

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

Presented by



Containment Technologies Group, Inc.

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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):  $\leq 12$  hours room temperature and/or  $\leq 24$  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  $\leq 3$  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)  $\geq 30$  ACPH- At least 15 ACPH of the total air change rate from room
  - ▶ ISO Class 8 room(s)  $\geq 20$  - 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

# Cleaning and Decontamination



# Segment 6 - Cleaning and Decontamination

## 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)  $\geq 20$  - No allowance for ACPH from PEC