21 Secondary Engineering Controls

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Introduction

Regulatory standards and professional guidelines (see Chapter 1 and Appendixes) require that pharmacists evaluate their sterile compounding facilities. Standards and guidelines specify that sterile preparations be compounded in an area separate from other pharmacy activities. The most prominent standard, USP Chapter <797>, Pharmaceutical Compounding—Sterile Preparations, requires that most sterile compounding be done within an ISO Class 5 primary engineering control that is properly placed in a buffer area supported by an ante-area[1] 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 primary engineering controls to work properly (see Chapter 4) and for personnel to maintain aseptic technique, a clean compounding area is mandatory. Further, Chapter <797> sets forth standards for handling hazardous drugs to protect the compounder and the environment from contamination with toxic substances.

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

Functional Requirements

Functional requirements follow USP Chapter <797> because this is the enforceable standard toward which most pharmacists strive. Anti-areas and buffer areas or cleanrooms are known collectively as "secondary engineering controls" because they provide the controlled environments in which primary engineering controls (laminar air flow workbenches, biological safety cabinets 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,[2] but FS 209 has been retired by the U.S. General Services Administration[3] in favor of the internationally-accepted definitions for cleanrooms and clean zones promulgated by the International Organization of Standardization (ISO).[4] See Table 21-1.

CSP Microbial Contamination Risk Levels

For the most part, USP Chapter <797> sets standards according to microbial contamination risk levels. The appropriate risk level—

Table 21-1.

International Organization of Standardization (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)[2]

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	3520	100
6	Class 1000	35,200	1000
7	Class 10,000	352,000	10,000
8	Class 100,000	3,520,000	100,000

Source: Adapted by USP from the Federal Standard 209e, General Services Administration, Washington, DC 20407 (September 11, 1992) and ISO 14644-1:1999 Cleanrooms and associated controlled environments—part 1: Classification of air cleanliness.

low, medium, or high—is assigned according to the corresponding probability of contaminating a CSP with (1) microbial contamination (e.g., microbial organisms, spores, endotoxins) and (2) chemical and physical contamination (e.g., foreign chemicals, physical matter).[1] Chapter <797> applies more stringent facility requirements to high risk level compounding as compared to low- and medium-risk compounding (see Table 21-2).

Low-Risk Level CSPs with 12-Hour or Less Beyond-use Date

If the primary engineering control (PEC) is a compounding aseptic isolator (CAI) or a compounding aseptic containment isolator (CACI) that does not meet the requirements described in USP Chapter <797> or is a laminar airflow workbench (LAFW) or a biological safety cabinet (BSC) that cannot be located within an ISO Class 7 buffer area, then only low-risk level nonhazardous 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 four of the following criteria[1]:

- PECs (LAFWs, BSCs, CAIs, and CACIs), must be certified and maintain ISO Class 5 as described in USP Chapter <797> for exposure of critical sites and must be in

Table 21-2.

Secondary Engineering Control Requirements by USP Chapter <797> Risk Level*

Low Risk

- Ante-area—An ISO Class 8 (see Table 21-1) or cleaner area where personnel hand hygiene and garbing procedures, staging of components, order entry, CSP labeling, and other high-particulate-generating activities are performed.
- Buffer area—An ISO Class 7 (see Table 21-1) or cleaner area where the primary engineering control is physically located. Activities that occur in this area include the preparation and staging of components and supplies used when compounding CSPs.
- Ante-area and buffer area may be separated by a line of demarcation or by a physical barrier like a wall, door, and pass-through.
- Buffer area must have at least 30 air changes per hour (ACPH), or as little as 15 ACHP if a laminar air-flow workbench provides as much as 15 ACHP.
- HEPA-filtered air must be introduced at the ceiling and air return vents should be mounted low on the walls.
- A temperature of 20 degrees Celsius (68 degrees Fahrenheit) or cooler should be maintained by the heating, ventilation, and air conditioning system.
- Surfaces of ceilings, walls, floors, fixtures, counters, and cabinets in the buffer area must be smooth, impervious, free from cracks and crevices, nonshedding, and resistant to damage by disinfectants.

Medium Risk

Same as low-risk level.

High Risk

Same as low-risk level except that:

- ante-area must be physically separated from the buffer area by a wall, door, and pass-through.

**Source:* U.S. Pharmacopeial Convention. Chapter <797> Pharmaceutical Compounding: Sterile preparations. http://www.usp.org/USPNF/pf/general Chapter797.html. Accessed on March 3, 2008.

a segregated compounding area restricted to sterile compounding activities.

- The segregated compounding area 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 Chapter <797> prior to compounding. Sinks should not be located adjacent to an ISO Class 5 PEC.
- The USP Chapter <797> specifications in cleaning and disinfecting the sterile compounding areas, personnel training and competency evaluation of garbing, aseptic work practices and cleaning/disinfection procedures, and viable and nonviable environmental air sampling must be followed as described in Chapter <797>.

See Table 21-3 for a summary of secondary engineering controls required for each classification of compounded sterile preparation (CSP).

CAIs and CACIs must be placed in an ISO Class 7 buffer area unless they meet all of the following conditions[1]:

- The isolator must provide isolation from the room and maintain ISO Class 5 during dynamic operating conditions, including transferring ingredients, components, and devices into and out of the isolator and during preparation of CSPs.
- Particle counts sampled approximately 6 to 12 inches upstream from the critical exposure site must maintain ISO Class 5 levels during compounding operations.
- Not more than 3520 particles (0.5 microns and larger) per cubic meter can be counted during material transfer, with the particle counter probe located as near to the transfer door as possible without obstructing the transfer.

Compounding personnel must obtain documentation from the manufacturer that the CAI or CACI will meet the conditions above when located in environments where the background particle counts exceed ISO Class 8.[1]

Hazardous Drugs

USP Chapter <797> states that hazardous drugs must be prepared only under conditions that protect healthcare workers and other personnel in the preparation and storage areas.[1] This means not just the sterile compounding areas but where ever hazardous drugs are received, stored, handled, compounded or transported. Hazardous drugs must be stored separately from other inventory so as to prevent contamination and personnel exposure. Many hazardous drugs have sufficient vapor pressures to allow volatilization at room temperature; thus storage should be within a containment area such as a negative pressure room. The storage area should have sufficient general exhaust ventilation, at least 12 air changes per hour (ACPH), to dilute and remove any airborne contaminants.[1] The USP's expert Sterile Compounding Committee (SCC)[5] states that the negative pressure storage conditions protect personnel outside the compounding area from hazardous drug exposure at a minimal risk of ingress of airborne contamination. Further, there may be no need for an additional negative pressure room for hazardous drug storage. That is, smaller volume hazardous compounding facilities can simply store the hazardous drugs in the chemotherapy compounding buffer room, which should already meet the minimum criteria for hazardous drug storage.[5]

All hazardous drugs must be prepared in a biological safety cabinet (BSC) or a compounding aseptic containment isolator (CACI). The ISO Class 5 BSC or CACI must be placed in an ISO Class 7 buffer area that is physically separated (i.e., a different room from other preparation buffer areas) and optimally has not less than 0.01-inch water column negative pressure to adjacent positive pressure ISO Class 7 or better ante-area, thus providing inward airflow to contain any airborne drug. A pressure indicator must be installed that can be readily monitored for correct room pressurization. The BSC and CACI should be 100% vented to the outside air through HEPA filtration.[1]

There is no requirement for a separate anteroom for the negative pressure ISO Class 7 buffer room. The same ante-room can be used for both non hazardous and hazardous buffer rooms. The difference in cost of making the ante-room ISO class 7 instead of ISO class 8 is minimal. For example, using a relatively large ante-room size of 10 foot x 10 foot with an 8-foot ceiling (total volume of 800 cubic feet) the difference to go from 20 ACPH (266 cubic feet per minute [CFM]) as appropriate for an ISO class 8 room to a minimum of 30

Table 21-3.

Summary of Secondary Engineering Controls Required for Each Classification of Compounded Sterile Preparation (CSP)

Type of CSP per USP Chapter <797>	ISO Class Requirement		Segregated Compounding Area
	Ante-Area	Buffer Area	
Low risk	Class 8 positive pressure to main pharmacy and either physically separated from buffer area by a wall or by displacement air flow	Class 7 positive pressure to ante-area	
Medium risk	Class 8 positive pressure to main pharmacy and either physically separated from buffer area by a wall or by displacement air flow	Class 7 positive pressure to ante-area	
High risk	Class 8 positive pressure to main pharmacy and physically separated from buffer area by a wall	Class 7 positive pressure to ante-area	
Low risk with less than 12-hour BUD*	Not required	Not required	Demarked area or room restricted to preparing low-risk CSPs with 12-hour or less BUD
Immediate use with one hour or less BUD	Not required	Not required	Not required
Hazardous drug	Separate Class 7 positive pressure to buffer room	Separate Class 7 negative pressure buffer room	
Radiopharmaceutical		Class 8 or better for Tc99m or Mo99	Low-risk with 12-hour or less BUD radiopharmaceutical with line of demarcation
Allergen extract appropriately preserved for intradermal or subcutaneous injection	Not required	Not required	Not required
Proprietary bag and vial system	Not required	Not required	Not required

*BUD, beyond-use date.

ACPH (399 CFM) for an ISO class 7 space only requires 133CFM. In either case, all of the supply air can be delivered through one HEPA filter.[5]

If a CACI that meets the USP Chapter <797> requirements above, is used outside of an ISO Class 7 buffer area, the separate compounding area must maintain a minimum negative pressure of 0.01-inch water column and have a minimum of 12 ACPHs.[1] In a health care institution that prepares a low volume of hazardous drugs, the use of two tiers of containment (i.e., a closed-system transfer device [e.g., PhaSeal®] with a BSC or a CACI that is located in a non-negative pressure

room) is acceptable.[1] The decision as to what is "low volume" is left to the sterile compounding institution.

Radiopharmaceuticals

USP Chapter <797> specifies that radiopharmaceuticals must be compounded using appropriately shielded vials and syringes in a properly functioning and certified ISO Class 5 PEC located in an ISO Class 8 or cleaner air environment to permit compliance with special handling, shielding, and negative air flow requirements. Storage and transport of properly shielded vials of radiopharmaceutical CSPs may occur in a limited access ambient environment without a specific ISO class designation.[1]

Technetium-99m/molybdenum-99 generator systems must be stored and eluted under conditions recommended by manufacturers and applicable state and federal regulations. Such generator systems must be eluted in an ISO Class 8 or cleaner air environment to permit special handling, shielding, and air flow requirements. Radiopharmaceuticals prepared as Low-Risk Level CSPs with 12-hour or less beyond-use dating must be prepared in a segregated compounding area. A line of demarcation defining the segregated compounding area must be established. Materials and garb exposed in a patient care and treatment area must not cross a line of demarcation into the segregated compounding area.[1]

See Chapter 8 on Radiopharmaceuticals as CSPs.

Allergen Extracts

The USP's expert Sterile Compounding Committee (SCC) added the new section titled "Allergenic Extracts as CSPs" based on evidence that 27,000 immunotherapy injections, which were not prepared in ISO classified controlled environments by personnel gloved and garbed according to standards specified in the chapter for low- and medium-risk level CSPs, were not associated with any infections.[6] USP Chapter <797> specifies suitably-preserved allergen extracts as CSPs are not subject to the environmental, and beyond-use date storage requirements for all CSP microbial contamination risk levels but *only* when all of eleven criteria listed in Chapter <797> are met. Non-preserved allergen extract CSPs must comply with the appropriate Chapter <797> CSP risk level requirements, regardless of whether compounded by pharmacist, physician or other trained personnel. Allergen extract compounders must follow specified hand cleansing, garbing and aseptic techniques and labeling standards.[1] Therefore, suitable space is required for compounding and storage of equipment, supplies and finished preparations.

Chapter <797> mandates no standards for allergen extract compounding facilities. However, the Joint Commission™ does have facility standards for medication preparation (see other regulatory requirements below). See also Chapter 9 on Allergen Extracts as CSPs.

Immediate-use Provision

USP Chapter <797> restricts the immediate-use provision to those situations where there is a need for emergency or immediate patient administration of a CSP, e.g., cardiopulmonary resuscitation, emergency room treatment, preparation of diagnostic agents, or critical therapy where the imposition of low-risk operating conditions subjects the patient to additional risk due to delays in therapy. When CSPs meet all six immediate use conditions, Chapter <797> mandates no standards for compounding facilities. However, the Joint Commission™ does have facility standards for medication preparation (see other regulatory requirements below).

Proprietary Bag and Vial Systems

USP Chapter <797> allows an exemption to risk level facility standards for proprietary bag and vial systems. The sterility storage and stability beyond-use times for attached and activated (where activated is defined as allowing contact of the previously separate diluent and drug contents) container pairs of drug products for intravascular administration (e.g., ADD-Vantage®, Mini Bag Plus®, AddAVial®, Add-Ease®, Duplex®) is to be applied as indicated by the manufacturer.[1] However, the Joint Commission™ does have facility standards for medication preparation (see other regulatory requirements below).

Other Regulatory Requirements for Facilities

In addition to USP Chapter <797> standards for air cleanliness, two regulatory organizations have requirements for sterile preparation

facilities. The Food and Drug Administration (FDA) requires pharmacists to use good manufacturing practices,[7] including a facility of suitable size, construction, and location to facilitate cleaning, maintenance, and proper operations. Second, the Joint Commission on Accreditation of Healthcare Organizations (Joint Commission™) standards for hospitals simply state[8]:

> Whenever medications are prepared, staff uses appropriate techniques to avoid contamination during medication preparation, which include but are not limited to:
>
> - Using clean or sterile techniques
> - Maintaining clean, uncluttered, and functionally separate areas for product preparation to minimize the possibility of contamination
> - Using a laminar-airflow hood or other Class 100 environment while preparing any intravenous (IV) admixture in the pharmacy, any sterile product made from non-sterile ingredients, or any sterile product that will not be used within 24 hours
> - Visually inspecting the integrity of the medications

Dispensing adheres to law, regulation, licensure, and practice standards, including record keeping.[9] In preventing pediatric medication errors, the Joint Commission™ sets forth risk reduction strategies, including, at a minimum, pediatric medications should be stored and prepared in areas separate from those where adult medications are stored and prepared.[10]

Buffer Area and Ante-area

Heating, Ventilation, and Air Conditioning (HVAC)

Under USP Chapter <797>, sterile compounding areas must provide a comfortable and well-lighted working environment, which typically includes a temperature of 20 °C. or cooler, to maintain comfortable conditions for compounding personnel to perform flawlessly when attired in the required aseptic compounding garb. Buffer areas are designed to maintain at least ISO Class 7 conditions for 0.5-micron particles under dynamic conditions and ISO Class 8 conditions for 0.5-micron and larger particles under dynamic conditions for the ante-areas. The buffer area must be segregated from surrounding, unclassified spaces to reduce the risk of contaminants being blown, dragged, or otherwise introduced into the filtered unidirectional airflow environment, and this segregation must be continuously monitored with a pressure gauge. For sterile compounding areas providing a physical separation between buffer and ante areas through the use of walls, doors, and pass-throughs, a minimum differential positive pressure of 0.02- to 0.05-inch water column is required. For buffer areas not physically separated from the ante-areas, the principle of displacement airflow must be employed. This concept utilizes a low pressure differential, high airflow principle. Using displacement airflow typically requires an air velocity of 40 feet per minute or more from the buffer area across the line of demarcation into the ante-area.[1] The displacement concept must not be used for high-risk compounding.

PECs must be placed within a buffer area in such a manner as to avoid conditions that could adversely affect their operation. For example, strong air currents from opened doors, personnel traffic, or air streams from the HVAC systems can disrupt the unidirectional airflow in open-faced LAFWs.[1]

HEPA filters should be located above the ceiling the air flowing in a unidirectional manner into the buffer area and ante-area. The HEPA filter in the ceiling air supply should be placed to avoid creating air currents inside the laminar-airflow workbench. Pre-filters on the heating, ventilation, and air conditioning (HVAC) air blower should be changeable from outside the ante-area/buffer area.[11]

Air return grills should be located low on the walls. Low wall mounted air returns are somewhat more difficult to install but are much more efficient in removal of airborne particulate contamination. Low wall returns should be well distributed throughout the room and ideally have adjustable louvers or dampers.[12]

Surface Characteristics

USP Chapter <797> stipulates that the surfaces of ceilings, walls, floors, fixtures, shelving, counters, and cabinets in the buffer area must be smooth, impervious, free from cracks and

crevices, and nonshedding, thereby promoting cleanability and minimizing spaces in which microorganisms and other contaminants may accumulate. The surfaces must be resistant to damage by disinfectant agents. Junctures of ceilings to walls must be coved or caulked to avoid cracks and crevices where dirt can accumulate.[1]

If ceilings consist of inlaid panels, the panels must be impregnated with a polymer to render them impervious and hydrophobic, and they must be caulked around each perimeter to seal them to the support frame. Walls may be constructed of flexible material (e.g., heavy gauge polymer) panels locked together and sealed, or of epoxy-coated gypsum board. Preferably, floors are overlaid with wide sheet vinyl flooring with heat-welded seams and coving to the side-wall. Dust-collecting overhangs, such as ceiling utility pipes, and ledges, such as windowsills, should be avoided. The exterior lens surface of ceiling lighting fixtures should be smooth, mounted flush, and sealed. Any other penetrations through the ceiling or walls must be sealed.[1]

The buffer area must not contain sources of water (e.g. sinks, eye washes) or floor drains. Work surfaces must be constructed of smooth, impervious materials, such as stainless steel or molded plastic, so that they are easily cleaned and disinfected. Storage shelving, counters, and cabinets must be smooth, impervious, free from cracks and crevices, nonshedding, cleanable, and disinfectable. Their number, design, and manner of installation must promote effective cleaning and disinfection.[1]

Placement of Equipment and Supplies

USP Chapter <797> explains that the quality of the environmental air improves with movement from the outer boundary of the ante-area to the direct compounding area (DCA) within PECs. Placement of devices in ante-areas and buffer areas is dictated by their effect on the designated environmental quality of atmospheres and surfaces, which must be verified by viable (microbial) and non-viable (particulate) air sampling.[1] See Chapter 24.

It is the responsibility of every sterile compounding supervisor to ensure that each PEC environment for exposure of critical sites and sterilization by filtration is properly located, operated, maintained, monitored, and verified (see Chapter 4). Placement of devices (e.g., computers, printers) and objects (e.g., carts, cabinets) that are not essential to compounding in buffer areas is dictated by their effect on the required environmental quality of air and surfaces, which must be verified by viable and nonviable air sampling. [1] Space must be provided in or convenient to the ante-area for storage of sterile garb (gowns, gloves, hair and shoe covers, face masks and goggles) and for supplies that are needed for equipment (e.g., pre-filters for PECs, automatic compounder sets, labels, etc.).

With regard to non-sterile chemicals used in high-risk compounding, USP Chapter <1075>: Good compounding practices says that bulk drugs and other chemicals or materials used in the compounding of drugs must be stored as directed by the manufacturer, or according to USP monograph requirements, in a clean, dry area, under appropriate temperature conditions (controlled room temperature, refrigerator or freezer).[13] Presterilization procedures for high risk level CSPs, such as weighing and mixing, must be completed in no worse than an ISO Class 8 environment (e.g. in a separate room with a controlled air environment). All high risk level CSP solutions subjected to terminal sterilization are pre-filtered by passing through a filter with a nominal pore size not larger than 1.2 microns preceding or during filling into their final containers to remove particulate matter. All nonsterile measuring, mixing, and purifying devices are rinsed thoroughly with sterile, pyrogen-free water, and then thoroughly drained or dried immediately before use for high-risk compounding.[1]

Environmental Sampling and Testing

USP Chapter <797> specifies that the environmental sampling and testing program must demonstrate that PECs (LAFWs, BSCs, CAIs, and CACIs) are maintaining an environment in the compounding area that consistently ensures acceptably low viable and nonviable particle levels. The compounding area includes the ISO Class 5 PEC, the buffer areas, and/or segregated compounding areas and the ante-areas.[1]

Environmental sampling must occur as part a comprehensive quality management program and must occur minimally under any of the following conditions: 1) as part of the commissioning and certification of new facili-

ties and equipment; 2) following any servicing of facilities and equipment; 3) as part of the re-certification of facilities and equipment (i.e., every six months); 4) in response to identified problems with end products or staff technique; or 5) in response to issues with CSPs, observed compounding personnel work practices, or patient-related infections (where the CSP is being considered as a potential source of the infection).[1] Therefore, suitable space must be provided for sampling swabs, agar plates, incubator, etc. See Chapter 24 on environmental quality and control.

Cleaning and Disinfecting

USP Chapter <797> states, "Environmental contact is a major source of microbial contamination of CSPs. Consequently, scrupulous attention to cleaning and disinfecting the sterile compounding areas is required to minimize this as a source of CSP contamination."[1] Therefore, appropriate space must be provided for cleaning supplies, sterile 70% isopropyl alcohol and other disinfectants, trash containers for all waste streams involved, etc. See Chapters 15 and 23.

Planning the Sterile Preparation Facility

Allen et al. presented a detailed planning process for designing and evaluating a sterile compounding facility.[14] The authors used a strategic functional planning approach. This allowed them to meet hospital goals for efficiency, functionality and a planned future relocation of the sterile compounding center. The functional program development took them through: work flow, work load, equipment, storage, arrangement of work areas, space requirements, floor plan and evaluation of the facility. They were able to improve pharmacist efficiency by 42% and technician efficiency by 29% within a modest-sized facility that met ASHP sterile compounding facility standards extant in 1995. The cost of the equipment and fixtures was $70,000–$75,000.[15]

The functional planning approach includes eight key steps that can be used for large or small construction projects[16]:

1. Strategic master facilities plan sets forth the implications of the hospital strategic plan in terms of the facilities needed to accommodate planned activities, along with a timeline to show when facility needs will occur. The pharmacy department should have its own master facilities plan, keyed to its strategic plan, and congruent with the hospital's strategic plan.
2. Analysis of existing facility includes as-built plans, space inventory room by room, equipment list showing age and replacement value, site surveys, assessment of structural, mechanical, and electrical systems, code conformity, and traffic patterns.
3. Functional program includes block diagrams that show department components, flow and traffic relationships, phases in development, new versus renovated space, gross cost estimate, and a statement of assumptions and priorities.
4. Architectural schematic plans include alternatives, showing layout and design of departments and relationships plus workflow of staff, materials, and patients (includes a brief description of fixtures, mechanical and electrical systems, and a cost estimate).
5. Architectural design adds all other architectural details, including the last review by the users.
6. Construction contract includes final drawings for regulatory approval and bidding plus the final cost estimate.
7. Construction includes demolition, construction, equipment ordering, and inspection.
8. Commissioning for occupancy includes installation of equipment, orientation of staff, moving, post-occupancy evaluation (i.e., validation, certifications), and follow-up.

Strategic Master Facilities Plan

The first step, developing a master facilities plan, involves identifying and justifying the need for a new facility.

Identifying Need

Before updated facilities can be justified, the pharmacy department must determine its specific need based on its patient population. Three questions can be asked to determine this need.

What guidelines apply to the patient popula-

tion? Some state pharmacy laws or regulations require that USP Chapter <797> standards be followed. See Chapter 1.

What are the highest level sterile preparations that will be compounded? Unless there is no chance that high-risk preparations will ever be compounded, following the USP Chapter <797> standards for high-risk compounding is the most conservative approach.

Will hazardous drugs be compounded? Compounding hazardous drugs will require additional primary (i.e., BSC or CACI) and secondary engineering (i.e., segregated negative pressure buffer room) controls.

Justifying Need

Pharmacy directors frequently face resistance (both from administrators and pharmacy personnel) when justifying the need to improve their facilities. Some commonly asked questions and their corresponding answers follow.

Q. If admixtures are made within a laminar-airflow workbench, why does its location matter? A. Laminar-airflow workbenches do not eliminate 100% of airborne particles. These workbenches have high-efficiency particulate air (HEPA) filters that remove 99.97% of particles over 0.3 microns when operating properly.[17] A significant increase in airborne contamination outside the workbench significantly increases contamination within the workbench. Workbenches cannot prevent microbial contamination introduced by poor aseptic technique downstream from the HEPA filter (e.g., from air currents pushing room air into the workbench).

Q. If the workbench is already in a separate room, do you really need a buffer area and ante-area? A. A separate room minimizes unnecessary traffic near the workbench but not the contamination already in a room. For example[17]:

- A person sitting motionless generates about 100,000 particles/cu ft/min.
- A person sitting down or standing up generates about 2,500,000 particles/cu ft/min.
- A person walking generates about 10,000,000 particles/cu ft/min.
- An open, non-airlocked door can add billions of particles/cu ft/min.

The primary functions of a well-designed buffer area are to remove internally generated contamination and to prevent it from adversely affecting the direct compounding area (i.e., inside workbench environment).[17]

Q. If pharmacy-prepared admixtures at this hospital have never been implicated in nosocomial infections, why should these facilities be upgraded? A. Pharmacy-prepared sterile preparations are not commonly implicated because few institutions thoroughly investigate the causes of nosocomial infections. In fact, pharmacy-compounded sterile preparations have often been traced back to poor pharmacy aseptic compounding technique (see Chapter 1).

Q. Isn't good aseptic technique more important than a buffer area in preventing microbial contamination? A. One study showed that when sterile preparations are contaminated, touch contamination (as evidenced by skin bacteria) is much more common that contamination from the environment.[18] However, well-maintained buffer areas provide a clean, comfortable, correctly-arranged environment for primary engineering controls optimally to create an aseptic direct compounding area where critical sites can be exposed. Requiring proper personnel garbing and hand cleansing prior to entering a buffer area also minimizes unnecessary traffic in the area of compounding.

Q. Since building an ante-area and buffer area will be expensive, why not return the responsibility for admixture preparation to nurses? A. True, in admixtures prepared just prior to administration, accidentally introduced microbes have less time to grow to pathological levels. But one study showed that 21% of the admixtures were made incorrectly (as to ingredients, dosage, unordered admixture, or incompatibility) on nursing units.[19] Moreover, nurses are less well trained to make admixtures today than when this study was published. Furthermore, since many sterile preparations are used for 24 hours or more (e.g., TPNs and patient-controlled analgesia syringes), microbes can easily grow to pathologic levels at room or body temperatures. USP Chapter <797> does exempt manufacturer's bag and vial systems from all chapter standards and this exemption is used in many hospitals for critical patient needs.[20]

Q. Finally, what agency is going to force our institution to adopt USP Chapter <797>

sterile compounding facility standards? A. The state board of pharmacy is the most powerful agency inspecting pharmacies. At least nine states require partial or full compliance with USP Chapter <797> and most state boards of pharmacy are reviewing the new Chapter <797> to decide whether or how to enforce this chapter. The Joint Commission™ requires accredited health care institutions to review and decide how to use Chapter <797>. Courts of law will use Chapter <797> as the "community standard" for sterile compounding. See Chapter 1.

Douglas recommends that pharmacy directors write a 5 to 10 page white paper to justify physical plant changes to bring pharmacy into conformance with USP Chapter <797>.[21] To be effective, the white paper should address: regulatory standards, patient safety improvement and reduced potential for litigation, fiscal impact as to personnel efficiency, capital expenditures and return on investment, competitive advantage in the health care market, alternative solutions and why they were ruled out.[22] Determine the stakeholders who will read the white paper. Use language that is familiar to the stakeholders, e.g., patient and employee safety, finances, regulations. Use tables to present more detailed information, like alternatives considered—pros and cons, effects on staff efficiency, building, equipment and supply costs.

Existing Facility

Once the need has been justified, the next step is to determine whether a current sterile compounding area can be updated, whether a new compounding area is needed, or whether a new type of environmental control (e.g., compounding isolator) should be employed. Room size and environment (e.g., temperature, humidity and lighting) as well as cleanliness levels are important considerations.

Size and Environment

A survey conducted in 2006 of 341 U.S. hospitals showed an average of 310 square feet of floor space allocated for compounding sterile preparations (see Table 21-4). Considering that a minority of hospitals had upgraded their sterile compounding facilities in line with USP Chapter <797>, 81.3% of respondents to this survey indicated that their space allocations were not adequate for sterile compounding.[23] Allen et al. found that their "open" sterile compounding center required 727 square feet in floor space including a separate hazardous drug compounding area for a teaching hospital with an average of 441 occupied beds and 800 IV admixtures per day.[14]

For hand washing, a sink with hot and cold running water should be in the ante-area but not the buffer area. Ventilation and room temperature control should be in accordance with USP Chapter <797> standards (See above discussion). In any enclosed space with heat-producing equipment, the air conditioning must keep personnel comfortable in cleanroom garb. Lighting should ensure that personnel can read packages easily (e.g., syringe gauges and drug labels) and visualize contaminants (e.g., glass fragments in ampuls and rubber cores in vials). [24]

Room Separation

An ISO Class 7 buffer area and ISO Class 8 ante-area are mandatory. Seventeen percent of hospital pharmacies compound high-risk preparations.[25] Any hospital that compounds, or has the potential to compound, high-risk preparations must have the ante-area separated from the buffer area by a solid wall with a door that closes.[1] See section on "open" and "closed" sterile compounding facilities below.

Table 21-4.

Space Allocation for Sterile Compounding Areas*

Number of Staffed Beds	Square Footage (mean ± S.E.)
< 50 (n = 40)	83 ± 15
50–99 (n = 65)	208 ± 21
100–199 (n = 57)	294 ± 37
200–299 (n = 52)	441 ± 52
300–399 (n = 61)	661 ± 108
≥ 400 (n = 66)	976 ± 280
All hospitals (n = 341)	310 ± 26

**Source:* Pederson CA, Schneider PJ, Schekkelhoff DJ. ASHP national survey of pharmacy practice settings: Monitoring and patient education-2006. *Am J Health-Syst Pharm.* 2007;64:507–20.

Functional Program

The functional program is a large volume of detailed performance specifications to provide the designer or architect with details for all sterile compounding and related activities, work flows, work loads, numbers of personnel to be accommodated, fixtures and equipment, storage needs, transportation and communications, services, utilities environmental controls, security considerations, etc.[16] The key point in functional programming is to identify every specific function along with the required methods and systems to be performed in the facility. After existing facilities have been analyzed, one primary decision has to be made: Should a custom-built ante-area/buffer area be planned or should a modular ante-area/buffer area be purchased? Or can an existing room be remodeled or procedures be implemented to create a facility that meets ante-area/buffer area air quality standards?

Ante-Areas and Buffer Areas

A high-cleanliness ante-area reduces the number of particles in the buffer area. Appropriate activities for the anteroom include but are not limited to hand washing, gowning and gloving, removal of packaging, and cleaning and disinfecting of hard-surface containers and supplies before they are placed in the buffer area.[1] See Chapter 15.

Figure 21-1, from proposed USP Chapter <797>, shows the important parts and spatial relationship of a buffer area to an ante area suitable for low and medium risk sterile compounding.[26] This configuration is sometimes referred to as an "open" cleanroom.

Figure 21-2 represents USP's schematic floor plan for a high-risk sterile compounding facility.[26] This configuration is sometimes referred to as a "closed" cleanroom. Access to the buffer room should be via the anteroom door for personnel and via an airlock pass through

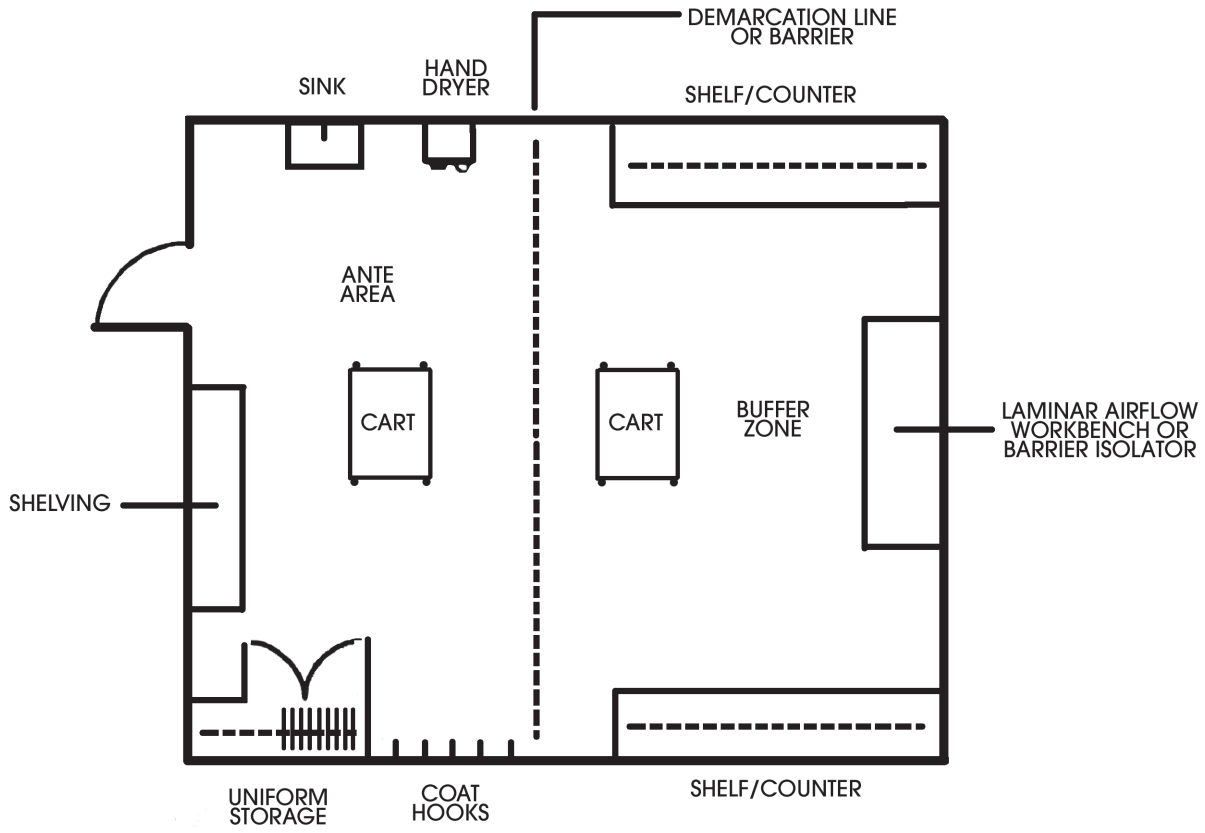

Figure 21-1. Schematic drawing of an "open" ante-area and buffer-area (not to scale).

for most supplies. As supplies are moved from the anteroom into the buffer room and then into the PEC, a series of cleaning steps should be followed (see Chapter 15).

Modular Ante-Area/Buffer Areas

Modular ante-area/buffer areas (as opposed to custom built) have several advantages:

1. Modular ante-area/buffer areas can be customized to specific needs of the institution.
2. No sanding, spackling, or painting of walls are necessary, leaving a cleaner environment.
3. Modularity allows future change if changes are anticipated in aseptic processes or volume, or relocation to another site.
4. Modular ante-area/buffer areas cost less and are more rapidly installed, reducing construction time by 20% to 40%.[27]
5. Modular systems use standard components that are often available from different suppliers.
6. Shipping costs for aluminum and vinyl components are less costly than steel and unassembled components.
7. Installation costs are less because the vendor will do most of the installation, with the exception of electrical, water and HVAC hook-ups.

For low-volume operations, soft-wall ante-area/buffer areas are available at a lower cost than modular hard-wall installations. The pharmacy at Memorial Hospital in Carthage, IL, had a soft-wall ante-area/buffer area (Figure 21-3) installed for under $20,000 (in 1995 dollars) that satisfied a JCAHO home care survey. Some facts about this ante-area/buffer area include[28]:

- Setup of tubular frame and vinyl plastic panels took 10-12 hours for two company personnel.
- Dimensions are 8 feet by 16 feet, with an 8-feet ceiling height.
- Three "movable" walls are connected to one rigid wall. The rigid wall contains elec-

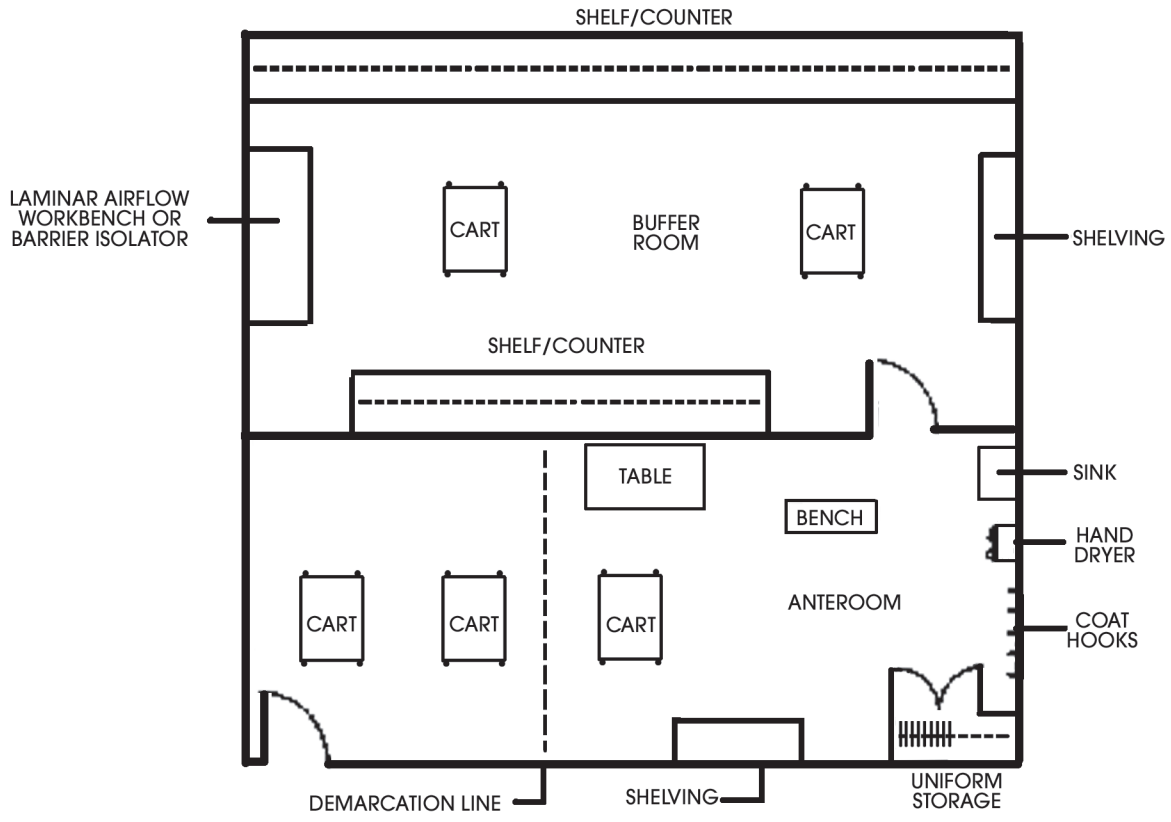

Figure 21-2. Schematic drawing of a "closed" anteroom and buffer room (not to scale).

trical and plumbing fixtures. It is made of aluminum stud supporting fire-rated dry wall and is painted with epoxy paint to provide durability and prevent particle shedding.

- Soft walls are made of 16-mil, replaceable, clear vinyl panels attached to a strong tubular frame.
- The ante-area/buffer area door is the same vinyl-on-tubular frame construction.
- The pass-through chamber is 16 inches by 16 inches.
- Two 2-feet by 4-feet HEPA filters are suspended in the ante-area/buffer area ceiling. Air from the pharmacy proper is blown through two standard fiberglass filters before passing through the HEPA filters into the ante-area/buffer area.
- Louvered dampers in the door and below the pass-through chamber permit airflow out of the positive-pressure room. They can be closed if power is lost to the blower.
- Ceiling tiles are vinyl-coated gypsum panels.
- Vinyl panels are easy to clean with detergent and water and can be replaced inexpensively if torn.
- A "hands free" faucet and hand dryer are just outside the ante-area/buffer area.
- The airborne particle count in the cleanroom is about 65 of 0.5 microns or larger per cubic foot, easily qualifying the environment as ISO Class 7 or even ISO Class 5. Particle counts inside the laminar-airflow workbench average 5–10 of 0.5 microns or larger.

Compared to soft-wall ante-area/buffer areas, hard-wall modular ante-area/buffer areas with rigid panels attached to a frame offer more stability and better seals to maintain ante-area/buffer area integrity.[29] Hard-wall ante-area/buffer areas are also easier to keep clean and are more durable.

Remodeling Existing Space

Kuster and Snyder gave reasons for renovating their pharmacy to create an ISO Class 7 ante-area/buffer area.[30] They prepared various sterile preparations, including high-risk preparations such as glycerin and phenol injection and sterile talc injection. To lessen the chance of error due to interruptions, they placed no phone in their ante-area/buffer area and included only a foot-activated intercom for outside communications.

Figure 21-3. Pharmacist in a soft-wall cleanroom at Memorial Hospital, a 67-bed hospital in Carthage, IL.

Samuelson and Clark described the planning for an ISO Class 7 buffer area with an ISO Class 8 anteroom at the University of Illinois Hospital.[31] They decided to convert an existing 32-feet by 22-feet sterile preparations room 40% into a buffer area and 60% into an ante-area by constructing a wall across it. The large anteroom was needed for stock storage and reference materials. A larger pass-through window was used for supplies going into the buffer area, and the smaller window, for completed preparations going back to the ante-area where a pharmacist checks them. The glass panel around the windows preserved a sense of openness and allows the pharmacist to monitor activities in the ante-area/buffer area. Since the existing walls and floor were seamless, they could be sealed with a polymer coating. However, ventilation had to be changed to incorporate HEPA filtration of the air supply in conjunction with a new two-inch ceiling grid system.

In a 321-bed community hospital, Schumock et al. described their remodeling project to create an ISO Class 7 buffer room.[32] The authors planned and implemented a 361 square foot facility that paid for itself ($39,486 in 1996 dollars) in less than two years via the batch production of selected unit-of-use

syringes not available commercially, i.e., savings were from reduced waste and extended expiration dating.

Minimal Facility Change

Pharmacy managers find it tempting to convert a traditional sterile compounding space to an ante-area, buffer area space. This is difficult for several reasons. Adding enough ante-area usually takes more space; there may not be enough overhead space for adding HEPA filters and their air grills; low wall air returns can be a problem; adding plumbing for a sink in the ante-area is tough if the pharmacy is on the bottom floor; exhausting a BSC or CACI to the outside for compounding hazardous drugs may be difficult and so on. Remodeling existing space also poses the difficulty of finding swing space for sterile compounding during weeks or months of construction.

As mentioned, the USP Sterile Compounding Committee believes that it is relatively easy to convert an ISO Class 8 buffer room to an ISO Class 7 buffer room. However, the American Society for Healthcare Engineering (ASHE) states that converting ISO 8 to ISO 7 and requiring HEPA air filtration will significantly increase the costs to design, construct, and operate the ventilation component of pharmacy buffer rooms, particularly if the design is to retrofit an existing ventilation system. They say increasing the air quality from ISO Class 8 to ISO 7 will require substantially greater air flow and cost (see Table 21-5.) Existing supply fans to ceiling air grills may be insufficient to overcome the resistance of HEPA filters, in which case hospitals must install in-line booster fans to maintain a positive pressure of the buffer area relative to the ante-area.[33]

In lower volume facilities or for pharmacy night shift or satellite operations, pharmacists might consider installing a compounding isolator in existing space. This is an option for low and medium risk compounding only. The CAI or CACI must meet USP Chapter <797> conditions to be considered for use outside an ISO Class 7 buffer room, i.e. complete isolation from the surrounding room, minimum air particle counts in the direct compounding area and at the transfer door when the surrounding room.[1] See Chapter 4. If a CACI that meets the Chapter <797> requirements is used for compounding hazardous drugs outside an ISO 7 buffer area, it must be in a segregated compounding room that maintains a minimum negative pressure of 0.01-inch water column and have a minimum of 12 air changes per hour.[1]

A non-ISO 7 alternative for low-risk compounding for sterile preparations with 12-hour or less beyond-use dates is to create a segregated compounding area. Placement of devices (e.g., computers, printers) and objects (e.g., carts, cabinets) that are not essential to compounding in the segregated area should be limited, based on their effect on air quality in the ISO Class 5 primary engineering control.[1]

Architectural Schematic Plan

Pharmacists should prepare plans with a hospital designer or architect in line with the detailed specifications in the functional program. For the hospital architect unfamiliar with ante-area/buffer area design, ISO Standard 14644-4 specifies the requirements for the design and construction of ante-area/buffer area facilities.[34] This standard is intended for use by purchasers, suppliers and designers of ante-area/buffer area installations and

Table 21-5.

Cost of Converting an ISO Class 8 Buffer Room to an ISO Class 7 Buffer Room*

ISO Class	Ceiling Covered by Air Grills	Approximate Cost of Ceiling Air Grills
8	5%–15%	$50 per square foot
7	15%–20%	$200–$250 per square foot

**Source:* Woodin D. Deputy Executive Director, American Society for Healthcare Engineering. Comments on summary of proposed revisions to <797>. http://www.ashe.org/ashe/codes/advisories/pdfs/comment090905_usp797rev3.pdf Accessed February 4, 2008.

provides a checklist of important parameters of performance. Construction guidance is provided, including requirements for qualification and start-up activities.

The pharmacist has the following roles in functional planning[16]:

- Derive pharmacy goals and objectives as to sterile compounding.
- Identify functions to be performed in the ante-area and buffer area.
- Determine workflow in the ante-area and buffer area.
- Determine the physical environment needed.
- Decide how to handle workload during the renovation process.
- Specify requirements for the ante-area and buffer area:
  - Workload (e.g., average and maximum daily numbers of parenteral nutrition solutions, batches of syringes, chemotherapy compounding, peritoneal dialysates, stat admixtures).
  - Equipment types and numbers. Will biological safety cabinets or isolators be exhausted to the outside (they should be)?
  - Storage requirements for supplies and finished preparations.
  - Personnel types and numbers.
  - Materials handling.
  - Communication systems (e.g., intercom, email, telephones, overhead paging).
  - Services expected from other departments (e.g., IV solution deliveries, housekeeping).
  - Security (e.g., locked doors, access control systems, video cameras).
  - Utilities (e.g., lighting, electrical outlets, plumbing, computer lines.)
  - Environmental quality control (i.e., ISO Class 5 or 7 or 8).
  - Housekeeping and cleaning routines.
  - Environmental sampling routines (e.g., laminar air-flow workbench testing, air and surface microbial counts, air particulate counts).

Together the pharmacist and designer/architect find optimal arrangements for work areas, find the best location, calculate space and develop trial schematics. The architect's role is to translate all of this into architectural plans, i.e., determining how much square footage is needed, designing the layout of the space, specifying construction materials, developing project budgets, producing blue prints and issuing change orders. The architect may be on the hospital staff, may be hired by the construction project or may be supplied by the construction company. Some hospital architects will need to review recommended practices in ante-area/buffer area design.[35,36]

Construction Contract

Preparing the Request for Information (RFI)

Before asking a vendor to bid on building an ante-area/buffer area, evaluate potential vendors by asking for information about their abilities and resources; solicit financials or Dun and Bradstreet reports and ask for a listing of recently completed projects in facilities like yours. Call for references or visit some of these facilities. Ask the vendor to submit a set of design plans for a similar project and resumes for the proposed project team. Select three to five vendors to whom you will submit a request for proposal.

Handling the Request for Proposal (RFP)

Together, the pharmacist and hospital engineer or architect should prepare the RFP and select the potential vendors most likely to serve the facility's needs. The request for proposal can follow these guidelines[37]:

1. Supply potential vendors with pertinent information to meet the requirements but not so detailed as to stifle their creativity.
2. Provide a general overview of the facility and its requirements, e.g., the type of work to be done, hours of operation.
3. Present the scope of work to be provided by the vendor, i.e., design, construction, electrical, heating, ventilation, and air conditioning (HVAC), institutional or vendor-supplied connections for electrical, ventilation, gases, etc. James T. Wagner (author of Chapter 4) recommends that Type C HEPA filters be used in pharmacy ante-area/buffer area air supplies.[38]

4. Ask for a proposed project schedule, floor plan, ceiling plan, elevations, equipment location plan, and air balance schematic, as well as details and catalog cuts of preparations and materials used as the basis of the design. Ask for heat load calculations and rough power requirements. Must construction and service personnel be union members? Use all this information to compare proposals and for interviews with potential vendors.
5. Show taxable status of the project so the vendor knows what to include or not include as regards permits, stamps, and fees.
6. Specify that your compounding area is to be an ISO 7 buffer area with an ISO Class 8 ante-area for airborne particles, temperature (i.e., 20 °C.), humidity (e.g., 45%–60% relative humidity), air pressure gradients between the buffer area and ante-area and the ante-area and surrounding space and air exchanges per hour (i.e., 30 air exchanges per hour in the buffer area). HVAC control is the biggest issue in design, because garb, workbenches and refrigerators increase warmth for people in ante-area/buffer areas. The number of people in the compounding area will also add heat and moisture to the environment.
7. Supply a schematic floor plan or bubble diagram, equipment list, material pathways, ceiling height (slab to slab), current floor construction, and any seismic or structural issues so the vendor can accurately assess construction requirements. What cleaning agents will be used on ceilings, walls, and floors? Are windows or viewing panels required? If so, where should they be? Are pass-through chambers required? If so, where and what size should they be in the ante-area and buffer area? Where are doors to be located in the ante-area and buffer area? What type of door (e.g., flexible vertical slats, swing, or sliding) should be installed? Do perimeter walls require fire rating? If so, identify rating in hours for the ante-area and buffer area. Are temperature recording and monitoring devices to be built in within the ante-area and buffer area?
8. Present a utility plan. Will additional electrical power be needed? Hospital engineering personnel can usually bring the power source to a single point of connection at a lower cost than having the ante-area/buffer area vendor arrange the power source. You may wish to have energy-saving setback controls if the ante-area/buffer area is not operating 24 hours per day, 7 days per week. What lighting levels are needed (in foot-candles) at 30 inches from the floor in the buffer area (e.g., 140) and ante-area (e.g., 100)? Requirements for a sprinkler system in the ante-area/buffer area are dependent on the occupancy code and use, as well as local building codes. Sprinkler heads should be flush with the ceiling. How far away is the tie-in point for sprinkler water supply? Will the water supply be shut down or will it need to operate during the tie-in process? What are the insurance policy requirements for the sprinkler system? Will smoke or fire alarms be needed in the ante-area/buffer area? Are hot and cold water available for the ante-area? Can a sink drain be installed in the ante-area? Who will remove waste material? How will hazardous and nonhazardous waste be handled? See Chapter 15.
9. Require the vendor to do an onsite inspection of your facility before developing a quotation.
10. Ask for the vendor to train your personnel who will use and maintain the ante-area/buffer area, e.g., engineers, housekeeping, pharmacy personnel.
11. Ask for a price breakdown, per building trade, allowing you to evaluate where there are differences in proposals. Is payment or performance bonding required?
12. Develop an evaluation matrix to compare proposals. Interview the two or three vendors who look most promising, based on criteria that you have set for your institution. Discuss architecture, mechanical systems, heat load calculations including wall insulation, and electrical and lighting systems.
13. Arrange to have the completed ante-area/buffer area evaluated by an independent company based on your RFP performance criteria. Determine who will pay for the final evaluation.
14. Negotiate the schedule that protects both parties from unforeseen delays and costs.
15. Ask what you, as the owner, will have to do to operate the ante-area/buffer area after the vendor's work is complete.
16. Finally, have the institution's pharmacist, engineer, administrator, and lawyer select the best ante-area/buffer area vendor.

Lawyers for the vendor and institution will finalize the contract for the administrator's approval.

Construction

Whether planning custom-built or modular construction, everyone involved in constructing an ante-area/buffer area should understand that this is no ordinary building project. The microbial contamination potential of all activities should be reviewed before they are begun. Institutional staff should monitor vendor personnel to ensure that they follow proper techniques so as not to build contamination into the ante-area/buffer area or its surroundings. Issues should be resolved with the vendor onsite, not after construction is complete.

Materials for walls, floors, and ceilings should never be stored outdoors. Packaging materials (usually doubled) cannot be torn or removed until the ante-area/buffer area vendor is ready for installation. A general wipe down of building materials with clean wipes is recommended both before and after installation.[39] After any cutting or drilling operation, the resealing should be done as soon as possible to prevent oxidation or deep contamination of building materials.

Once the floor is laid, construction workers should wear gowns and shoe covers to reduce contamination and prevent damage to the floor. No eating, smoking, chewing, etc., should be allowed in the area. All spills, filings, etc., should be cleaned up immediately. After walls and ceilings are in place (even before the air supply is turned on), the area should be restricted to authorized personnel. Finally, once the air supply is on, construction workers should be gowned like the operators will be.[39]

Commissioning for Occupancy

Final steps are inspecting and approving the new facility, installing and evaluating equipment, moving supplies, assessing workflow, and following up on needed changes (which are inevitable). Use of a qualified independent testing agency is recommended to assure unbiased test results.

The sterile compounding supervisor must be sure that air quality (balance and particle levels), surface conditions, environmental requirements (temperature and humidity), and working conditions (e.g., space, sound, and lighting levels) are as specified in the original bidding process.

These requirements must be satisfied before any equipment or supplies are moved into the ante-area or buffer area. The vendor should supply an operation and maintenance manual that will help identify problems and possible solutions. This manual should also provide scheduling for maintenance and parts replacement.

Furthermore, the institution's facilities management personnel must check that all policies regarding electrical fixtures, heating, ventilation, etc., have been met. An agreement must be reached with the vendor to rectify deficiencies before the contract can be considered satisfied.

Ante-area/buffer area vendor should be required to pay to have independent facility certification and validation. This may involve three phases of certification[40]:

- Phase 1—Installation Qualification. As-built testing or construction approval. This proves the environment was correctly installed and that it meets functional design specifications.
- Phase 2—Operational Qualification. At-rest testing or functional approval. This testing is performed with all the equipment present and operating but without personnel present. It is necessary to see that primary and secondary engineering controls work properly together.
- Phase 3—Performance Qualification. Also called dynamic operational testing, it is a series of tests or certifications that determine whether the completed installation achieves the functional standards during routine operations. USP Chapter <797> requires that secondary engineering controls meet standards during dynamic operations like those in the CETA Certification Guide for Sterile Compounding Facilities.[41] The Controlled Environment Testing Association (CETA) guide covers tests for airflow testing including smoke patterns, room pressurization, airflow displacement, HEPA filter installation leaks, air particle counts and optional tests for lighting and noise levels, temperature and humidity controls.

Facility Maintenance

Clearly, planning, building, and implementing an ante-area/buffer area is a detailed process. All that preparation, however, must be preserved with proper maintenance. Preventive maintenance of ante-area/buffer area pre-filters, HEPA filters, and ducts should be arranged with appropriate maintenance personnel or a service vendor. Similarly, lighting should be checked periodically and/or bulbs should be changed.

Cleaning and Disinfecting (see also Chapter 23)

Each day, work surfaces near the primary engineering control(s) (e.g., counter tops and carts) should be wiped clean with a freshly prepared mild detergent solution followed by an approved disinfectant. Sufficient time must be allowed for the agent to exert its antimicrobial effect. Furthermore, storage shelving should be emptied of all supplies, cleaned, and disinfected at least monthly. Re-cleaning should be performed if spillage or other events indicate the need.[1]

When no aseptic operations are in progress, floors should be mopped once daily by trained and supervised personnel. Floors should not be waxed because dried, worn wax adds to airborne particulates.[42] All cleaning and sanitizing agents should be approved, with careful consideration of compatibilities, effectiveness, and inappropriate or toxic residues. In addition, all cleaning tools (e.g., wipers, sponges, and mops) should be nonshedding and used only in the buffer area (first) and ante-area.

Most wipers should be discarded after one use. If cleaning tools are reused, their cleanliness should be maintained by thorough rinsing and sanitizing and by storage in a clean environment. Ceilings and walls should be cleaned monthly with a mild detergent solution followed by an approved sanitizing agent.[1]

Trash should be collected in suitable plastic bags and removed with minimal agitation. Routine monitoring is used to control the quality of the air and surfaces in the ante-area/buffer area.

Re-Certification

USP Chapter <797> requires that recertification procedures such as those in the CETA Certification Guide for Sterile Compounding Facilities be performed by a qualified individual no less often than every six months and whenever a secondary engineering control is relocated or altered or major service to the facility is performed.[41] This applies to segregated compounding areas as well as ante-area/buffer area sterile compounding facilities.[1] See Chapter 24.

Environmental Sampling and Testing

In addition to recertification, USP Chapter <797> stipulates that routine monitoring and testing of secondary engineering controls: air microbial and surface testing, air pressure differential monitoring in "closed" ante-area/buffer areas and differential airflow velocity in "open" ante-area/buffer areas, temperature and humidity controls.[1] See Chapter 24.

Corrective Actions

Whenever monitoring and testing fall outside acceptable ranges, corrective actions are required. If colony-forming unit counts are too high in microbial air or surface testing, a review of personnel garbing, traffic patterns, cleaning and disinfecting, etc., is required. If air pressure differential or airflow velocity monitoring, temperature or humidity are outside the normal range, the heating, ventilation, and air conditioning system must be inspected by a qualified engineer and corrections must be made. See Chapters 24 and 27.

Summary

Facilities used for sterile compounding play an integral role in guaranteeing sterility, as does proper garbing, hand hygiene, and aseptic technique. Therefore, pharmacy departments should assess their current facilities and, if needed, upgrade or replace them. Once facilities have been brought up to USP Chapter <797> standards, a proper maintenance program for the ante-area/buffer area must be followed.

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