnel

***New in Proposed 797

- If using a restricted-access barrier system (RABS), such as a CAI or CACI, disposable gloves (e.g., cotton, either nonsterile or sterile) must be worn inside gauntlet gloves.
Segment 4 - Personnel

**Individuals must:**

- **New** - Remove personal outer garments.
- Remove all cosmetics because they shed flakes and particles.
- Remove all hand, wrist, and other exposed jewelry including piercings.
- Not wear ear buds or headphones.
- Not bring electronic devices that are not necessary for compounding or other required tasks into the compounding area.
- Keep nails clean and neatly trimmed to minimize particle shedding and avoid glove punctures. Nail polish, artificial nails, and extenders must not be worn.
- Additional restrictions on items may be necessary based on the risk of contaminating the environment and the CSP.
Segment 5 - Air and Surface Quality Standards

Air and Surface Quality Standards
Segment 5 - Air and Surface Quality Standards

- CSPs must be prepared in an ISO Class 5 or better PEC. If compounding only Category 1 CSPs, the PEC may be placed in an unclassified SCA.
Segment 5 - Air and Surface Quality Standards

- **ACPH Requirements for Non-HD Sterile Compounding Areas Unclassified SCA**
  No requirement:
  - ISO Class 7 room(s) ≥ 30 ACPH - At least 15 ACPH of the total air change rate from room
  - ISO Class 8 room(s) ≥ 20 - No allowance for ACPH from PEC
Microbiological Air and Surface Monitor

- Viable air sampling
  - ***New - Sampling device, test at least 1 cubic meter or 1000 liters of air each location sampled.
  - The times and locations of sampling should be carefully selected based on their relationship to the activities performed in the area.

- ***New - Surface sampling all classified areas must be conducted at least monthly.
  - The interior of the PEC and the equipment contained in it
  - Staging or work area(s) near the PEC
  - Frequently touched surfaces
  - Pass-through chamber(s) (new)

- Sampling must be at the end of the compounding activities or shift, before cleaned & disinfected.
Segment 6 - Cleaning and Decontamination

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Cleaning and Decontamination

- Surfaces must be cleaned prior to being disinfected unless an Environmental Protection Agency (EPA) registered one-step disinfectant cleaner is used.
- Cleaning and disinfecting surfaces must occur at the minimum frequencies specified.
- If compounding is not performed daily, cleaning and disinfecting must be completed before initiating compounding in the SCA.
Frequency for Cleaning and Disinfecting Surfaces and Applying Sporicidals in Classified Areas and within the Perimeter of the SCA Site PEC(s) and Equipment inside the PEC(s).

- **Cleaning** -
  - The horizontal work surface at the beginning and end of each shift, after spills, and when surface contamination is known or suspected.
  - The ceiling, walls, bars and any equipment inside the PEC on each day.

- **Disinfect** all interior surfaces of the PEC at the beginning and end of each shift, after spills, and when surface contamination is known or suspected.
  - Disinfect the horizontal work surface at least every 30 minutes while compounding
  - If compounding takes 30 minutes compounding must not be disrupted and the work surface of the PEC must be disinfected immediately after compounding.
## Segment 6 - Cleaning and Decontamination

<table>
<thead>
<tr>
<th>Frequency</th>
<th>Cleaning</th>
<th>Disinfecting</th>
<th>Apply Sporicidal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surfaces of sink(s)</td>
<td>Daily</td>
<td>Daily</td>
<td>Monthly</td>
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<tr>
<td>Pass-through(s)</td>
<td>Daily</td>
<td>Daily</td>
<td>Monthly</td>
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<tr>
<td>Work surface(s)</td>
<td>Daily</td>
<td>Daily</td>
<td>Monthly</td>
</tr>
<tr>
<td>outside the PEC</td>
<td>Daily</td>
<td>Daily</td>
<td>Monthly</td>
</tr>
<tr>
<td>Floor(s)</td>
<td>Daily</td>
<td>Daily</td>
<td>Monthly</td>
</tr>
<tr>
<td>Wall(s), door(s), and door frame(s)</td>
<td>Monthly</td>
<td>Monthly</td>
<td>Monthly</td>
</tr>
<tr>
<td>Ceiling(s)</td>
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<tr>
<td>Storage shelving and storage bins</td>
<td>Monthly</td>
<td>Monthly</td>
<td>Monthly</td>
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</tbody>
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Note: Apply Sporicidal - Monthly
Segment 7 - Omissions

***New in Proposed 797

Omissions
Segment 7 - Omissions

***New in Proposed 797

- **Omissions**
  - Robotic enclosure no indication of type of SEC required
  - Minimum Requirements for Placement of Robotic enclosure
  - ISO Class 8 room(s) ≥ 20 - No allowance for ACPH from PEC