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Compounding Pharmacies

Background

- USP 797 - Sterile Compounding
  - Purpose: General Protection of sterile compounds and spaces from contamination
  - First published in 2004, latest revision released in 2008
- USP 800 - Hazardous Drugs
  - Purpose: Guide for the safe handling of hazardous drugs
  - Official implementation date was December 1, 2019
- Revision to 797 were made to harmonize with USP 800
  - The long anticipated revised USP 797, was published on November 1, 2022. USP 797 becomes official on November 1, 2023, allowing 1 year for final adoption and implementation of these standards. Additionally, USP 800 becomes enforceable on the same date.

Compounding Pharmacies

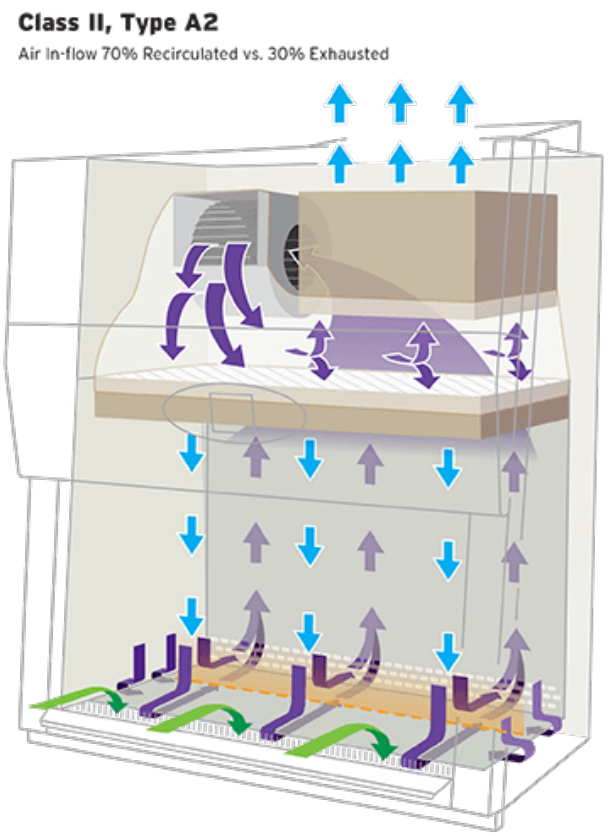
Definitions

- Compounding Sterile Preparation (CSP)
  - A substance (medication) that is not commercially available in the strength, concentration or form needed for a specific patient
- Hazardous (Harmful) Drug (HD)
  - Any drug identified as hazardous or potentially hazardous on the basis of at least one of the following criteria:
    - Carcinogenicity
    - Teratogenicity or developmental toxicity
    - Reproductive toxicity in humans
    - Organ toxicity at low doses in humans or animals
    - Genotoxicity or new drugs that mimic existing HDs in structure or toxicity

Compounding Pharmacies

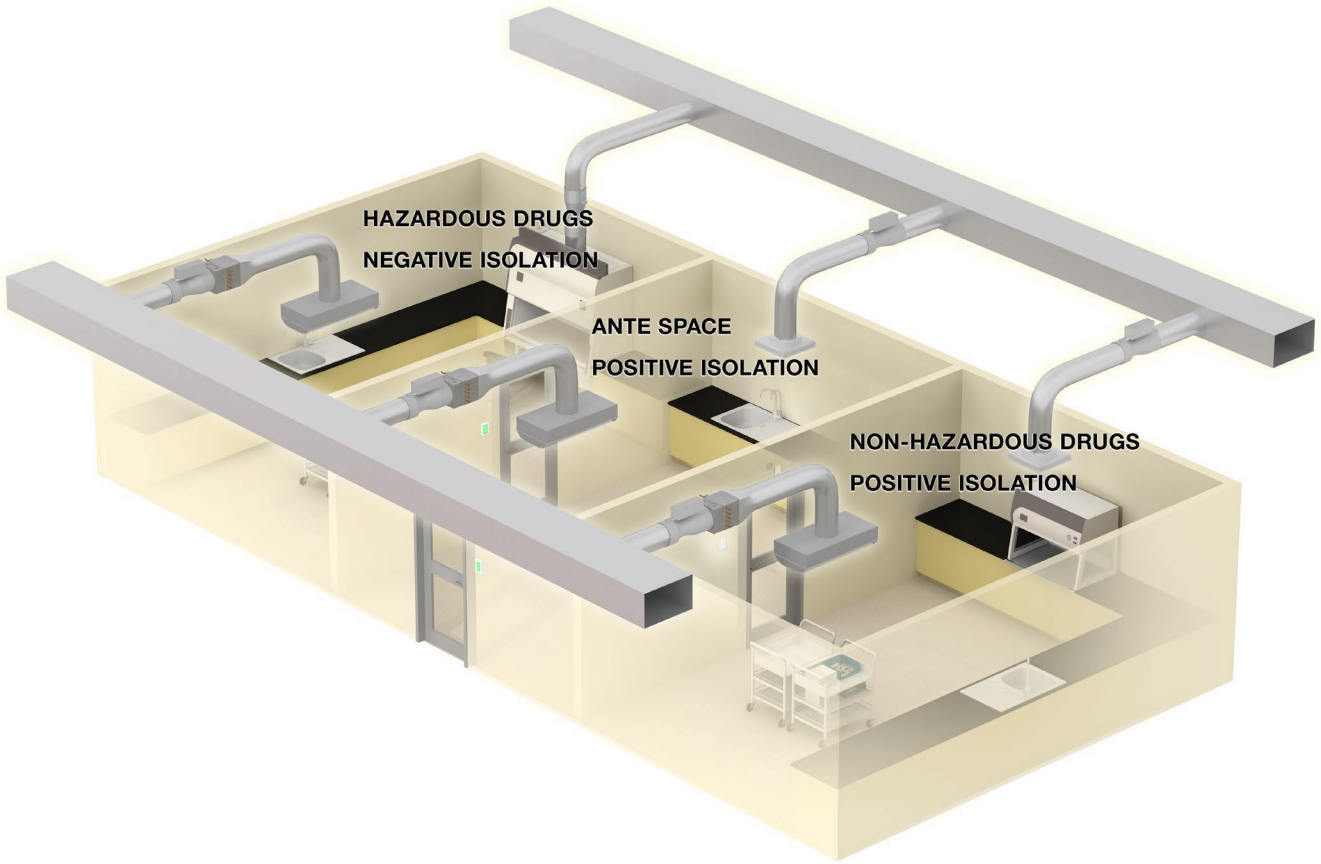
Different Types of Primary Engineering Controls (PEC)

+ Biological Safety Cabinet (BSC)
  - An inflow ventilated cabinet often used for preparations of hazardous drugs
  - Divided into 3 classes (Class 2 is divided in 4 types)
+ Laminar Airflow Work Bench (LAFW)
  - An inflow or outflow work bench typically used to protect either a compounded substance or employee
+ Compounding Aseptic Isolator (CAI)
  - Isolator designed for compounding sterile, non-hazardous pharmaceutical preparations
  - Designed to provide an aseptic environment
+ Compounding Aseptic Containment Isolator (CACI)
  - Type of CAI designed for compounding sterile hazardous drugs
  - Designed to provide worker protection from undesirable levels of airborne drugs though out the compounding and material transport process



Compounding Pharmacies

Applications



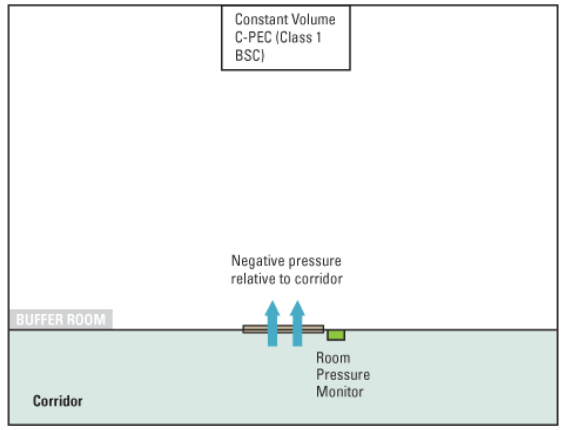
+ Types of isolation (and airflow direction)
  - Buffer Rooms
  - Anterooms

+ Types of compounding
  - Sterile
  - Non-sterile
  - Hazardous
  - Non-hazardous

Compounding Pharmacies

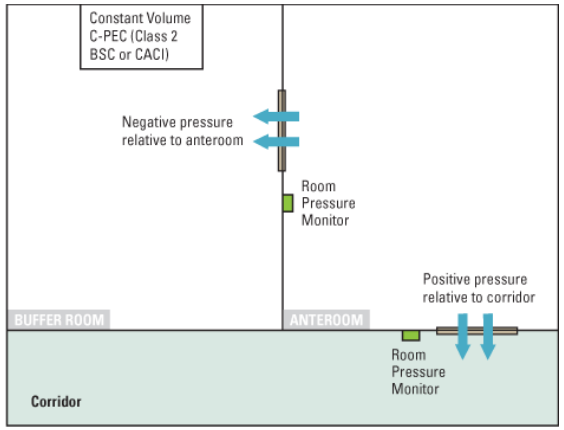
Applications

+ **Non-Sterile Compounding:**
  - Involves creating medication in a clean environment, but does not require the environment to be completely free from all microorganisms
  - Also used for medications that are administered topically



NON-STERILE HAZARDOUS

+ **Sterile Compounding:**
  - Anything that is not a nonsterile preparation
  - Does not have any microbial contamination, meaning that the C-PEC must prevent the CSP from being contaminated by microorganisms



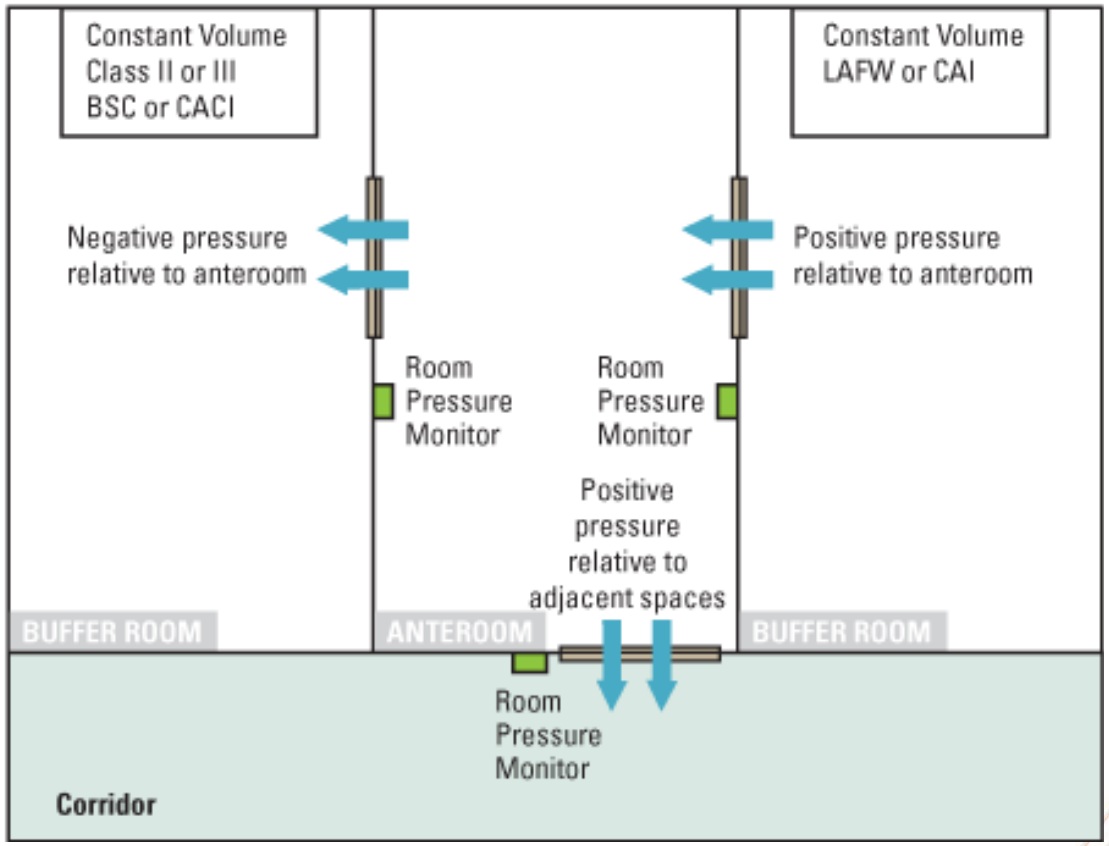
STERILE HAZARDOUS

Compounding Pharmacies

Applications

- **Sterile Hazardous and Non-Hazardous:**
  - HD buffer and non-HD buffer share an anteroom which provides:
    - Barrier from the corridor contaminants
    - PPE gowning space
    - Drug prep area

STERILE HAZARDOUS AND NON-HAZARDOUS
(common design)



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Standard Requirements – USP 795, 797, 800

+ A pressure indicator shall be installed that can be readily monitored for room pressurization measurements.
  - Pressure measurements must be logged daily
  - Annually checked for calibration

+ Required upgrades:
  - A containment primary engineering control devices (C-PEC) must be located in a room that will function as a secondary engineering control (C-SEC)
  - Must be directly ventilated outside
  - Minimum room pressure differential relative to adjacent spaces
    - HD storage areas are subject to the same negative air pressure requirements

Exemption permitted under USP 797 allowing HDs to be compounded in the same areas as non-HDs has been eliminated

Compounding Pharmacies

Standard Requirements – USP 795, 797, 800

- Minimum room pressure differential relative to adjacent spaces and air change requirements
  - HD storage areas are subject to the same negative air pressure requirements

	Sterile	Non-Sterile
Hazardous Drugs Room	Negative (-0.01 in.w.c. to -0.03 in.w.c.) 30 ACH	Negative (-0.01 in.w.c. to -0.03 in.w.c.) 12 ACH
Non Hazardous Drugs Room	Positive (+0.02 in.w.c. to +0.05 in.w.c.) 30 ACH	Positive 4 ACH
Hazardous Drugs Anteroom	Positive (Minimum +0.02 in.w.c.) 30 ACH	Positive (Minimum +0.02 in.w.c.) 12 ACH
Non Hazardous Drugs Anteroom	Positive (Minimum +0.02 in.w.c.) 30 ACH	N/R

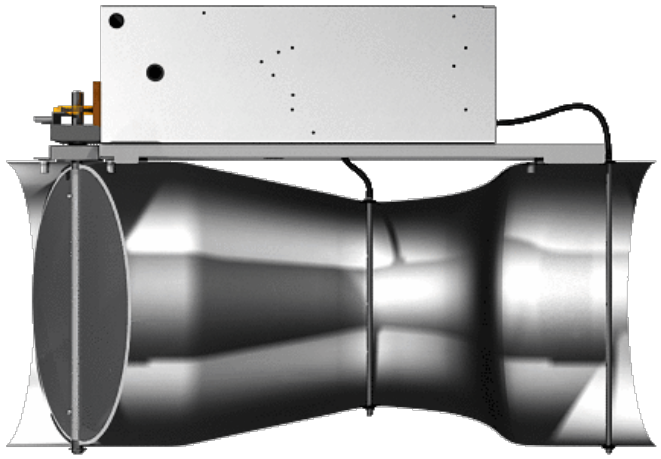
Design Considerations

Compounding Pharmacies

Airflow Control Devices

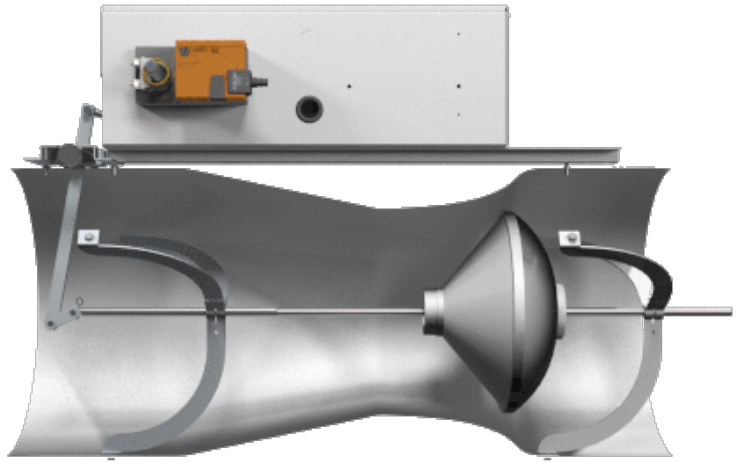
Mechanically Pressure Dependent

- Actuator moves when there is change in airflow target **and** change in duct pressure
- Also known as electronically pressure independent
- Examples: Terminal boxes, high accuracy terminal units



Mechanically Pressure Independent

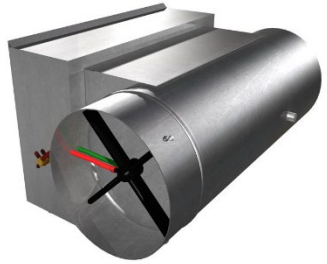
- Actuator moves when there is change in airflow target, **not** when there is change in duct pressure
- Examples: Venturi valves

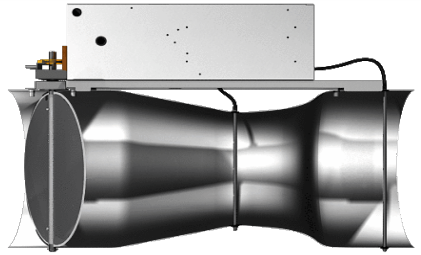


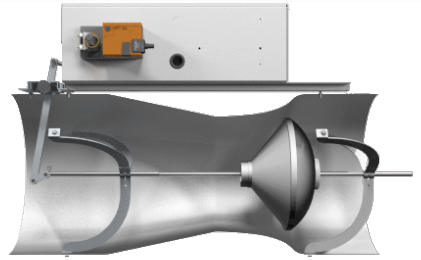
Either airflow control devices can be provided with standard or high speed actuation – typically standard speed actuation is used in pharmacy applications

Compounding Pharmacies

Airflow Control Devices Comparison







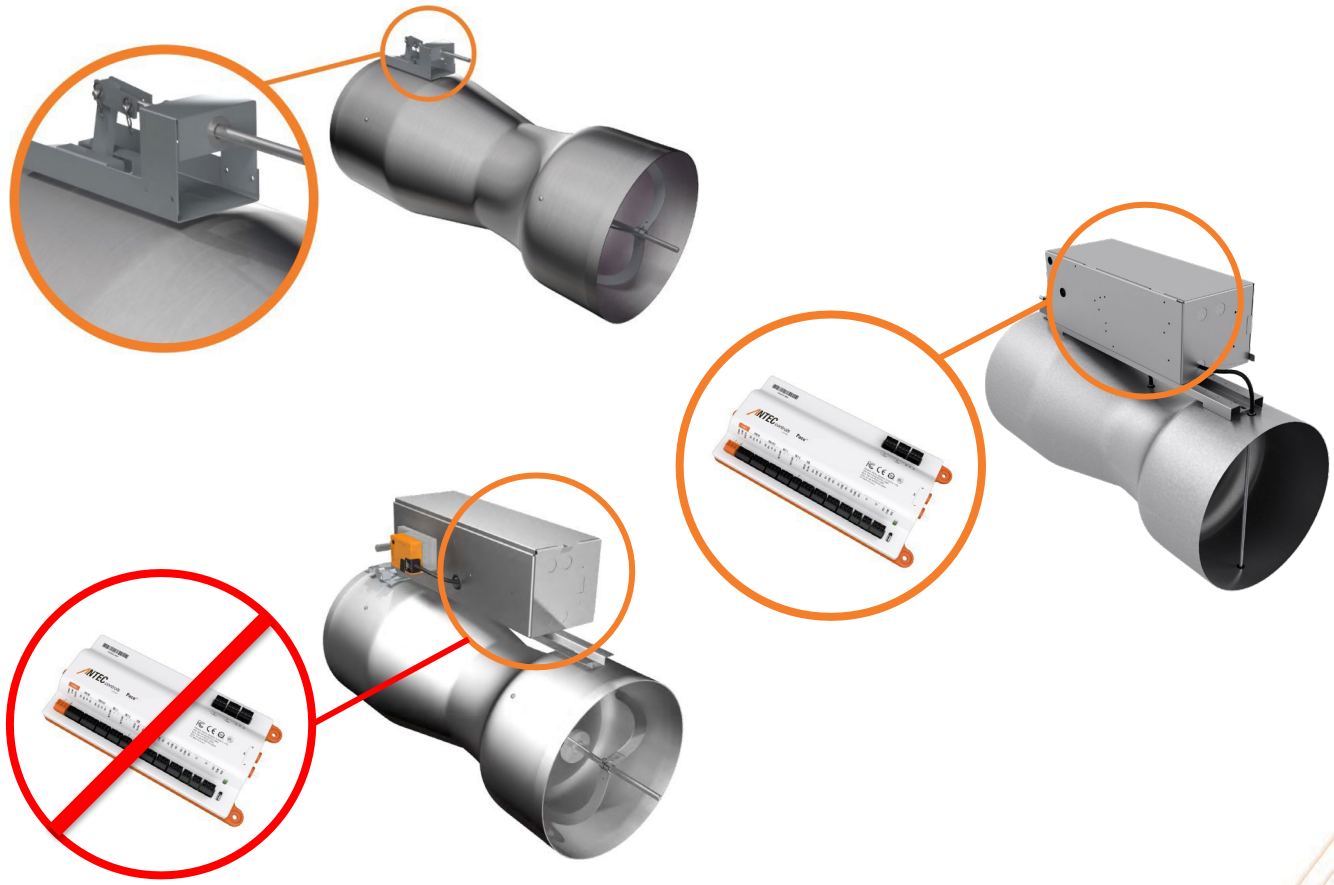
	Terminal Unit (VAV Boxes)	High-Accuracy Terminal Units	Venturi Valves
Pressure Independence	Electronically	Electronically	Mechanically
Airflow Measurement	Total – Static = Velocity pressure	Differential static pressure	Position
Airflow Feedback	Measured	Measured	Electronic
Contamination Resistant	No	Yes	Yes
Turndown Ratio	Up to 6:1	Up to 11:1	Up to 20:1
Pressure Drop (TU, HAT) Operating Pressure (VV)	~ 0.01 in.w.c.	> 0.3 in.w.c.	Low: 0.3 – 3.0 in.w.c. Medium: 0.6 – 3.0 in.w.c.
Coating Options	None	Phenolic (Class 1)	Phenolic (Class 1 & 2), Kynar

Compounding Pharmacies

Airflow Control Devices

+ Constant air volume
  - Mechanically set constant volume Venturi valve
  - High accuracy terminal unit controlled to a constant volume

+ Two position operation
  - 2P actuator with relay for feedback
  - High accuracy terminal unit controlled to two separate airflows (dual flow setpoint)



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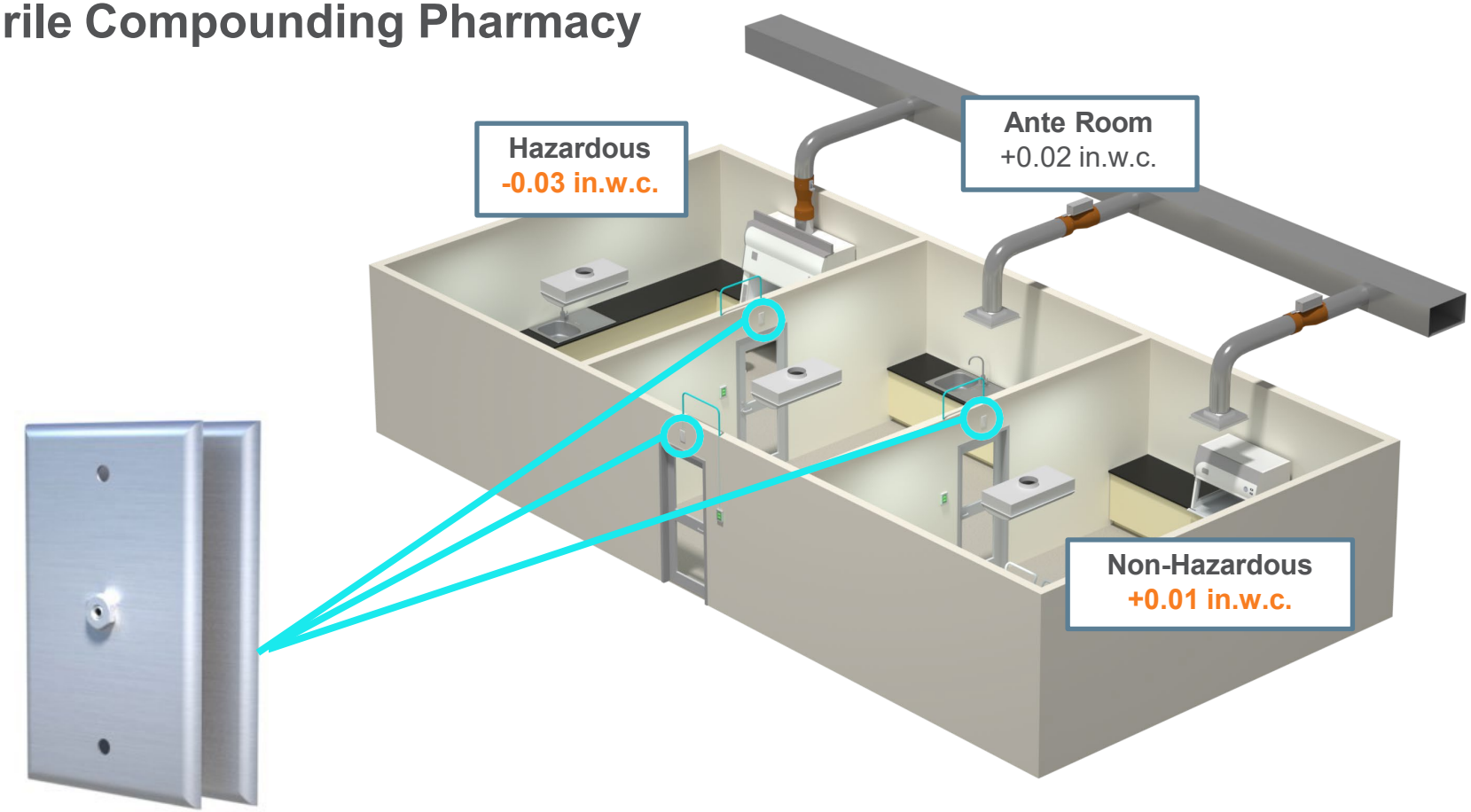
Room Pressure Monitoring

Sterile Compounding Pharmacy



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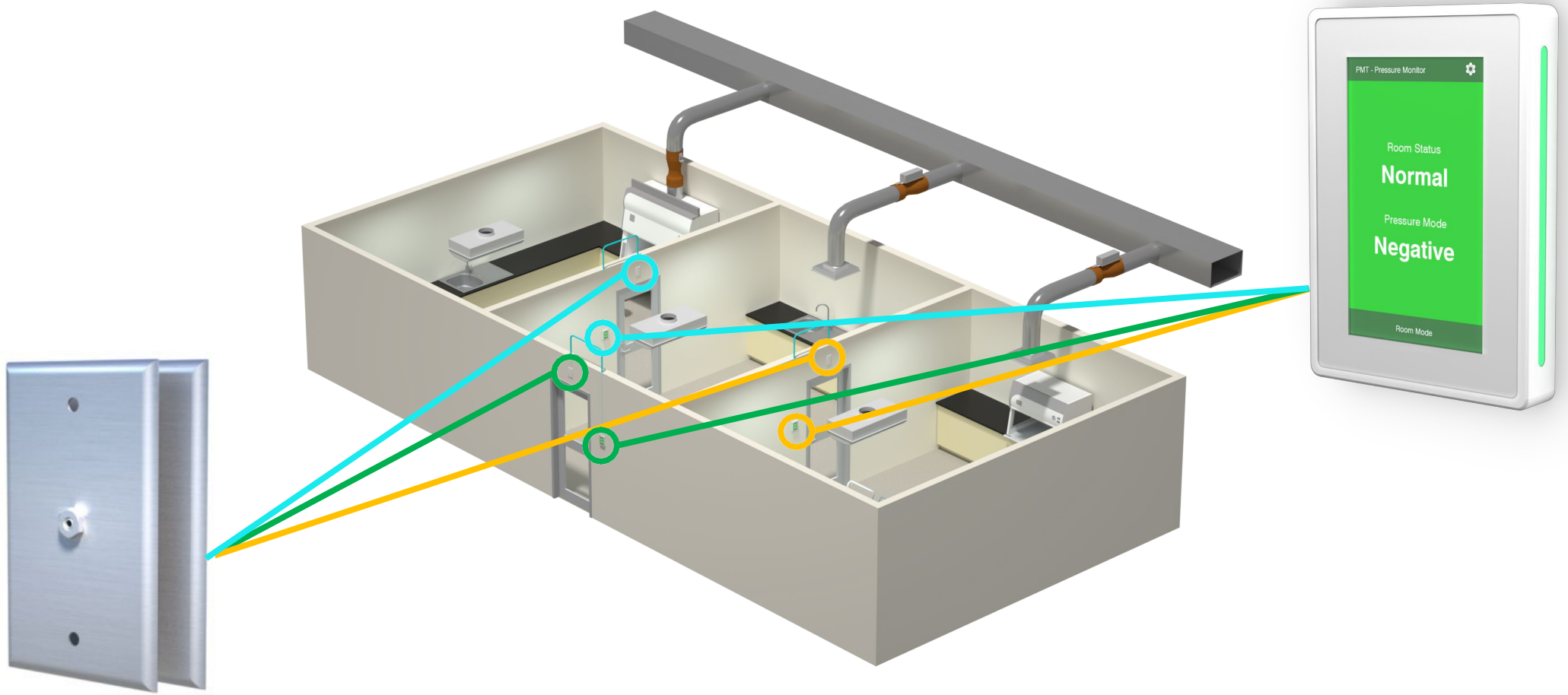
Room Pressure Monitoring

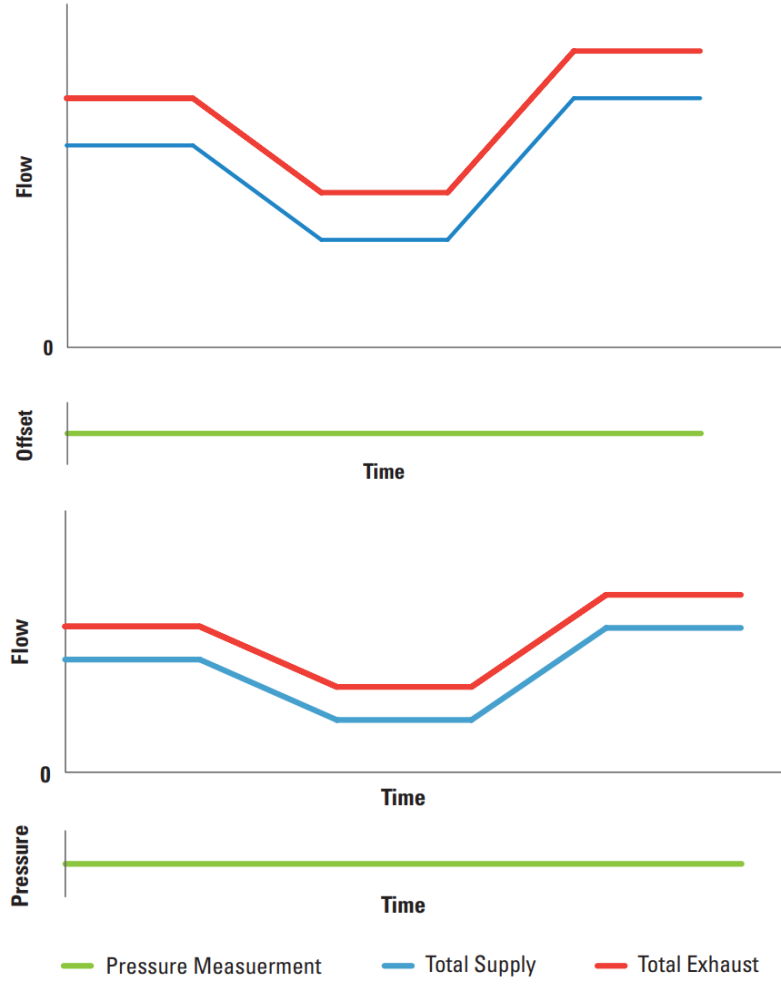


Compounding Pharmacies

Room Pressurization Control

+ **Volumetric offset control**
  - Maintains a constant CFM offset between supply and exhaust valves
  - Independent of room pressure
  - Most common solution (especially in laboratory applications)
  - Room pressure sensor and door contact switches can be used for **monitoring**

+ **Direct pressure control**
  - Airflow adjustment based on room pressure
  - Independent of room offset
  - Becoming more common in pharmacy applications
  - Room pressure sensor and door contact switches can be used for **control**

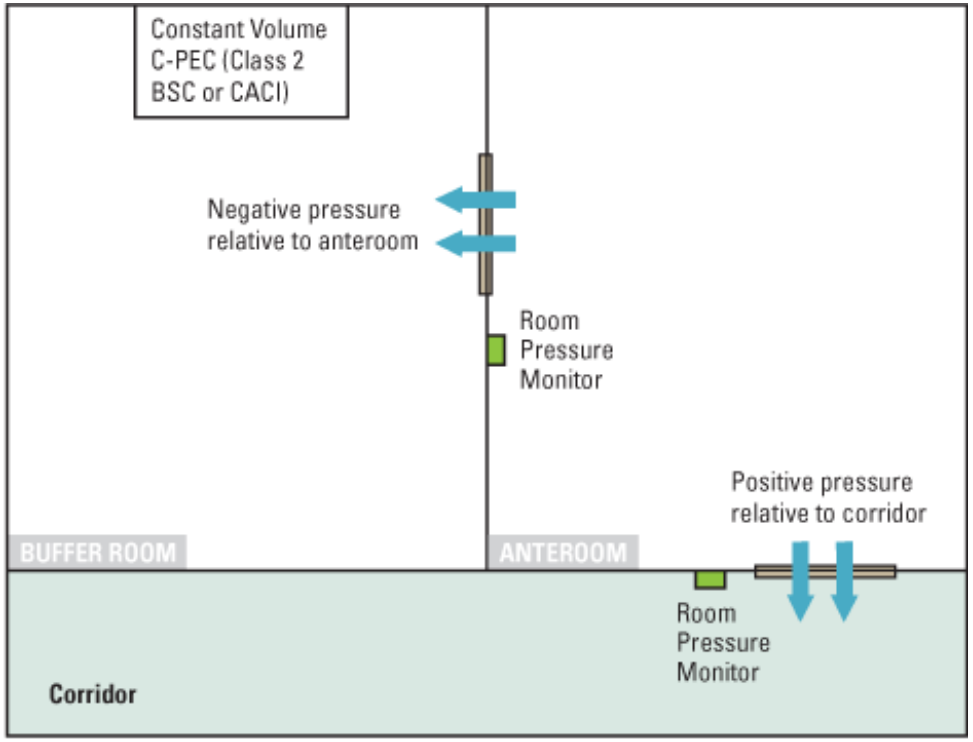


Compounding Pharmacy Design Example

Compounding Pharmacies

Example: Sterile Hazardous Room and Anteroom

+ Minimum ventilation rate for a pharmacy space is typically driven by dilution and displacement of contaminants

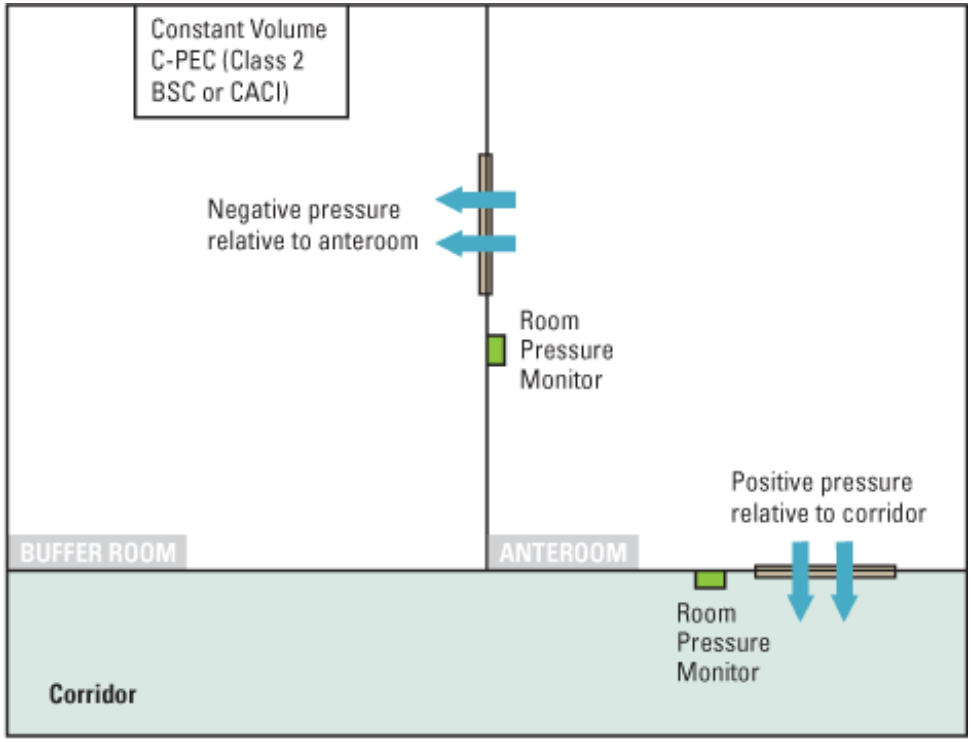


+ Some assumptions made for the spaces are as follows:
  - One (1) supply valve per space
  - One (1) general exhaust valve per space
  - Room dimensions are both 14ft x 14ft x 9ft
  - Minimum 30 ACH for both spaces
  - Class II C-PEC exhausting 500 CFM in sterile HD space

Compounding Pharmacies

Example: Sterile Hazardous Room and Anteroom

+ Minimum ventilation rate for a pharmacy space is typically driven by dilution and displacement of contaminants



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  - One (1) supply valve per space
  - One (1) general exhaust valve per space
  - Room dimensions are both 14ft x 14ft x 9ft
  - Minimum 30 ACH for both spaces

Room volume

= W x D x H = 14ft x 14ft x 9ft = 1764 ft^3

Minimum room airflow based on air change requirement

= Volume * ACH / 60 = 1764 ft^3 x 30 ACH / 60

= **882 CFM**

Compounding Pharmacies

Example: Sterile Hazardous Room and Anteroom

+ Minimum ventilation rate for a pharmacy space is typically driven by dilution and displacement of contaminants = **882 CFM**

+ Some assumptions made for the space as follows:
  - Negatively pressurized sterile HD room and positively pressurized anteroom
  - Class II C-PEC exhausting **500 CFM** in sterile HD space
    - Since ACH requirement exceeds equipment airflow, space is ACH driven
  - Room offset = **80 CFM**
    - Typically estimated as 75-200 CFM per door or 10% of maximum flow

Room State	Supply (1)	General Exhaust (1)	Equipment Exhaust (1)
Sterile HD Room Minimum ACH			
Ante Room Minimum ACH			N/A

Compounding Pharmacies

Example: Sterile Hazardous Room and Anteroom

+ Minimum ventilation rate for a pharmacy space is typically driven by dilution and displacement of contaminants = **882 CFM**

+ Some assumptions made for the space as follows:
  - Negatively pressurized sterile HD room and positively pressurized anteroom
  - Class II C-PEC exhausting **500 CFM** in sterile HD space
    - Since ACH requirement exceeds equipment airflow, space is ACH driven
  - Room offset = **80 CFM**
    - Typically estimated as 75-200 CFM per door or 10% of maximum flow

Room State	Supply (1)	General Exhaust (1)	Equipment Exhaust (1)
Sterile HD Room Minimum ACH	882 CFM		500 CFM
Ante Room Minimum ACH	882 CFM		N/A

Compounding Pharmacies

Example: Sterile Hazardous Room and Anteroom

+ Minimum ventilation rate for a pharmacy space is typically driven by dilution and displacement of contaminants = **882 CFM**

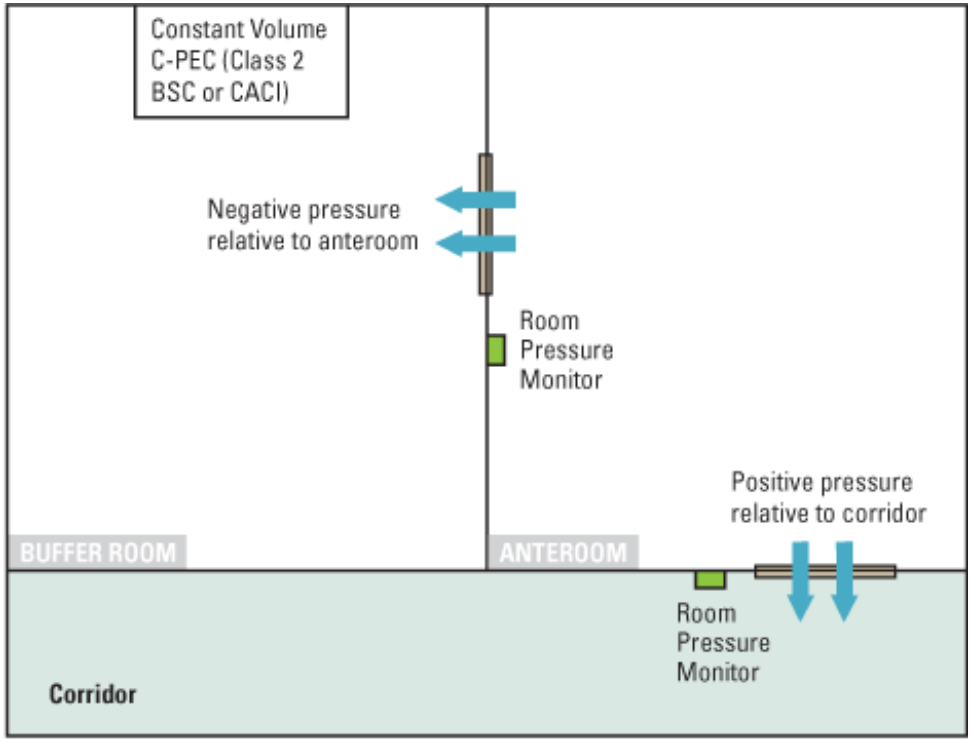
+ Some assumptions made for the space as follows:
  - Negatively pressurized sterile HD room and positively pressurized anteroom
  - Class II C-PEC exhausting **500 CFM** in sterile HD space
    - Since ACH requirement exceeds equipment airflow, space is ACH driven
  - Room offset = **80 CFM**
    - Typically estimated as 75-200 CFM per door or 10% of maximum flow

Room State	Supply (1)	General Exhaust (1)	Equipment Exhaust (1)
Sterile HD Room Minimum ACH	882 CFM	462 CFM	500 CFM
Ante Room Minimum ACH	882 CFM	802 CFM	N/A

Compounding Pharmacies

Example: Non-Sterile Hazardous Room and Anteroom

+ Minimum ventilation rate for a pharmacy space is typically driven by dilution and displacement of contaminants

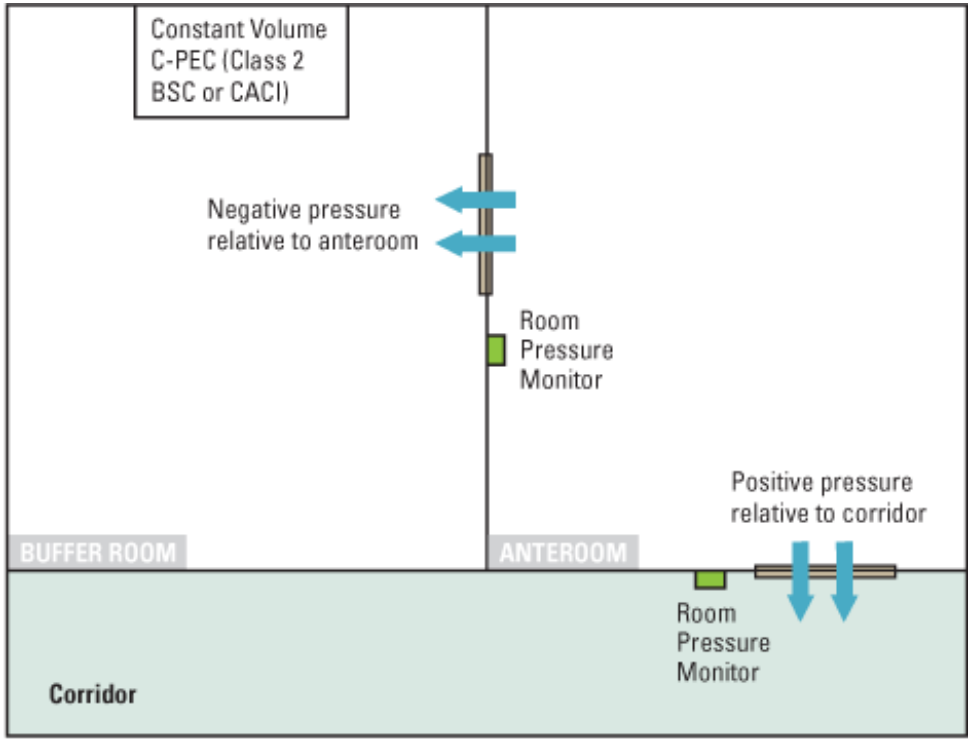


+ Some assumptions made for the spaces are as follows:
  - One (1) supply valve per space
  - One (1) general exhaust valve per space
  - Room dimensions are both 10ft x 10ft x 9ft
  - Minimum 12 ACH for both spaces
  - Class II C-PEC exhausting 500 CFM in non-sterile HD space

Compounding Pharmacies

Example: Non-Sterile Hazardous Room and Anteroom

+ Minimum ventilation rate for a pharmacy space is typically driven by dilution and displacement of contaminants



+ Some assumptions made for the spaces are as follows:
  - One (1) supply valve per space
  - One (1) general exhaust valve per space
  - Room dimensions are both 10ft x 10ft x 9ft
  - Minimum 12 ACH for both spaces

Room volume

= W x D x H = 10ft x 10ft x 9ft = 900 ft^3

Minimum room airflow based on air change requirement

= Volume * ACH / 60 = 900 ft^3 x 12 ACH / 60

= **180 CFM**

Compounding Pharmacies

Example: Non-Sterile Hazardous Room and Anteroom

+ Minimum ventilation rate for a pharmacy space is typically driven by dilution and displacement of contaminants = **180 CFM**

+ Some assumptions made for the space as follows:
  - Negatively pressurized non-sterile HD room and positively pressurized anteroom
  - Class II C-PEC exhausting **500 CFM** in non-sterile HD space
    - Since equipment requirement exceeds ACH airflow, space is equipment driven
  - Room offset = **50 CFM**
    - Typically estimated as 75-200 CFM per door or 10% of maximum flow

Room State	Supply (1)	General Exhaust (1)	Equipment Exhaust (1)
Sterile HD Room Minimum ACH			
Ante Room Minimum ACH			N/A

Compounding Pharmacies

Example: Non-Sterile Hazardous Room and Anteroom

+ Minimum ventilation rate for a pharmacy space is typically driven by dilution and displacement of contaminants = **180 CFM**

+ Some assumptions made for the space as follows:
  - Negatively pressurized non-sterile HD room and positively pressurized anteroom
  - Class II C-PEC exhausting **500 CFM** in non-sterile HD space
    - Since equipment requirement exceeds ACH airflow, space is equipment driven
  - Room offset = **50 CFM**
    - Typically estimated as 75-200 CFM per door or 10% of maximum flow

Room State	Supply (1)	General Exhaust (1)	Equipment Exhaust (1)
Sterile HD Room Minimum ACH	180 CFM		500 CFM
Ante Room Minimum ACH	180 CFM		N/A

Compounding Pharmacies

Example: Non-Sterile Hazardous Room and Anteroom

+ Minimum ventilation rate for a pharmacy space is typically driven by dilution and displacement of contaminants = **180 CFM**

+ Some assumptions made for the space as follows:
  - Negatively pressurized non-sterile HD room and positively pressurized anteroom
  - Class II C-PEC exhausting **500 CFM** in non-sterile HD space
    - Since equipment requirement exceeds ACH airflow, space is equipment driven
  - Room offset = **50 CFM**
    - Typically estimated as 75-200 CFM per door or 10% of maximum flow

Room State	Supply (1)	General Exhaust (1)	Equipment Exhaust (1)
Sterile HD Room Minimum ACH	180 CFM	270 CFM	500 CFM
Ante Room Minimum ACH	180 CFM	130 CFM	N/A

Compounding Pharmacies

Example: Non-Sterile Hazardous Room and Anteroom

+ Minimum ventilation rate for a pharmacy space is typically driven by dilution and displacement of contaminants = **180 CFM**

+ Some assumptions made for the space as follows:
  - Negatively pressurized non-sterile HD room and positively pressurized anteroom
  - Class II C-PEC exhausting **500 CFM** in non-sterile HD space
    - Since equipment requirement exceeds ACH airflow, space is equipment driven
  - Room offset = **50 CFM**
    - Typically estimated as 75-200 CFM per door or 10% of maximum flow

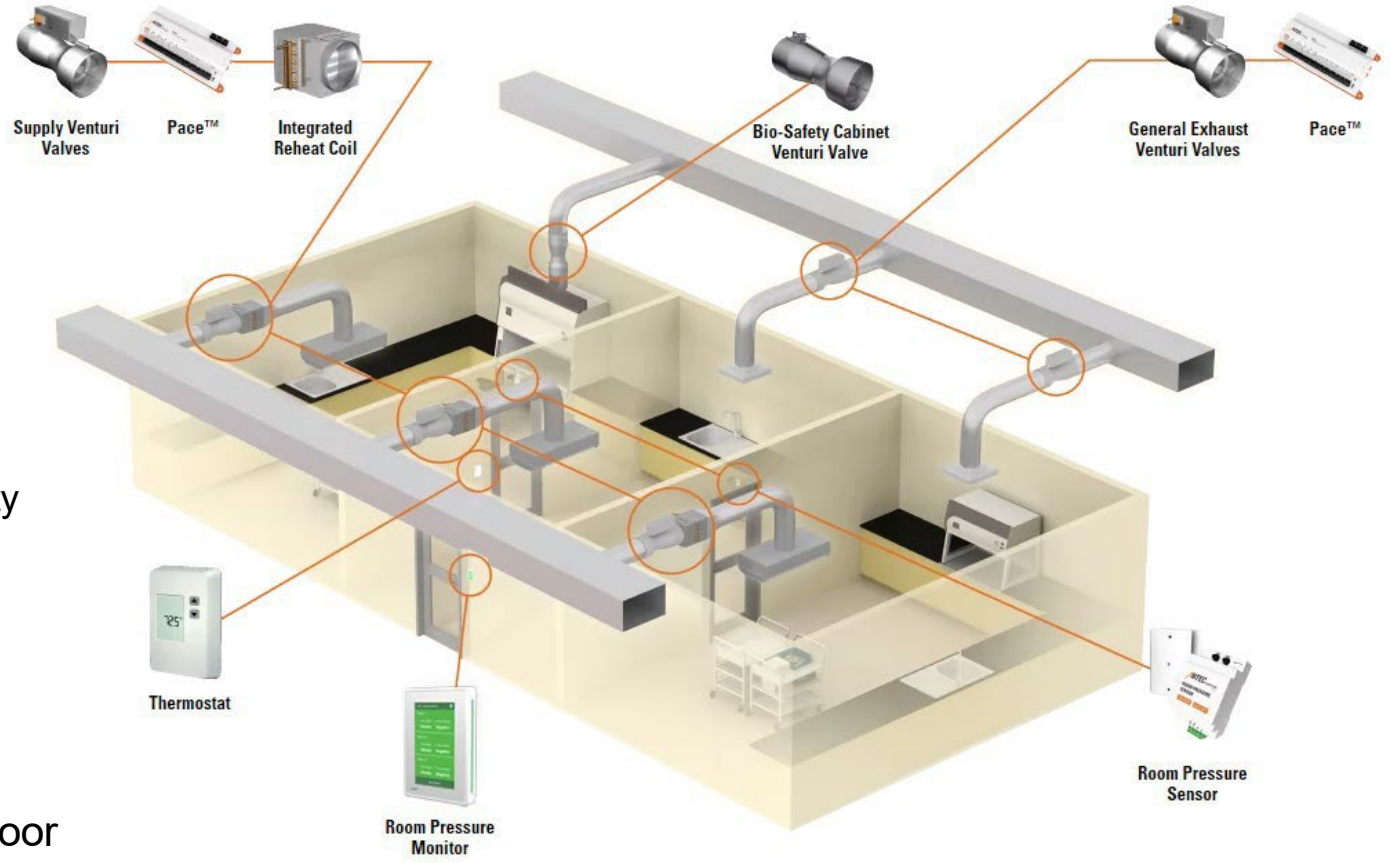
Room State	Supply (1)	General Exhaust (1)	Equipment Exhaust (1)
Sterile HD Room Minimum ACH	**450 CFM**	**N/A**	500 CFM
Ante Room Minimum ACH	180 CFM	130 CFM	N/A

Summary and Recommendations

Compounding Pharmacies

Summary and Recommendations

+ Both High Accuracy Terminals and Venturi Valves are acceptable
  - Standard speed actuation is acceptable
+ Volumetric offset or direct pressure control can be used
  - Extreme air change rates in small spaces and room pressure requirements prescribed as ranges, not minimums, presents a challenge to ensure stability
+ Rooms controlled as constant volume systems
  - Separation of HD and non-HD rooms
+ Ensure reference spaces remain in control
  - Tight construction with low leakage rates
+ Room pressure monitoring and display at each door



*"Perhaps the biggest—and most important—aspect of USP <800> is that unlike the current NIOSH, ONS, and ASHP guidelines, this chapter is a standard and many aspects will be enforced. Organizations must comply with the standards or face consequences," Eisenberg says. "**USP has the support of major players in health care, and enforcement will be via one or more of the following agencies: state boards of pharmacy, U.S. Food and Drug Administration, Centers for Medicare and Medicaid Services, and Joint Commission. Failure to comply can result in loss of Medicare funding, accreditation status, and potentially pharmacy licensure.** This is the greatest strength of USP <800>: we've had good guidelines for decades, but they were never enforced until now."*

ANTEC controls by price

Questions?

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MAP
MICHIGAN AIR PRODUCTS

ANTEC controls
by price