USP 797 Standards and Guidelines for Pharmaceutical Compounding – Sterile Preparations

Sterile compounding procedures require clean facilities, specific training for operators, air quality evaluations, and a sound knowledge of sterilization and stability principles. USP 797 provides guidelines, procedures and compliance requirements for compounding sterile preparations.

The following USP 797 Q&A helps answer your questions.

What Is USP 797?

USP 797 refers to chapter 797 "Pharmaceutical Compounding – Sterile Preparations," in the USP National Formulary. It is the first set of enforceable sterile compounding standards issued by the United States Pharmacopeia (USP). USP 797 describes the guidelines, procedures and compliance requirements for compounding sterile preparations and sets the standards that apply to all settings in which sterile preparations are compounded.

To Who Do USP 797 Standards Apply?

The standards in this chapter are intended to apply to all persons who prepare compounded sterile preparations (CSPs) and all places where CSPs are prepared (e.g., hospitals and other healthcare institutions, patient treatment clinics, pharmacies, physicians' practice facilities, and other locations and facilities in which CSPs are prepared, stored, and transported). USP 797 requirements affect all disciplines involved in sterile compounding, including physicians, nurses, pharmacists, and pharmacy technicians.

How Do I Comply With USP 797 Standards And Requirements?

Products manufactured as an aseptic parenteral have the greatest risk of contamination and must be manufactured in an area tolerating only the lowest level of risk. Therefore, the greatest level of control over manufacturing must be proven. To comply with USP 797 requirements, first determine the risk level of the compounding done in your facility, then perform a practice gap analysis of your compounding activities, and finally develop an action plan for USP 797 compliance. Your compliance action plan may include simple procedures (e.g., improved gowning, gloving, and hand washing procedures) and monitoring the air quality of your compounding room regularly for viable and non-viable particulates.

What Is The USP 797 Compliance Standard For Non-viable Particulates?

In critical areas, such as Class 100 or ISO 5 (the area in immediate proximity of exposed sterilized containers/closures and filling/closing operations), the particle per cubic meter must be no more than 3520 particles/m^3 in a size of 0.5 micrometers or larger when counted at representative locations normally not more than 1 foot away from the work site, within the airflow, and during filling/closing operations. In critical areas such as Class 100 or ISO 5 (area in immediate proximity of exposed sterilized containers/closures and filling/closing operations), the particle per cubic meter must be no more than 3520 particles/m^3 in a size of 0.5 micrometers or larger when counted at representative locations normally not more than 1 foot away from the work site, within the airflow, and during filling/closing operations. Supporting areas, or clean room areas where the laminar flow stations are located, must meet at least Class 100,000 (ISO 8) air quality. See table below.

Clean Air Classification	ISO Designation	≥ 0.5 µm particles/m^3
100	5	3,520

1,000	6	35,200
10,000	7	352,000
100,000	8	3,520,000

The nature of your activities conducted in a supporting clean room area determines its classification. USP 797 requires that the area immediately adjacent to the aseptic processing line meet, at a minimum, Class 10,000 (ISO 7) standards under dynamic conditions. Manufacturers can also classify this area as Class 1,000 (ISO 6) or maintain the entire aseptic filling room at Class 100 (ISO 5). An area classified at a Class 100,000 (ISO 8) air cleanliness level is appropriate for the anteroom used for garbing.

What Type of Viable Sampling Do I Need To Perform For USP 797 Compliance?

You will need to take both air and surface samples. Impaction on a media plate is the preferred method for viable air sampling. Settling plates that were once suggested in earlier National Formulary guidelines are not permitted in the 2008 USP 797 revision since all sampling must now be volumetric. Surface sampling is required in all ISO classified areas on a periodic basis. Surface sampling can be accomplished using contact plates and/or swabs. In addition, "media-fill tests" must be conducted at least annually by each person authorized to make sterile compounds to verify that they can do so aseptically.

What Specific Locations Must Be Sampled To Determine Viable Particle Counts In CSP Areas?

Sampling for airborne viable particles must be conducted based on a risk assessment of your compounding activities. The sampling sites you select must include multiple locations within each ISO Class 5 environment, ISO Class 7 and 8 areas and in the segregated compounding areas at greatest risk of contamination (e.g., work areas near the ISO Class 5 environment, counters near doors, pass-through boxes). For low, medium, and high-risk level compounding, perform air sampling at locations that are prone to contamination during compounding activities and during other activities such as staging, labeling, gowning, and cleaning. Locations must include zones of air backwash turbulence within laminar airflow workbenches (LAFW) and other areas where air backwash turbulence may enter the compounding area (doorways, in and around ISO Class 5 primary engineering control and environments). Consideration must be given to the overall effect the chosen sampling method may have on the uni-directional airflow within a compounding environment. For low-risk level CSPs with 12-hour or less beyond-use date prepared in an aseptic isolator located outside of a clean room that maintains an ISO Class 5 area in its interior, perform air sampling at locations inside the ISO Class 5 environment and other areas that are in close proximity to the ISO Class 5 environment. During your sampling, in addition to documenting sample location, volume of air collected, etc. also note the time of day as related to activity in the compounding area when the sample was collected.

What Types of Media Do I Use For Viable Sampling?

A general microbiological medium such as Trypticase Soy Agar (TSA) or Soybean-Casein Digest Medium should be used to support the growth of bacteria. For fungi, Malt Extract Agar (MEA) or some other media that supports the fungal growth must be used. Media used for surface sampling must be supplemented with additives to neutralize the effects of disinfecting agents (e.g., TSA with lecithin and polysorbate 80).

How Do I Sample For Viable Particulates For USP 797 Compliance?

Air Sampling: Using an impaction sampler collect as much air as possible without drying the media. The 2008 revision bulletin requires a sampling volume of 400 to 1000 liters of air, subject to recommendations by the manufacturer of the sampling device and the volume needed to meet the limits of detection for the ISO rating of the area being tested.

Surface Sampling: Surface sampling can be accomplished using contact plates and/or swabs. When swabbing is used in sampling, the area covered should be at least 24 cm^2 but no larger than 30 cm^2.

Gloved Finger Sampling: TSA plates should be used to sample gloved fingertips after compounding CSPs immediately after exiting the ISO Class 5 environment. Glove fingertip sampling must occur outside of the ISO Class 5 environment. Do not disinfect gloves with Isopropyl alcohol immediately prior to sampling. Personnel should "touch" the agar with the fingertips of both hands in a manner to create a slight impression in the agar.

According To USP 797, What Levels of Viable Colony Counts Are Considered Elevated?

The following table lists the action levels adapted from the Pharmaceutical Compounding - Sterile Preparations <797>, that when exceeded must initiate further investigation.

ISO Class	Active Airborne (cfu*/m^3)	Glove Fingertip (cfu/contact plate)	Inanimate Surfaces** (cfu/contact plate)
5	> 1	> 3	> 3
7	> 10	not required	> 5
8	> 100	not required	> 100

* cfu = colony forming units
** Contact plate areas vary from 24 to 30 cm^2. When swabbing is used in sampling, the area covered should be at least 24 cm^2 but no larger than 30 cm^2.

Regardless of the cfu counts, corrective actions must be dictated by identifying the microorganisms recovered. If pathogenic microorganisms are found, you must be immediately remedy the situation.

What USP 797 Requirements Are Needed If Action Levels Are Exceeded?

Environmental monitoring data must be collected and trended as a means of evaluating the overall control of the compounding environment. Any colony forming unit (cfu) counts that exceeds its respective action level should prompt you to re-evaluate personnel work practices, cleaning procedures, operational procedures, and air filtration efficiency within your aseptic compounding location. If any highly pathogenic microorganisms are detected, regardless of the cfu count, you must remedy immediately with the assistance of a competent microbiologist, infection control professional, or industrial hygienist. An investigation into the source of the contamination must be conducted. Sources may include HVAC systems, damaged HEPA filters, and changes in personnel garbing or work practices. Once determined, the source of the problem must be eliminated, the affected area cleaned, and re-sampling performed.

How Can EMLab P&K Help Me With USP 797 Compliance?

EMLab P&K can help you with your scheduled environmental monitoring of the CSP areas. We offer environmental monitoring supplies and perform the analysis you need to meet USP 797 compliance requirements including identification to genus level and quantification to cfu/area or cfu/m^3. You receive online reports and emailed PDF reports of your sample data to help you chart trends in evaluating the overall control of the compounding environment. Contact us to learn how to meet the USP 797 standards and compliance requirements.

USP 797 Compliance – Quality and Accuracy

You can count on our reputation and commitment to superior quality, accuracy and service. We are dedicated to your success. When your USP 797 testing requires identification of a bacteria or fungal species, make sure your testing lab is using superior identification systems. EMLab P&K performs Biolog*, MIDI and API. Biolog alone contains over 1,900 species in the reference database — that's twice as many species than other laboratories offer through the methods they currently use. Are you providing your clients with this technology? Or are you missing out on proper identification of bacteria and fungi?

*Contact EMLab P&K for availability of the bacterial identification systems at specific lab locations.

For further information and guidelines please refer to The United States Pharmacopoeia (USP) General chapter <797> "Pharmaceutical Compounding - Sterile Preparations," and Chapter <1116> "Microbiological Evaluation of Clean Rooms and Other Controlled Environments."

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