

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

Presented by



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Introduction

- ▶ 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.

Segment 1- Buildings and Facilities

▶ 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.

Segment 2 - Primary Engineering Controls (PEC)

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▶ 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.

Segment 2 Primary Engineering Controls (PEC)

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)

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- ▶ **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

Segment 4 - Personnel

- ▶ 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

Segment 5 - Air and Surface Quality Standards

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

Segment 6 - Cleaning and Decontamination

Frequency for Cleaning and Disinfecting Surfaces and Applying Sporocidals 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

<u>Frequency</u>	<u>Cleaning</u>	<u>Disinfecting</u>	<u>Apply Sporicidal</u>
▶ Surfaces of sink(s)	Daily	Daily	Monthly
▶ Pass-through(s)	Daily	Daily	Monthly
▶ Work surface(s) outside the PEC	Daily	Daily	Monthly
▶ Floor(s)	Daily	Daily	Monthly
▶ Wall(s), door(s), and door frame(s)	Monthly	Monthly	Monthly
▶ Ceiling(s)	Monthly	Monthly	Monthly
▶ Storage shelving and storage bins	Monthly	Monthly	Monthly

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