CHAPTER 21-4.10 - DESIGN REQUIREMENTS FOR COMPOUNDED STERILE AND HAZARDOUS DRUG PREPARATION AREAS

21-4.10.1 INTRODUCTION

A. Purpose

This chapter provides guidance on minimum requirements for the designing of IHS pharmacies to ensure safe and contamination free storage and processing of compounded sterile preparations (CSP) and hazardous drugs (HD).

B. Scope

This Section 10 of Chapter 21-4 applies to all new construction and renovation for IHS health care facilities.* This Section addresses aspects of the built environment, e.g., architectural, mechanical, and electrical, etc., as these relate to the environmental conditions for compounding sterile preparations and storage and processing of hazardous drugs. This document should be used in conjunction and/or consultation with the IHS Pharmacist, the Area Institutional Environmental Health officer, and the Director of Facilities Management.

* Note: For facilities constructed prior to the adoption date of this section and not otherwise scheduled for renovation, the multi-disciplinary team listed above should evaluate facility compounding needs, practices, equipment, and environment to determine appropriate actions to address United States Pharmacopeia (USP) 797-2008 and USP 800-2016.

C. Background

In 2002, the Centers for Disease Control and Prevention (CDC) published a Morbidity and Mortality Weekly Report, which advised that “clinicians should consider the possibility of improperly compounded medications as a source of infection in patients.” This recommendation from the CDC was the beginning of an increased focus to provide controlled environments and practices when compounding sterile preparations.

This update reflects incorporation of updated requirements from the publication of USP 797 (2008) and the initial issuance of USP 800 (2016).

Previous editions of this Technical Handbook Chapter.

- Dec 9, 2008

D. Definitions

Ante Area/Room – An International Standards Organization (ISO) Class 8 or better area/room where personnel hand hygiene and garbing procedures, staging of components, order entry, CSP labeling, and other high- particulate generating procedures are performed (USP-797-2008).

Biological Safety Cabinet (BSC) – A ventilated cabinet for protection of Compounded Sterile Preparations, personnel, product and/or the environment, which has an open front with inward airflow for personnel protection, downward high-efficiency particulate air (HEPA)-filtered laminar airflow for product protection, and HEPA-filtered exhausted air for environmental protection (USP-797-2008).

Buffer Area/Zone – An ISO Class 7 or better area/zone where the primary engineering control (PEC) is physically located (USP-797-2008).

Compounding Aseptic Containment Isolator (CACI) – A compounding aseptic isolator (CAI) designed to provide worker protection from exposure to undesirable levels of airborne drug throughout the compounding and material transfer processes and to provide an aseptic environment for compounding sterile preparations.

Air exchange with the surrounding environment should not occur unless the air is first passed through a microbial retentive filter (HEPA minimum) system capable of containing airborne concentrations of the physical size and state of the drug being compounded. Where volatile hazardous drugs are prepared, the exhaust air from the isolator should be appropriately removed by properly designed building ventilation. (USP-797-2008)

Compounding Aseptic Isolator (CAI) – A form of isolator specifically designed for compounding sterile, non-hazardous pharmaceutical ingredients or preparations. It is designed to maintain an aseptic compounding environment within the isolator throughout the compounding and material transfer processes. Air exchange into the isolator from the surrounding environment should not occur unless the air has first passed through a microbially retentive filter (HEPA minimum). (USP-797-2008)

Compounded Sterile Preparation (CSP) - For the purposes of this chapter, CSPs include any of the following:
(1) Compounded biologics, diagnostics, drugs, nutrients, and radiopharmaceuticals, including but not limited to the following dosage forms that must be sterile when they are administered to patients: aqueous bronchial and nasal inhalations, baths and soaks for live organs and tissues, injections (e.g., colloidal dispersions, emulsions, solutions, suspensions), irrigations for wounds and body cavities, ophthalmic drops and ointments, and tissue implants.
(2) Manufactured sterile products that are either prepared strictly according to the instructions appearing in manufacturers' approved labeling (product package inserts) or prepared differently than published in such labeling. (USP-797-2008)

Containment Ventilated Enclosure (CVE) - A full or partial enclosure that uses ventilation principles to capture, contain, and remove airborne contaminants through HEPA filtration and prevent their release into the work environment

Hazardous Drugs (HD) - A group of drugs that are associated with or suspected of causing adverse health effects. A current list of drugs commonly classified as “hazardous drugs” is published by the National Institute for Occupational Safety and Health (NIOSH) and titled “NIOSH List of Antineoplastic and Other Hazardous Drugs in Healthcare Settings”. This current published list may be found at http://www.cdc.gov/niosh/topics/hazdrug/. Additional “hazardous drug” information and IHS requirements may be found at The Indian Health Manual (IHM) Part 3 – Professional Services, Chapter 27, “Controlling Occupational

Exposure to Hazardous Drugs." (https://www.ihs.gov/ihm/index.cfm?module=dsp_ihm_pc_p3c27)

Laminar Air Flow Workbench (LAFW) – A controlled environment created by a high efficiency particulate air (HEPA) filter to retain airborne particles and microorganisms (Compounding Sterile Preparations, 2nd ed., Buchanan, Schneider).

Primary Engineering Control (PEC) – A device or room that provides an ISO Class 5 environment for the exposure of critical sites when compounding CSPs. Examples include BSCs, CACIs and LAFWs (USP-797-2008).

21-4.10.2 GUIDELINES

A. General Design Criteria for facilities

(1) Elements Common to Sterile and Hazardous Drug Compounding

(a) When practical, locate air handling unit outside of pharmacy area to avoid dust/debris generation within pharmacy area during maintenance activities, e.g., filter replacement, etc.
(b) PECs should operate continuously to maintain the required pressure differentials and ISO Class environments. These systems should be considered for inclusion on emergency power supply.
(c) In locations with a physical barrier and a doorway or other penetration is present between locations (buffer room, ante room, hazardous drug prep room and/or adjacent hallways), a permanently installed pressure gauge must be used to constantly monitor the relative pressure status. This gauge must include an audible alarm to alert staff when improper relative pressure occurs.
(d) For CSP and hazardous drug buffer rooms/areas, the square footage should be as small as functionally necessary, to limit the storage of unnecessary materials.

(2) Elements specific to Sterile Drug Compounding

(a) For facilities that perform "Low" and/or "Medium" risk procedures, as defined in the USP 797-2008, an ante area or ante room shall be provided adjacent to the buffer room.

(b) For facilities that perform “High” risk procedures, as defined in USP 797-2008, the buffer room shall be physically separated and adjacent to the ante room.
(c) In sterile drug compounding areas, supply air diffusers should be located in or near the ceiling, while air returns should be located low on the wall.

(3) Elements specific to Hazardous Drug Compounding

(a) LAFW and CAI shall not be used for hazardous drug preparation or compounding. Class I BSCs may only be used for non-sterile hazardous drug procedures. Only Class II or III BSCs, or CACIs shall be used for hazardous drug procedures. Refer to the Tables below for environmental requirements related to selection of the PEC.
- For occasional nonsterile HD compounding, a Class II BSC or CACI used for sterile compounding may be used but must be decontaminated, cleaned, and disinfected before resuming sterile compounding in that containment PEC.

(b) All BSCs and CACIs used for hazardous drugs must have the exhaust HEPA filtered and be vented to the exterior, or have redundant HEPA filters before recirculation for non-sterile preparations.
(c) Hazardous drug compounding areas must be separated from other preparation areas and must maintain between 0.01 and 0.03 inches of water column negative pressure differential.
(d) Antineoplastic HDs must be unpacked (i.e., removal from external shipping containers) in an area that is neutral/normal or negative pressure relative to the surrounding areas. HDs must not be unpacked from their shipping containers in sterile compounding areas or in positive pressure areas.
(e) Hazardous drug non-sterile compounding areas require 12 Air Changes per Hour (ACH). Hazardous drug sterile compounding areas require either 12 ACHs or 30 ACHs, depending upon Beyond Use Dates (BUDs) for segregated compounding areas.
(f) Hazardous drug storage areas should have at least 12 ACHs and be externally vented.
- Items such as refrigerated anti-neoplastic HDs must be stored in a dedicated refrigerator in a negative pressure area with 12 ACH. If a refrigerator is placed in a negative pressure buffer room, an exhaust

located adjacent to the refrigerator's compressor and behind the refrigerator should be considered.

(g) An eyewash station and/or other emergency or safety precautions that meet applicable laws and regulations must be readily available. However, care must be taken to locate them in areas where their presence will not interfere with required ISO classifications.

(h) Exhaust from hazardous drug compounding area should be clearly marked as to the hazard where the exhaust leaves the building.

B. Design Criteria for facilities using BSCs and LAFWs

The rooms used for compounding sterile and hazardous drug preparations shall comply with the design recommendations listed below in the Tables.

C. Design Criteria for facilities using CAIs and CACIs

If a facility uses a CAI or CACI that meet USP 797-2008 requirements as listed below in Subsection (1), the environmental requirements as listed in Subsection (2) are not as strict as for facilities using a BSC or a LAFW.

(1) CAI/CACI requirements for reduced environmental requirements *(Copied from USP 797-2008, "Placement of Primary Engineering Controls" Section):*

- *The isolator shall 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 of the critical exposure site shall maintain ISO Class 5 levels during compounding operations.*
- *Not more than 3520 particles (0.5 µm and larger) per m3 shall be counted during material transfer, with the particle counter probe located as near to the transfer door as possible without obstructing the transfer.*

It is incumbent on the compounding personnel to obtain documentation from the manufacturer that the CAI/CACI will meet this standard when located in environments where the background particle counts exceed ISO Class 8 for 0.5-µm and larger particles. When isolators are used for sterile compounding, the recovery time to achieve ISO Class 5 air quality shall be documented and internal procedures developed to ensure that adequate recovery time is allowed after material transfer before and during compounding operations.

(2) Potentially applicable reduced environmental requirements

(a) Sterile Drug Compounding

- CAI’s may be placed outside a Class 7 buffer area if they meet the above requirements. The unclassified area must maintain at least 0.02 to 0.05 inch water column positive pressure and 12 air changes per hour.
- If the PEC is a CAI or CACI that does not meet the requirements above or is a LAFW or 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 order for a specific patient may be prepared, and administration of the CSP shall commence within 12 hours of preparation or as recommended in the manufacturer's package insert, whichever is less.

(b) Hazardous Drug Compounding

- Low- and medium risk hazardous drug CSPs may be prepared in a Class II BSC or CACI placed outside an ISO Class 7 buffer area, if the compounding area maintains a minimum negative pressure of 0.01 in water column, is vented to the exterior, and has a minimum of 12 ACHs.
- Facilities should consider placing the CACI in a negative pressure room with the stored hazardous drugs.

D. Typical Room Layouts

Refer to USP-800 (Feb 2016), appendix 2, for illustrative examples of typical room layouts. You may contact the IHS Pharmacist or the Area Institutional Environmental Health Officer to request a copy.

21-4.10.3 Tables: Construction Guidelines for Pharmacy Compounding Rooms

Table 1: Requirements Common to All Locations and Compounded Pharmaceuticals (Note 1)

Requirement Category	Requirement
Buffer Area Minimum Outdoor ACH (Note 2)	2 ACH
Buffer Area Humidity (Note 3)	≤60% RH
Buffer Area Temperature °C / °F	≤20'C (≤68'F) Note 4.
Ante Room Pressure Differential to Adjacent Areas	Positive to all other adjacent areas (out): At least 0.01" H_2O for ISO Class 8 or unclassified areas and at least 0.02" H_2O for ISO Class 7 areas.
Provisions for hand-washing.	Faucets should be designed to be hands-free, such as motion sensitive or foot controlled.
Ceilings *(Note 5)*	Smooth, impervious, free from cracks and crevices, non shedding and resistant to sanitizing agents. For example: • Smooth finish drywall with epoxy-painted finish • Vinyl coated ceiling tiles in anodized aluminum T-bar grid (lock down clips required). Ceiling tiles should be sealed to the grid and perimeter of grid should be caulked.
Floor *(Note 5)*	Smooth, impervious, free from cracks and crevices, non shedding and resistant to sanitizing agents. Typically: • Seamless sheet vinyl with joint sealing technique of grooved, melted, welded, vinyl for an impervious waterproof seal. Provide seamless sheet vinyl base integral with the flooring, using the same joint sealing technique.
Wall finish *(Note 5)*	Smooth, impervious, free from cracks and crevices, non shedding and resistant to sanitizing agents. For example: • Smooth finish drywall with epoxy-painted finish or FRP sheets (FRP=Fiber Reinforced Plastic)
Shelving & Fixtures	Smooth, impervious, free from cracks and crevices, non shedding and resistant to sanitizing agents.
Doors	Epoxy-painted door/frame with no ledges (flush with walls).
Windows	Anodized aluminum frames with no ledges with tempered safety glass.
Light fixtures	Recessed "clean room" fixture sealed to grid or fixture frame. Acrylic lens with baked enamel finish.

Note 1: References USP 797, 2008 revision and USP-800, 2016 revision, except as otherwise noted.

Note 2: Source: ANSI/ASHRAE/ASHE Standard 170-2013: Ventilation of Health Care Facilities. Extrapolated value for Outside Air. See tables 2 – 5 for minimum total ACH.

Note 3: Humidity range recommendation based on central supply clean workroom guidelines in Table 7.1 from ANSI/ASHRAE/ASHE Standard 170-2013: Ventilation of Health Care Facilities. Table 7.1 has no humidity requirement for pharmacies. USP 797 states that bulk or unformulated drug substances and added substances or excipients shall be stored in tightly closed containers under temperature, humidity, and lighting conditions that are either indicated in official monographs or approved by suppliers.

Note 4: Temperature range of <68F is designed for staff comfort while in PPE. Where buffer area is also used for storage, USP 797 recommends 68-77F

Note 5: Avoid condensation /trapping warm moist air on cold, impervious surfaces resulting in moisture accumulating on gypsum wall board

Table 2A: Standard Requirements for Low and Medium Risk CSPs
(Note 1)

Requirement Category	Standard Sterile CSP Requirement	Standard Sterile Haz. Drug Requirement
Types of PECs	LAFW, BSC	Class II BSC (A2, B1 and B2), Class III BSC, or CACI
Air Quality within PEC	ISO Class 5	ISO Class 5
PEC Exhaust (Note 2)	Not Specified	To Exterior
Air Quality in buffer area	ISO Class 7	ISO Class 7
Buffer Area Minimum total ACH (Note 3)	15 ACH (Note 4)	30 ACH **supply** air
Buffer and Ante-area Air filtration	HEPA (Note 5)	HEPA (Note 5)
Physical separation between Buffer, Ante-Areas, or other Compounding Areas	Required	Required
Buffer Area Air Movement and Pressure Differential (Note 6)	Positive (Out) 0.02 to 0.05" H_2O	Negative (In) 0.01 to 0.03" H_2O
Exhaust for buffer area	Not Specified	To Exterior (Note 4)
Ante Room Air Quality	ISO Class 8	ISO Class 7
Ante Room Minimum ACH	20 ACH Note 7	30 ACH HEPA filtered **supply** air
Storage area Air Movement	Not specified	Negative (In)
Storage Areas Minimum ACH	Not specified	12 ACH for antineoplastic requiring manipulation or any active pharmaceutical ingredient
Floor drains and sinks	No sinks or floor drains in ISO 7 buffer area	Sink is at least 1 meter from the PEC - A sink and eyewash station must be available for emergency access to water for removal of hazardous substances from skin and eyes.

Note 1: References USP 797, 2008 revision and USP-800, 2016 revision, except as otherwise noted.
Note 2: Outdoor air intakes and exhaust discharges shall meet the requirements of ANSI/ASHRAE/ASHE Standard 170-2013: Ventilation of Health Care Facilities, Section 6.3 to ensure adequate separation
Note 3: In order to maintain the specified relative pressure relationships, the PEC's rate of exhausted air must be considered. More than 15 ACH (Supply) may be required to overcome the PEC's exhaust rate
Note 4: This minimum of 15 ACH are to be provided exclusively by the room, with up to an additional 15 ACH to be provided by the PEC. A total of 30 ACH must be maintained.
Note 5: As an alternative to HEPA filters, MERV-14 rated filters may be used as the secondary filter bank at that Air Handling Unit if tertiary HEPA filters are installed within the portion of the HVAC system serving these spaces. (Based on principle from ANSI/ASHRAE/ASHE Standard 170-2013: Ventilation of Health Care Facilities, Table 6.4, Footnote C related to protective environment rooms)
Note 6: Rapid movements can create unacceptable turbulence in a critical area. Such movements disrupt the unidirectional airflow, presenting a challenge beyond intended cleanroom design and control parameters. The principle of slow, careful movement should be followed throughout the cleanroom.
Note 7: Source: FDA Aseptic Processing Guide recommends a minimum of 20 ACPH to maintain ISO 8.

Table 2B: Reduced Requirements for Low and Medium Risk CSPs in Compliant Isolators (Notes 1 and 2)

Requirement Category	Sterile CSP Reduced Requirement Allowances	Sterile Haz. Drug Reduced Requirement Allowances
Types of PECs	Compliant CAI or CACI (Note 2)	Compliant CACI (Note 2)
Air Quality within PEC	ISO Class 5	ISO Class 5
PEC Exhaust (Note 3)	Not Specified	To Exterior
Air Quality in buffer area	Unclassified	Unclassified
Buffer Area Minimum total ACH (Note 4)	12 ACH	12 ACH **supply** air
Buffer and Ante-area Air filtration (Note 5)	filters rated as 90% efficient filter (MERV 14)	filters rated as 90% efficient filter (MERV 14)
Physical separation between Buffer, Ante-Areas, or other Compounding Areas	Not required	Required
Buffer Area Air Movement and Pressure Differential (Note 6)	Positive (Out) 0.02 to 0.05" H_2O (Note 7)	Negative (In) 0.01 to 0.03" H_2O
Exhaust for buffer area	Not Specified	To Exterior (Note 3)
Ante Room Air Quality	Unclassified	Unclassified
Ante Room Minimum ACH	10	10
Storage area Air Movement	Not specified	Negative (In)
Storage Areas Minimum ACH	Not specified	12 ACH for antineoplastic requiring manipulation or any active pharmaceutical ingredient
Floor drains and sinks	Sink is at least 1 meter from the CAI/CACI	Sink is at least 1 meter from the PEC - A sink and eyewash station must be available for emergency access to water for removal of hazardous substances from skin and eyes.

Note 1: References USP 797, 2008 revision and USP-800, 2016 revision, except as otherwise noted.
Note 2: Compliant or Non-compliant with requirements in USP 797, 2008, as excerpted in Section 21-4.10.2.C in this document.
Note 3: Outdoor air intakes and exhaust discharges shall meet the requirements of ANSI/ASHRAE/ASHE Standard 170-2013: Ventilation of Health Care Facilities, Section 6.3 to ensure adequate separation.
Note 4: In order to maintain the specified relative pressure relationships, the PEC's rate of exhausted air must be considered. More than 15 ACH (Supply) may be required to overcome the PEC's exhaust rate
Note 5: Source: ANSI/ASHRAE/ASHE Standard 170-2013: Ventilation of Health Care Facilities. Extrapolated value for filtration
Note 6: Rapid movements can create unacceptable turbulence in a critical area. Such movements disrupt the unidirectional airflow, presenting a challenge beyond intended cleanroom design and control parameters. The principle of slow, careful movement should be followed throughout the cleanroom.
Note 7: Locations with a line of demarcation, (buffer area and ante area) shall be designed such that air will move/flow from "clean" to "less clean" areas)

Table 3: Requirements for Low Risk CSPs w/ BUD <12 hours (Note 1)

Requirement Category	Sterile CSP Requirement	Sterile Haz. Drug Requirement
Types of PECs	LAFW, BSC, Noncompliant CAI or CACI (Note 2)	Class II BSC (A2, B1 and B2), Class III BSC, or CACI
Air Quality within PEC	ISO Class 5	ISO Class 5
PEC Exhaust (Note 3)	Not Specified	To Exterior
Air Quality in buffer area	Unclassified	Unclassified
Buffer Area Minimum total ACH (Note 4)	15 ACH (Note 5)	12 ACH HEPA filtered **supply** air
Buffer and Ante-area Air filtration (Note 6)	filters rated as 90% efficient filter (MERV 14)	filters rated as 90% efficient filter (MERV 14)
Physical separation between Buffer, Ante-Areas, or other Compounding Areas	Not required	Required
Buffer Area Air Movement and Pressure Differential (Note 7)	Positive (Out) 0.02 to 0.05" H_2O (Note 8)	Negative (In) 0.01 to 0.03" H_2O (Note 8)
Exhaust for buffer area	Not Specified	To Exterior (Note 3)
Ante Room Air Quality	Unclassified	Unclassified
Ante Room Minimum ACH	10	10
Storage area Air Movement	Not specified	Negative (In)
Storage Areas Minimum ACH	Not specified	12 ACH for antineoplastic requiring manipulation or any active pharmaceutical ingredient
Floor drains and sinks	Sink is at least 1 meter from the PEC	Sink is at least 1 meter from the PEC - A sink and eyewash station must be available for emergency access to water for removal of hazardous substances from skin and eyes.

Note 1: References USP 797, 2008 revision and USP-800, 2016 revision, except as otherwise noted.
Note 2: Compliant or Non-compliant with requirements in USP 797, 2008, Section: Placement of Primary Engineering Controls, Paragraph 2, Bullets 1 - 3 regarding maintaining ISO Class 5 conditions during dynamic operating conditions.
Note 3: Outdoor air intakes and exhaust discharges shall meet the requirements of ANSI/ASHRAE/ASHE Standard 170-2013: Ventilation of Health Care Facilities, Section 6.3 to ensure adequate separation.
Note 4: In order to maintain the specified relative pressure relationships, the PEC's rate of exhausted air must be considered. More than 15 ACH (Supply) may be required to overcome the PEC's exhaust rate
Note 5: This minimum of 15 ACH are to be provided exclusively by the room, with up to an additional 15 ACH to be provided by the PEC. A total of 30 ACH must be maintained.
Note 6: Source: ANSI/ASHRAE/ASHE Standard 170-2013: Ventilation of Health Care Facilities. Extrapolated value for filtration
Note 7: Rapid movements can create unacceptable turbulence in a critical area. Such movements disrupt the unidirectional airflow, presenting a challenge beyond intended cleanroom design and control parameters. The principle of slow, careful movement should be followed throughout the cleanroom.
Note 8: Locations with a line of demarcation, (buffer area and ante area) shall be designed such that air will move/flow from "clean" to "less clean" areas).

Table 4: Requirements for High Risk CSPs(Note 1)

Requirement Category	Sterile CSP Requirement	Sterile Haz. Drug Requirement
Types of PECs	LAFW, BSC, CAI, CACI	Class II BSC (A2, B1 and B2), Class III BSC, or CACI
Air Quality within PEC	ISO Class 5	ISO Class 5
PEC Exhaust	Not Specified	To Exterior (Note 2)
Air Quality in buffer area	ISO Class 7	ISO Class 7
Buffer Area Minimum total ACH (Note 3)	15 ACH (Note 4)	30 ACH **supply** air
Buffer and Ante-area Air filtration	HEPA (Note 5)	HEPA (Note 5)
Physical separation between Buffer, Ante-Areas, or other Compounding Areas	Required	Required
Buffer Area Air Movement and Pressure Differential (Note 6)	Positive (Out) 0.02 to 0.05" H_2O	Negative (In) 0.01 to 0.03" H_2O
Exhaust for buffer area	Not Specified	To Exterior (Note 2)
Ante Room Air Quality	ISO Class 8	ISO Class 7
Ante Room Minimum ACH	20 ACH (Note 7)	30 ACH HEPA filtered **supply** air
Storage area Air Movement	Not specified	Negative (In)
Storage Areas Minimum ACH	Not specified	12 ACH for antineoplastics requiring manipulation or any active pharmaceutical ingredient
Floor drains and sinks	No floor drains or sinks in ISO Class 7 buffer area/zone	- No floor drains or sinks in buffer area/zone, and at least 1 meter from entrance to buffer room - A sink and eyewash station must be available for emergency access to water for removal of hazardous substances from skin and eyes.

Note 1: References USP 797, 2008 revision and USP-800, 2016 revision, except as otherwise noted.

Note 2: Outdoor air intakes and exhaust discharges must meet the requirements of ANSI/ASHRAE/ASHE Standard 170-2013: Ventilation of Health Care Facilities, Section 6.3 to ensure adequate separation.

Note 3: In order to maintain the specified relative pressure relationships, the PEC's rate of exhausted air must be considered. More than 15 ACH (Supply) may be required to overcome the PEC's exhaust rate

Note 4: This minimum of 15 ACH are to be provided exclusively by the room, with up to an additional 15 ACH to be provided by the PEC. A total of 30 ACH must be maintained.

Note 5: As an alternative to HEPA filters, MERV-14 rated filters may be used as the secondary filter bank at that Air Handling Unit, if tertiary HEPA filters are installed within the portion of the HVAC system serving these spaces. (Based on principle from ANSI/ASHRAE/ASHE Standard 170-2013: Ventilation of Health Care Facilities, Table 6.4, Footnote C related to protective environment rooms)

Note 6: Rapid movements can create unacceptable turbulence in a critical area. Such movements disrupt the unidirectional airflow, presenting a challenge beyond intended cleanroom design and control parameters. The principle of slow, careful movement should be followed throughout the cleanroom.

Note 7: Source: FDA Aseptic Processing Guide recommends a minimum of 20 ACPH to maintain ISO 8.

Table 5: Requirements for Non-sterile Hazardous Drug Manipulations
(Notes 1, 2, and 3)

Requirement Category	Non-Sterile Hazardous Drug Requirement
Types of PECs	BSC Class I or II, CVE or CACI
Air Quality within PEC	Unclassified
PEC Exhaust (Note 4)	To Exterior or redundant HEPA filters in series
Air Quality in buffer area	Unclassified
Buffer Area Minimum total ACH	12 ACH
Buffer and Ante-area Air filtration (Note 5)	filters rated as 90% efficient filter (MERV 14)
Physical separation between Buffer, Ante-Areas, or other Compounding Areas	Required
Buffer Area Air Movement and Pressure Differential (Note 6)	Negative (In) 0.01 to 0.03" H_2O
Exhaust for buffer area	To Exterior (Note 4)
Ante Room Air Quality	Unclassified
Ante Room Minimum ACH	10
Ante Room Pressure Differential to Unclassified Areas	Not Specified
Storage area Air Movement	Negative (In)
Storage Areas Minimum ACH	12 ACH for antineoplastic requiring manipulation or any active pharmaceutical ingredient
Floor drains and sinks	Sink is at least 1 meter from the PEC - A sink and eyewash station must be available for emergency access to water for removal of hazardous substances from skin and eyes.

Note 1: References USP 797, 2008 revision and USP-800, 2016 revision, except as otherwise noted.
Note 2: A PEC is not required if manipulations are limited to handling of final dosage forms (e.g., counting or repackaging of tablets and capsules) that do not produce particles, aerosols, or gasses.
Note 3: For occasional non-sterile HD compounding, a PEC used for sterile HD compounding (e.g., Class II BSC or CACI) may be used, but must be decontaminated, cleaned, and disinfected before resuming sterile HD compounding
Note 4: Outdoor air intakes and exhaust discharges shall meet the requirements of ANSI/ASHRAE/ASHE Standard 170-2013: Ventilation of Health Care Facilities, Section 6.3 to ensure adequate separation.
Note 5: Source: ANSI/ASHRAE/ASHE Standard 170-2013: Ventilation of Health Care Facilities. Extrapolated value for filtration
Note 6: Rapid movements can create unacceptable turbulence in a critical area. Such movements disrupt the unidirectional airflow, presenting a challenge beyond intended cleanroom design and control parameters. The principle of slow, careful movement should be followed throughout the cleanroom.

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Revision Notes: