Chapter 25

Secondary Engineering Controls

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Introduction

Regulatory standards and professional guidelines (see Chapter 2 and Appendixes) require that pharmacists evaluate their sterile compounding facilities. Standards and guidelines specify that sterile preparations should be compounded in an area separate from other pharmacy activities. The most prominent standards, USP Chapter <797> Pharmaceutical Compounding—Sterile Preparations and USP Chapter <800> Hazardous Drugs—Handling in Healthcare Settings, require that most sterile compounding be done within an ISO Class 5 primary engineering control (PEC) that is properly placed in a buffer area supported by an ante-area.[1,2] USP Chapter <797> stresses that employee training and evaluation on garbing, hand cleansing, maintaining aseptic technique in an ISO Class 5 environment, and disinfecting gloves are the most important determinants leading to compounded preparations that are free from viable microorganisms and pyrogens. However, for PECs to work properly and for personnel to maintain aseptic technique, a very clean compounding area is mandatory. In addition, USP Chapter <800> sets forth standards for handling hazardous drugs (HDs) to protect personnel, patients, and the environment from contamination with these hazardous substances. ASHP has promulgated guidelines that supplement USP Chapters <797> and <800>.[3,4]

This chapter explains the functional requirements of sterile compounding areas, how to plan new sterile compounding areas or to alter existing ones, and how to justify, purchase, validate and certify sterile compounding facilities.

Functional Requirements

Functional requirements follow USP Chapters <797> and <800> because these are the enforceable standards toward which most pharmacists strive. Ante-areas and buffer areas or cleanrooms are known collectively as *secondary engineering controls* (SECs) because they provide the controlled environments in which PECs (laminar air flow workbenches [LAFWs], biological safety cabinets [BSCs], and compounding isolators) are placed.

Air Cleanliness

To follow USP Chapter <797>, pharmacists must understand controlled environment classifications. For nearly 40 years, U.S. Federal Standard 209 (FS 209) defined air cleanliness in contamination control, but FS 209 has been retired by the U.S. General Services Administration in favor of the internationally accepted definitions for cleanrooms and clean zones promulgated by the International Organization of Standardization (ISO).[5,6] (**Table 25-1.**)

Compounded Sterile Preparation Microbial Contamination Risk Levels

For the most part, USP Chapter <797> sets standards according to microbial contamination risk levels. The appropriate risk level—low, medium, or high—is assigned according to the corresponding probability of contaminating a compounded sterile preparation (CSP) with (1) microbial contamination (e.g., microbial organisms, spores, and endotoxins); and (2) chemical and physical contamination (e.g., foreign chemicals and physical matter).[1] USP Chapter <797> applies more stringent facility requirements to high-risk level compounding as compared to low- and medium-risk compounding (**Table 25-2**).

Low-Risk Level, Nonhazardous CSPs with 12-Hour or Less Beyond-Use Date

If the PEC is a compounding aseptic isolator (CAI) that does not meet the requirements described in USP Chapter <797> or is an LAFW or a BSC that is not located within an ISO Class 7 buffer area, then only low-risk level CSPs and radiopharmaceutical CSPs pursuant to a physician's order for a specific patient may be prepared, and administration of such CSPs must commence within 12 hours of preparation or as recommended in the manufacturers' package insert, whichever is less.

Low-risk level CSPs with a 12-hour or less beyond-use date (BUD) must meet all of the following criteria[1]:

- PECs (LAFWs, BSCs, and CAIs) must be certified and maintain ISO Class 5 as described in USP Chapter <797> for exposure of critical sites and must be in a segregated compounding area (SCA) restricted to sterile compounding activities.
- The SCA cannot be in a location that has unsealed windows or doors that connect to the outdoors or high-traffic flow or that is adjacent to construction sites, warehouses, or food preparation, etc.
- Personnel must follow cleansing, garbing and other personnel procedures described in USP

Table 25-1.
ISO Classification of Particulate Matter in Room Air as Limits in Particles 0.5 Microns and Larger per Cubic Meter (Current ISO) and Cubic Feet (Former FS 209E)

Class Name		Particle Counts Per	
ISO Class	U.S. FS209E	ISO, m^3	FS209E, ft^3
3	Class 1	35.2	1
4	Class 10	352	10
5	Class 100	3,520	100
6	Class 1,000	35,200	1,000
7	Class 10,000	352,000	10,000
8	Class 100,000	3,520,000	100,000

ISO = International Organization of Standardization
Source: Adapted by USP from General Services Administration. Federal Standard 209e. Washington, DC: General Services Administration; 1992 Sep 11 and ISO 14644-1:2015 cleanrooms and associated controlled environments—part 1: classification of air cleanliness.