HVAC Design of Compounding Pharmacies

White Paper Developed by

ASHRAE Standing Standard Project Committee 170,
Pharmacy Work Group

Peachtree Corners

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Introduction

This white paper provides recommendations for the HVAC design of compounding pharmacies located within health care facilities. This document aims to coordinate between United States Pharmacopeia (USP) publications and ANSI/ASHRAE/ASHE Standard 170, *Ventilation of Health Care Facilities*, to provide consolidated design parameters for engineers.

This white paper will cover the major areas of concern for HVAC design engineers, from basics on the International Standardization Organization's (ISO) classifications to humidity and temperature control within the compounding spaces. These discussions are meant to be informative. Always reference the local state boards of pharmacies having jurisdictions responsible for each individual project for the most up-to-date requirements of compounding pharmacies within a health care setting.

Background

The United States Pharmacopeia (USP) serves as the main referenced standard for designing and operating compounding pharmacies. For over 200 years, USP has worked to create standards for the world's medicines, dietary supplements, and foods. USP is an independent, scientific nonprofit organization focused on building trust in the supply of safe, quality medicines. USP's mission is to strengthen the global supply chain so that the medicines people rely on are available when needed and work as expected.

USP standards for compounding were first recognized in Section 503A of the *Food and Drug Administration (FDA) Modernization Act of 1997*, which states that a compounder must use bulk drug substances and ingredients that comply with the standards of an applicable USP chapter on pharmacy compounding. This directly resulted from multiple patient fatalities due to poor compounding practices.

The first USP compounding standard was released in 2004 to provide background and certification of general pharmaceutical compounding practices. The USP published Chapter 797 on November 27, 2007 and emphasized the individual training and evaluation of sterile compounding standards. In 2013, Congress enacted the *Drug Quality and Security Act (DQSA) of 2013* to clarify the FDA's authority over drug compounding. This guidance states that compounded preparations by a licensed pharmacist or physician qualify for an exemption from the requirements of a new drug application if they are compounded in compliance with the USP chapters on pharmacy compounding. The guidance specifically references USP General Chapter <795> Pharmaceutical Compounding—Nonsterile Preparations (USP 795) and USP General Chapter <797> Pharmaceutical Compounding—Sterile Preparations (USP 797).

On February 1, 2016, USP General Chapter <800> Hazardous Drugs—Handling in Healthcare Settings was published. This chapter was meant to supplement the hazardous drug requirements found in USP 797. In 2019, USP released a proposed revision of USP General Chapter <797> Pharmaceutical Compounding—Sterile Preparations, which now references USP 800 for hazardous drug preparations, and USP General Chapter <825> Radiopharmaceuticals—Preparation, Compounding, Dispensing, and Repackaging was published at the same time. Subsequently, USP also adopted revisions to General Chapters 795 and 797 on May 1, 2020, and USP General Chapter 800 on July, 1, 2020. Furthermore, on November 1, 2022, USP <797> was republished.

For reference, from USP General Notices and Requirements, "Applicable general chapters" means general chapters numbered below 1000 or above 2000 that are made applicable to an article through reference in General Notices, a monograph, or another applicable general chapter numbered below 1000. Where the requirements of a monograph differ from the requirements specified in these General Notices or an applicable general chapter, the monograph requirements apply and supersede the requirements of the General Notices or applicable general chapters, whether or not the monograph explicitly states the difference. General chapters numbered 1000 to 1999 are for informational purposes only. They contain no mandatory tests, assays, or other requirements applicable to any official article, regardless of citation in a general chapter numbered below 1000, a monograph, or these General Notices. General chapters numbered above 2000 apply only to articles that are intended for use as dietary ingredients and dietary supplements. General chapter citations in NF monographs refer to USP general chapters.

Within the USP standards, ISO classifications are used to identify the cleanliness of each designated space within the health care pharmacy setting. ISO 14644-1, *Classification of Air Cleanliness by Particle Concentration*, provides particle counts for various ISO classifications. The first document of the ISO 14644 series was published in 1999 (ISO 14644-1) and has been updated over the years, with the current version being ISO 14644-1:2015. The Controlled Environmental Testing Association (CETA) also plays a key role in pharmacy compounding requirements. CETA created testing guidelines to maintain a higher level of integrity; improve testing quality, accuracy, and repeatability; and aid in the understanding and practical application of complex standards and guidelines, including those of USP.

Sterile Compounding Secondary Engineering Control (SEC) Recommendations

Two main buffer areas, referred to as secondary engineering controls in USP 797 and 800, typically separated by a common anteroom, constitute a cleanroom suite of ISO Class 7 cleanliness for compounding hazardous and nonhazardous medications. A buffer area is a cleanroom that generally houses a primary engineering control (laminar airflow workbench, biosafety cabinet, or compounding aseptic isolator) in which medications are compounded for intravenous administration.

The following bulleted lists represent ASHRAE's recommendations for the type of ISO Class 5 device to be used, as well as the recommended temperature, humidity, air diffusion, air filtration, air change rate, and pressure relationships for the space.

Buffer/Anteroom/Storage Room Requirements

Acceptable ISO Class 5 Unidirectional Flow Containment—Primary Engineering Control (C-PEC)

- Nonhazardous Buffer Room
  - Laminar airflow workbench (vertical or horizontal)
  - Biosafety cabinet (Class II, A2 not exhausted)
  - Compounding aseptic isolator (CAI) positive pressure recirculating
- Hazardous Buffer Room
  - Biosafety cabinet (Class II, Type A2 or B2 exhausted)
  - CAI (externally exhausted)

Acceptable Temperature and Humidity

- **For USP 797 Spaces (Nonhazardous Compounding Rooms)**
  - The temperature must be monitored and recorded at least daily. The monitoring device must be tested for accuracy at least annually and calibrated or replaced as required.
  - The temperature in the suite should be maintained at or below 20°C (68°F) at a relative humidity of 60% or less. Rooms designed to 18.3°C (65°F) are common. The maximum humidity value mini-

mizes microbial growth risk and maintains product quality, especially with powder-based drugs.
    - While not mentioned in USP 797, a minimum relative humidity of 30% is recommended to maintain occupant comfort as well as minimize potential for the static electricity within the cleanroom, which affects particle movement and removal.
    - If the suite is used for storage, USP 659 requirements may also come into play (see USP 795 room recommendations for additional information). If this is the case, tight control over the variability of temperature and humidity may be required as the minimum temperature in the range for storage is the maximum temperature in the range for the cleanroom.
- **For USP 800 Spaces (Hazardous Compounding Rooms)**
    - USP 800 spaces must meet USP 797 requirements for temperature and humidity.
- **For USP 825 Spaces (Radiopharmaceuticals)**
    - The temperature must be monitored and recorded at least daily. The monitoring device must be tested for accuracy at least annually and calibrated/replaced as required.
    - The temperature in the suite should be maintained at or below 25°C (77°F) and at a relative humidity of 60% or less.
    - While not mentioned in USP 825, a minimum relative humidity of 30% is recommended to maintain comfort as well as minimize the potential for static electricity within the cleanroom, which affects particle movement and removal.
    - If the suite is used for storage, USP 659 requirements may also come into play (see USP 795 room recommendations for additional information).

Air Pattern and Diffuser Location

- Diffuser type: ASHRAE Group E, nonaspirating laminar flow with integral HEPA room side replaceable filter (99.97% minimum).
- For nonhazardous sterile compounding (USP 797 spaces), it is recommended to use ceiling-mounted HEPA fan filter units (FFUs) or a local recirculating fan through ceiling-mounted HEPA-filtered laminar flow diffusers and low returns. This is done to increase air change rates while minimizing air-handling unit size.
    - FFUs are recommended to be ducted and/or within a sealed and clean plenum with no other infrastructure within it except required fire protection piping.
    - Returns to FFUs are recommended to be independent of the air-handling unit return or hazardous exhaust ductwork.
- For hazardous sterile compounding (USP 800 spaces), recirculating FFUs may be considered in addition to the recommended minimum exhaust from the room for added cleanliness. Consideration should be given to the volatility of the hazardous compounds in use, the effec-

tiveness of HEPA filtration on the hazardous compounds in use, and the effective extraction rate from the room. A risk assessment process may prove beneficial in determining if recirculation is appropriate.

- Best diffuser and grille placement practices should be used to maintain as clean a space as possible. Recommended practices include:
  - Supply at the ceiling with low wall return (nonhazardous buffer and anteroom) or low wall exhaust (hazardous buffer and anteroom).
    - For a hazardous buffer room, when all the air changes are met by the airflow through the primary engineering control (PEC), an additional low wall exhaust grille is not required in addition to the airflow through the PEC, so long as it can be proven through engineering analysis or smoke test that stagnant air will not be created within the clean space.
  - Locating supply outlets such that air is distributed as evenly as possible throughout the space.
  - Locating return/exhaust air inlets on at least two walls along the room's long dimensions to ensure maximum airflow uniformity.
  - Locating inlets so that return/exhaust openings are not blocked by equipment and furniture.
- When cleanroom spaces include sinks, such as an anteroom, locating low wall return (or exhaust) grilles near the sink is recommended to capture airborne contaminates as efficiently as possible before spreading out throughout the room.
- It is not recommended to locate refrigerators in buffer areas; however, USP allows hazardous medication refrigerators to be located within the hazardous buffer area. A low wall exhaust must be provided adjacent to the refrigerator when located in the buffer area.
- HEPA filters should be room-side replaceable unless space is available for top-side access.
- HEPA filters and/or ductwork should have challenge ports to allow for HEPA filter leakage testing for room certification.
- Air supplied to a secondary engineering control (SEC) must be distributed to keep temperature gradients and air currents to a minimum. Air outlets must not discharge in a way that disrupts the face velocity of the C-PEC (i.e., a laminar airflow workbench or biological safety cabinet). Where independent HEPA FFU recirculating units are used to increase airflow in the room, they must be carefully evaluated to ensure room temperature/humidity and temperature uniformity are not impacted.

Acceptable Filtration Rate

- HEPA 99.97% minimum located in room at the ceiling. Using minimum MERV 14 upstream of HEPA filters in air-handling equipment is recommended to minimize HEPA filter replacement frequency.

Acceptable Air Change Rate

- Calculate air change rates such that the room maintains ISO 7 air cleanliness. While USP recommends 30 ACH as a minimum, 30 ACH may not maintain ISO 7 air cleanliness conditions, and the designer should consider higher air change rates (USP 1116 provides guidance suggesting a minimum of 50 ACH). In rooms that may include a sink, such as anterooms, consideration should be provided to increase the air change rate above the minimum value to accommodate for contaminants that may be provided by the sink and drain assembly. In nonsterile hazardous rooms and hazardous drug storage rooms, the minimum ACH required is 12. The minimum ACH is based on exhaust air.
- The occupancy of the space is typically one person per PEC device. The per-person minimum outdoor air rate R_p and area-based outdoor air rate R_a can follow ASHRAE Standard 62.1's pharmacy (prep area) criteria of R_p = 5 cfm/person and R_a = 0.18 cfm/ft^2 (ASHRAE 2022).

Acceptable Room Differential Pressure

- Nonhazardous buffer room and anteroom: +0.020 in. w.c. in alignment with IEST-RP-CC006 (IEST 2004)
- Anteroom to unclassified work area: +0.020 in. to +0.050 in.
- Hazardous buffer room and hazardous drug (HD) storage room: –0.010 in. to –0.030 in. with respect to adjacent anteroom
- The target ΔP pressures are recommended to be set higher than the minimum values indicated to allow for fluctuations in ΔP during normal operation of the facility and avoid nuisance alarms. Room ΔPs tend to oscillate around a band instead of a straight line.
- HD drug storage room: ≤–0.010 in.
- To the extent possible, achieve pressure differentials between rooms using gaps around doors and door undercut or door sweeps.
- It is recommended to locate the pressure monitor sensor above the door frame to avoid interference from PECs or other HVAC distributions.

Ventilation Criteria

- One hundred percent exhaust with adequate outdoor air (OA) to compensate for the exhausted air is recommended for hazardous, and recirculating systems are recommended for nonhazardous. For hazardous, recirculating FFUs may be considered in addition to the required minimum exhaust from the room for added cleanliness. Consideration should be given to the volatility of the hazardous compounds in use, the effectiveness of HEPA filtration on the hazardous compounds in use, and the effective extraction rate from the room. A risk assessment process may prove beneficial in determining if recirculation is appropriate. If multiple recirculated units are used in classified spaces, return from these spaces is not recommended to be recirculated in areas where there is a risk of cross-contamination.

Pass-Through

- A material pass-through chamber is a type of airlock designed to transfer materials between rooms of differing risk, classification, and/or differential pressure to reduce the risk of contamination. A cart pass-through chamber is installed at the floor level.
- Pass-throughs shall be fully gasketed with double interlocked doors made from appropriate materials that can withstand cleaning chemicals without corrosion.

Nonsterile Compounding Secondary Engineering Control (SEC) Recommendations

The following bulleted lists represent ASHRAE's recommendations for the type of PEC to be used as well as the recommended temperature, humidity, air diffusion, air filtration, air change rate, and pressure relationships for the SEC.

Primary Engineering Control (C-PEC)

- **Nonhazardous Compounding.** The following C-PECs are only required when compounding could generate airborne particles. This must be assessed and stated within the facility standard operating procedure (SOP) when required.
  - Containment ventilated enclosure (CVE)
  - Laminar airflow workbench
  - Biosafety cabinet (Class II, A2 not exhausted)
  - Compounding aseptic isolator (CAI) positive pressure recirculating
- **Hazardous Compounding**
  - Externally vented and HEPA filtered
  - CVE
  - Biosafety cabinet (Class I, Class II)
  - Compounding aseptic containment isolator (CACI)

Acceptable Temperature and Humidity

- **For USP 795 Spaces (Pharmacy Workroom, Receiving, Storage)**
  - Temperature must be monitored and recorded at least daily. Monitoring device must be tested for accuracy at least annually and calibrated or replaced as required.
  - Temperature and humidity levels must meet the storage requirements indicated by the specific drug monographs published by USP. These generally require drugs to be stored to a "controlled room temperature," which is defined in USP 659 as 20°C to 25°C (68°F to 77°F). If a specific drug must be stored in a "dry place," this is defined by USP 659 as not exceeding 40% RH at 20°C (68°F). The "dry place" requirement in hospital/healthcare pharmacies is rare and generally limited to larger pharmacy production centers where bulk materials are in use.

- **For USP 800 Spaces (Hazardous Compounding Rooms)**
  - USP 800 spaces must meet USP 795 requirements for temperature and humidity.
- **For USP 825 Spaces (Radiopharmaceuticals)**
  - Temperature must be monitored and recorded at least daily. Monitoring device must be tested for accuracy at least annually and calibrated or replaced as required. .
  - Temperature in the suite should be maintained at or below 25°C (77°F) at a relative humidity of 60% or less. The maximum humidity value is to minimize risk of microbial growth and to maintain product quality, especially with powder-based drugs.
  - While not mentioned in USP 825, a minimum relative humidity of 30% is recommended to maintain comfort as well as minimize potential for static electricity within the cleanroom, which affects particle movement and removal.
  - If the suite is used for storage, the requirements of USP 659 may also come into play (see USP 795 room recommendations for additional information).

Air Pattern and Diffuser Location

- Type: ASHRAE Group A or E supply air distribution
- Best practices for diffuser and grille placement should be employed with the intent of maintaining as clean a space as possible. Recommended practices include:
  - Supply at ceiling with low wall or ceiling return (nonhazardous compounding room) or low wall exhaust (hazardous compounding room or hazardous drug storage room).
  - Locate inlets such that equipment and furniture does not block return/exhaust openings.
  - Return/exhaust grilles shall be located behind refrigerators and equipment that generate particulate or air contaminates.
- Air supplied to an SEC must be distributed to keep temperature gradients and air currents to a minimum. Air outlets must not discharge into the face of C-PEC (i.e., a laminar airflow workbench or biological safety cabinet) such that the protective environment of the device is compromised.

Acceptable Filtration Rate

- Minimum MERV 14 located in air-handling equipment is recommended and required within some applications as indicated in ASHRAE Standard 170 (ASHRAE 2021).

Acceptable Air Change Rate

- In nonsterile hazardous rooms and hazardous drug storage rooms, the minimum ACH required is 12. The minimum ACH is based on exhaust air.
- The traffic in the space is typically limited to just the person working at the PEC. The occupancy of the space can be assumed to be one per PEC device. The per person minimum outdoor air rate *Rp* and area-based outdoor air rate can follow ASHRAE Standard 62.1's pharmacy (prep area) criteria of *Rp* = 5 cfm/person, *Ra* = 0.18 cfm/ft^2 (ASHRAE 2022).

Acceptable Room Differential Pressure

- Nonsterile, nonhazardous, compounding room: +0.010 in. w.c.
- Nonsterile, hazardous compounding room and HD drug storage room: –0.010 in. to –0.030 in. with respect to adjacent room.
- The target Δ*P* pressures are recommended to be set higher than the minimum values indicated, to allow for fluctuations in Δ*P* during normal operation of the facility and avoid nuisance alarms. Room Δ*Ps* tend to oscillate around a band instead of a straight line.
- To the extent possible, achieve pressure differentials between rooms using gaps around doors and door undercut.
- It is recommend to locate the pressure monitor sensor above a door frame to avoid interference from PECs or other means of air distribution within the room.

Ventilation Criteria

- One hundred percent exhaust with adequate outdoor air (OA) to compensate for the exhausted air is recommended for hazardous, and recirculating systems are recommended for nonhazardous. For hazardous, recirculating FFUs may be considered in addition to the required minimum exhaust from the room for added cleanliness. Consideration should be given to the volatility of the hazardous compounds in use, the effectiveness of HEPA filtration on the hazardous compounds in use, and the effective extraction rate from the room. A risk assessment process may prove beneficial in determining if recirculation is appropriate. If multiple recirculated units are used in classified spaces, return from these spaces is not recommended to be recirculated in areas where there is a risk of cross-contamination.

Sterile Segregated Compounding Area (SCA) Pharmacy Recommendations

A containment-segregated compounding area (C-SCA) is defined in USP 797 as "a designated space, either a demarcated area or room, that is restricted to preparing low-risk level compounded sterile preperations (CSPs) with 12-hour or less beyond-use date (BUD). Such area shall contain a device that provides unidirectional airflow of ISO Class 5 (see Table 1 in USP General Chapter <797>) air quality for preparation of CSPs and shall be void of activities and materials that are extraneous to sterile compounding." It is important to note that the 12-hour BUD may have a shorter time duration based on the medications being compounded, per the medication manufacturer's directions. A C-SCA is not recommended for high-risk HD compounding.

The ISO Class 5 environment is provided by a containment primary engineering control (C-PEC), which may be a laminar airflow workbench, biosafety cabinet, or compounding aseptic isolator. Locate the C-PEC in a space away from operable windows or doors to the exterior of the building or other areas of high traffic flow and away from circulating air currents. The absence of an ISO 7 environment surrounding the C-PEC device may increase the potential for airborne microbial growth. The environment surrounding the device should therefore be considered to have an air cleanliness equivalent to or greater than inpatient care areas of a health care facility. Follow proper personnel cleansing and garbing in compliance with USP General Chapters <797> and <800> to help minimize the airborne transfer of contaminants from the personnel working in the space and should be coordinated with staff during design.

The following bulleted lists represent ASHRAE's recommendation for the type of ISO Class 5 device to be used as well as the recommended temperature, humidity, air diffusion, air filtration, air change rate, and pressure relationships for the space.

Nonhazardous Sterile Segregated Compounding Area

Acceptable ISO Class 5 Containment—Primary Engineering Control (C-PEC)

- Laminar airflow workbench (vertical or horizontal)
- Biosafety Cabinet (Class II, A2 not exhausted)
- Compounding Aseptic Isolator (CAI) Positive Pressure Recirculating

Acceptable Temperature and Humidity

- Maximum 68°F (20°C)
- Maximum 60% RH
- Minimum humidity of 25% recommended.

Air Pattern and Diffuser Location

- Type: ASHRAE Group A or E.
- Supply at ceiling, return at ceiling or low wall.
- Air supplied to a SEC must be distributed to keep temperature gradients and air currents to a minimum. Air outlets must not discharge into the face of C-PEC (i.e., a laminar airflow workbench or biological safety cabinet) such that the protective environment of the device is compromised.

Acceptable Filtration Rate

- Minimum MERV 13
- Can be located at air-handling unit or at air delivery point

Acceptable Air Change Rate

- Minimum six total air changes per hour
- The space is limited in traffic to just the person working at the PEC. The occupancy of the space is therefore easily determined—one per PEC device. The per-person minimum outdoor air rate *Rp* and area-based outdoor air rate can follow ASHRAE Standard 62.1's pharmacy (prep area) criteria of *Rp* = 5 cfm/person, *Ra* = 0.18 cfm/ft^2 (ASHRAE 2022). Occupant density should not be less than 10 people per 1000 for determining occupants in the room.

Acceptable Room Differential Pressure

- Positive to adjacent spaces

Hazardous Sterile Segregated Compounding Area

Acceptable ISO Class 5 Containment—Primary Engineering Control (C-PEC)

- Biosafety Cabinet (Class II, A2 or B2, exhausted)
- Compounding aseptic containment isolator (CACI) externally exhausted

Acceptable Temperature and Humidity

- See Nonhazardous Sterile SCA criteria.

Air Pattern and Diffuser Location

- Type: ASHRAE Group A or E.
- Supply at ceiling, room fully exhausted. Low wall exhaust recommended for maximum air change rate effectiveness.
- Air supplied to a SEC must be distributed to keep temperature gradients and air currents to a minimum. Air outlets must not discharge into the face of C-PEC (i.e., a laminar airflow workbench or biological safety cabinet) such that the protective environment of the device is compromised.

Acceptable Filtration Rate

- Minimum MERV 13.
- Can be located at air-handling unit or at air delivery point.

Acceptable Air Change Rate

- Minimum 12 total air changes per hour, exhaust. Exhaust system should be dedicated to the purpose of hazardous drug exhaust. The hazardous drug exhaust may also serve the hazardous drug storage area, and the C-PEC device where acceptable by the AHJ. NSF 49 Annex I recommends Type B2 hoods be exhausted by a dedicated exhaust fan. Redundant exhaust fans are recommended.
- Outdoor air change rate: See Nonhazardous Sterile SCA criteria.

Acceptable Room Differential Pressure

- –0.010 in. to –0.030 in. to adjacent spaces.

Nonsterile Segregated Compounding Area (SCA) Pharmacy Recommendations

The following bulleted lists represent ASHRAE's recommendation for the type of ISO Class 5 device to be used as well as the recommended temperature, humidity, air diffusion, air filtration, air change rate, and pressure relationships for the space.

Nonhazardous Nonsterile Segregated Compounding Area

Acceptable Containment—
Primary Engineering Control (C-PEC)

The following C-PEC's are only required when compounding could generate airborne particles. This must be assessed and stated within the facility SOP when required.

- Containment ventilated enclosure (CVE)
- Biosafety cabinet (Class II, A2 not exhausted)
- Compounding aseptic isolator (CAI) positive pressure recirculating

Acceptable Temperature and Humidity

- Maximum 68°F (20°C). The purpose of the temperature is due to the personnel's garb that leads to discomfort when compounding at warmer space temperatures.
- Maximum 60% RH.
- Minimum humidity of 25% recommended.

Air Pattern and Diffuser Location

- Type: ASHRAE Group A or E.
- Supply at ceiling, return at ceiling or low wall.
- Air supplied to a SEC must be distributed to keep temperature gradients and air currents to a minimum. Air outlets must not discharge into the face of C-PEC (i.e., a Laminar airflow workbench or biological safety cabinet) such that the protective environment of the device is compromised.

Acceptable Filtration Rate

- Minimum MERV 8.
- Can be located at air handling unit, or at air delivery point.

Acceptable Air Change Rate

- Minimum 6 total air changes per hour.
- The space is limited in traffic to just the person working at the PEC. The occupancy of the space is therefore easily determined, 1 per PEC device. The per person minimum outdoor air rate *Rp* and area-based outdoor air rate can follow ASHRAE Standard 62.1's pharmacy (prep area) criteria. *Rp* = 5 cfm/person, *Ra* = 0.18 cfm/ft^2. Occupant density should not be less than 10 people per 1000 for determining occupants in the room.

Acceptable Room Differential Pressure

- ≥ +0.01 in. w.c.

Hazardous Nonsterile Segregated Compounding Area

Acceptable Containment—
Primary Engineering Control (C-PEC)

- Containment ventilated enclosure (CVE)
- Biosafety cabinet (Class II, A2, or B2 exhausted)
- Compounding Aseptic Isolator (CACI) Externally Exhausted.

Acceptable Temperature and Humidity

- See Nonhazardous Sterile SCA criteria.

Air Pattern and Diffuser Location

- Type: ASHRAE Group A or E.
- Supply at ceiling, room full exhausted. Low wall exhaust recommended for maximum air change rate effectiveness.
- Air supplied to a SEC must be distributed to keep temperature gradients and air currents to a minimum. Air outlets must not discharge into the face of C-PEC (i.e., a laminar airflow workbench or biological safety cabinet) such that the protective environment of the device is compromised.

Acceptable Filtration Rate

- See Nonhazardous Sterile SCA criteria.

Acceptable Air Change Rate

- Minimum 12 total air changes per hour, exhaust. Exhaust system should be dedicated to the purpose of Hazardous drug exhaust. The hazardous

drug exhaust may also serve the Hazardous drug storage area, and the C-PEC device where acceptable by the AHJ. NSF 49 Annex I recommends Type B2 hoods be exhausted by a dedicated exhaust fan. Redundant exhaust fans are recommended.
- Outdoor air change rate: See Nonhazardous Sterile SCA criteria.

Acceptable Room Differential Pressure

- –0.010 in. to –0.030 in. to adjacent spaces.

Ductwork Material Recommendations

Pharmaceutical applications have proven that G60 galvanized steel is an adequate product for applications of supply, return, and exhaust ductwork under normal operations. Where surfaces may become wet from condensation, such as cooling coils, drain pans, etc., the condensate due to cleaning chemicals can become corrosive to galvanized steel. Where condensate may come in contact with metallic materials, use appropriate aluminum or stainless steel. Compounding drugs do not have a corrosive attribute to them that warrants the usage of stainless steel or coated ductwork. Furthermore, it is recommended that all ductwork within a pharmaceutical compounding application receives duct sealant in accordance with the Sheet Metal and Air Conditioning Contractors' National Association's (SMACNA) duct seal class A to minimize leakage. Specifically, provide duct sealant at all joints, seams, and all applicable wall penetrations with ductwork seams and joints. It is acceptable to provide welded seams on the ductwork; however, welded seams are considered to be beyond the minimum needs of care for compounding pharmacies. Welded joints are known to be more reliable and durable as compared to sealant-filled, mechanically locked joints.

It is recommended during the design stage for the owner to provide a list of products with material safety data sheets (MSDS) that will be compounded within the hoods, as well as those used for cleaning of the spaces, to allow the design team to verify the appropriate ductwork material is specified. Additionally, it is recommended for the owner to only clean ductwork with cleaning materials and decontamination gases that will not lead to corrosion on the ductwork and sealant material provided.

Intake and Exhaust Clearance Recommendations

Intake air for pharmacy areas should be as free of contaminants as possible to protect compounded medications from exposure and extend the life of filtration media required for some compounding areas. ASHRAE Standards 62.1 and 170, as well as consensus mechanical codes, outline the requirements for the location of air intakes in relation to potential contaminant sources. Based on these references, intakes should generally be located at least 25 ft from all known sources of contamination. However, the required distance varies by type and spatial relationship to the intake.

Environmental air from general pharmacy and compounding pharmacy areas that are not used to compound hazardous drugs or radiopharmaceuticals is nonhazardous and may be classified as Class 2 air under the classification system provided by ASHRAE Standard 62.1 (ASHRAE 2022). Air exhausted from hazardous-drug-compounding hoods, HD buffer rooms, and HD storage areas may contain elevated levels of compounds that may be harmful and should be considered Class 4 air under the classification system provided by ASHRAE Standard 62.1, similar to laboratory hood exhaust and chemical storage rooms. HD room air may be reclassified using ASHRAE Standard 62.1's documented method and recirculated within the space of origin through HEPA FFUs to increase the particulate removal rate within the space to aid in maintaining the required ISO cleanliness level.

ASHRAE Standards 62.1 and 170 and other consensus mechanical codes outline requirements for protecting air intakes and building openings from exhaust sources. Care should be taken when locating exhaust sources from hazardous drug areas to ensure air is not re-entrained and personnel working in the vicinity are properly protected from exposure. This may include distancing exhaust from intakes and openings, elevating exhaust discharge above areas of concern, increasing dilution rates to safe levels, and/or employing containment measures. Equipment utilized for the exhaust from these sources should be clearly labeled as to the function and nature of the hazard.

Air exhaust from radiopharmaceutical compounding areas, including the compounding hood, buffer room, restricted areas, and storage spaces, may contain radioactive isotopes. This air should be considered Class 4, just like HD air

sources. Additional protective measures may be required based on the radiopharmaceuticals in use. The radiation safety consultant or facility radiation safety officer should be consulted to determine these exhaust sources' hazard levels and physical control requirements.

Refer to NRC Regulatory Guide 8.18 for further information.

Emergency Power Recommendations

To be prepared for the event of a power failure, a facility must develop a plan that governs pharmacy operations upon the loss of power, including what is the allowable time prior to requiring a terminal clean. A reliable backup power source is critical to maintaining operations within a pharmacy. All compounding pharmacies should have an emergency preparedness plan outlined at the onset of the design of a facility that includes confirmation of the following:

- All components on emergency backup power (e.g., air conditioning, lighting, door operators, hoods, convenience receptacles, building automation controls, electronic pressure monitors, electronically operated faucets, electric hand dryers, etc.)
- UPS power requirements
- Generator capacity
- Required on-site fuel oil storage capacity and generator runtime capability

The PEC and room air-conditioning systems must be on the essential electrical system (EES) if the facility is a licensed care hospital. The pharmacy is considered an essential function of the facility unless the facility performs a risk assessment to authorize excluding the pharmacy from the essential services.

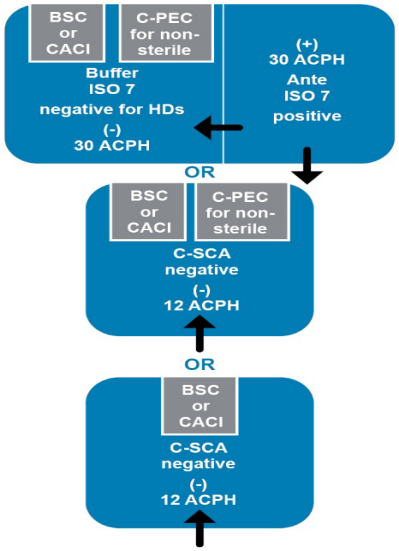
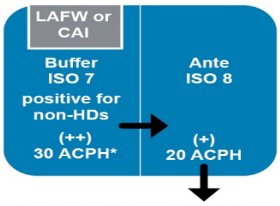
HVAC Equipment Considerations/ Recommendations

- Dedicated air-handling equipment for cleanroom compounding pharmacy spaces is recommended. Segregated compounding areas can share other building air-handling infrastructure. When dedicated AHUs cannot be provided for the cleanroom compounding spaces, it is recommended to utilize automatic airflow regulating devices (i.e., air valves) to regulate the airflow when unsteady airflow is provided to the rest of the area served by the AHU.
- Locate equipment in easily serviceable locations. Locating major equipment, including air terminals (VAV boxes, air valves, etc.), outside the classified boundary to allow maintenance staff easy access to equipment and devices is recommended. Access to field calibration, testing, and repair should be considered.
- Individual rooms should receive dedicated temperature sensors/humidity sensors, pressure monitors, and associated zone controls. It is recommended to provide centralized monitoring panels outside the cleanrooms to allow end users and maintenance staff to observe and document conditions without entering the clean rooms.
- Select sensors for space temperature/humidity and pressure for high accuracy and repeatability; they should be National Institute of Standards and Technology (NIST) traceable, located for easy access and recalibration and not be placed next to biological safety cabinet (BSCs) or heat-producing equipment where they may impact temperature control and uniformity, and be resistant to damage from cleaning chemicals.
- Room differential pressure should be measured to the nearest thousandth of an inch to confirm compliance within the required range.
    - Example: Required pressure range (Between –0.01 in. w.c. and –0.03 in. w.c.). Acceptable pressure range must be measured to the thousandth of an inch—between 0.010 in. and 0.030 in. Specifically, it is unacceptable to rely on rounding to the nearest hundredth (between 0.0050 in. and 0.0349 in.) to allow the system to operate at a broader range.
- Redundancy within the equipment such as N+1 fan redundancy is highly recommended.
- Direct-drive motors without the ability for fan belts to slip/break/wear are highly recommended.

- In hazardous drug storage rooms and hazardous drug compounding rooms, it is acceptable for low wall exhaust grilles to be shared with the same exhaust fan as hoods (including when they are in separate rooms) where acceptable by the authority having jurisdiction (AHJ). A means of automatic balancing (i.e., air valves) should be provided to allow consistent airflow levels for each exhaust device. Note for design consideration: NSF 49 Annex I recommends Type B2 hoods be exhausted by a dedicated exhaust fan.
- During the project's design phase, review having redundant exhaust fans or having a plan for equipment replacement or repair with the facility owner/operator to ensure their expectations are met.

Environmental Conditions Out of Tolerance Range

It is anticipated and acceptable that room pressurization and temperature will fluctuate outside of the design range during activities such as opening/closing doors for the operation of the space and during HVAC equipment shutdown during a fire alarm and transfer to emergency backup power. Being out of the design tolerance range for minutes as these activities occur is within the industry standard for acceptance. If prolonged operation out of the design tolerances persists after these activities cease, the facilities, operating, design, and construction team members should be consulted to remediate the issue. The owner should set forth and provide the acceptance criteria for tolerance of operating outside of the design parameters during these conditions before the design of a compounding pharmacy. Temperature, humidity, and pressure are recommended parameters. If the sensed value exceeds the requirements of the drugs compounded within the facility by up to 5% for a period of greater than six hours, the facility engineer should take corrective action and adjust the mechanical system. If the excursion of up to 5% occurs for a total of 24 hours, consider halting operation. If the excursion is greater than 5%, consider halting operation.

Use	Optimal Primary and Secondary Control	Limitations Primary and Secondary Control	Notes for Limitations
Both sterile HD and nonsterile HD compounding	A separate room for sterile and nonsterile compounding is recommended.		For rooms used for both sterile and nonsterile compounding, particle-generating activity must not be performed when sterile compounding is in process. C-PECs must be at least 1 meter apart. Maximum BUD as described in <797> for segregated compounding area. Maximum BUD as described in <797> for segregated compounding area.
Sterile NonHD compounding	 *30 ACPH Combined—Minimum 15 ACPH from LAFW and 15 ACPH from room air		

[a]the arrows indicate direction of airflow

Figure 1 Examples of Drug Compounding Areas Designs.

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