



Pharmacies USP 797 & 800

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Learning Objectives

- Explain the purpose of USP 797 and USP 800, including their significance and key differences.
- Identify how the commissioning team can support designers in avoiding design challenges that may lead to compliance or performance issues.
- Recognize the certifier's critical role in achieving compliance and enabling successful pharmacy operations.
- Compare methods for maintaining required pressure relationships in pharmacy spaces, including pressure-based, volumetric, and hybrid approaches.
- Identify key elements of an ongoing commissioning plan to support future pharmacy recertification.

AGENDA

What are the USP requirements: General and ACH and pressure requirements of spaces
Design priorities to provide benefits to the certification process
What are certifiers really looking for when doing their certification test (the petri dishes)...the purpose
Room types (Ante, IV Prep, Haz Compounding) and their pressure individual requirements
What about the work room
What is the primary source of containment (it might not be what you are thinking)
Volumetric, Pressure, Hybrid control
Lock and holds for pressure control (hold one room, hold them all, are they necessary)
Cascading pressure relationships (the reference point)
AHU's using a dedicated unit or using a unit that serves other areas besides the pharmacy
Exhaust control
Economizer is not your friend
Where is cooling coming from
Humidification & De-Humidification
What does fail safe (safe egress) look like
Energy Code (is this process unit)

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What does fail safe (safe egress) look like
Energy Code (is this process unit)



A lot of content on this list;
let's concentrate on the
highlighted ones.....

USP

United States Pharmacopeia

- What is USP?
- Importance of USP 797/800
- What is the difference between 797/800?
- HVAC requirements
- Design of Pharmacy Clean Rooms
- Testing & Certification requirements
- Maintaining Pharmacy Clean Rooms
- Other Considerations



WHAT IS USP?



United States Pharmacopeia

- It is an independent scientific nonprofit organization that was founded over 200 years ago.
- In 1938 legislation was passed that required companies to test all new drugs to verify they meet USP standards. The data had to be submitted to FDA prior to marketing.
- The main focus of USP is to ensure safe and reliable medicine, dietary supplements and foods.
- USP also focuses on protecting patient safety.
- USP sets high quality and rigorous standards which have become recognized and used world-wide.
- 140 countries around the globe recognize USP standards.

USP 797 VS. USP 800

USP General Chapter 797

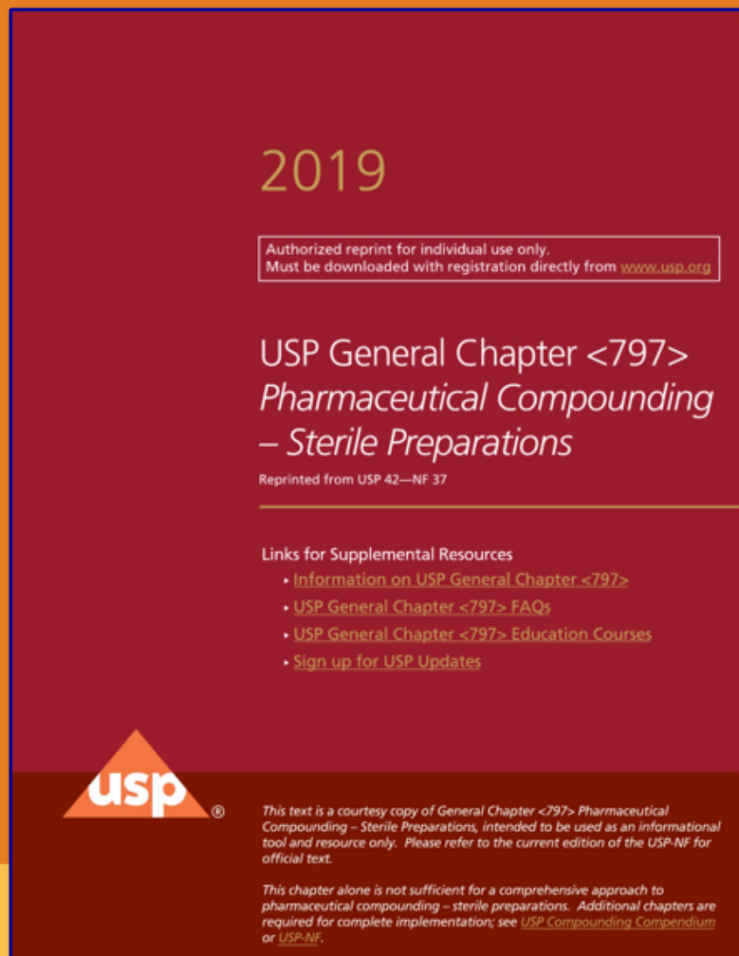
Pharmaceutical Compounding – Sterile Preparations

The requirements of this chapter intend to ensure the sterility of compounded sterile preparations (CSPs) to provide safe medicine.

USP General Chapter 800

Hazardous Drugs – Handling in Healthcare Settings

This chapter covers standards for handling hazardous drugs that protects patients, workers, and the environment.



USP 797 Overview

USP General Chapter 797 – Pharmaceutical Compounding – Sterile Preparations

Covers all requirements for sterile compounding including:

- Personnel training, Hygiene and Garbing
- Facilities and Engineering Controls
- Certification and Recertification
- Microbial Air and Surface Monitoring
- Cleaning and Disinfecting
- Master Formulation and Compounding Records
- Labeling
- CSP Handling, Storage, Packaging
- and more....

USP 800 Overview

USP General Chapter 800 – Hazardous Drugs – Handling in Healthcare Settings

Covers all requirements for sterile compounding including:

- Lists of Hazardous Drugs
- Types of Exposure
- Facilities and Engineering Controls
- Responsibilities of Personnel Handling Hazardous Drugs
- Environmental Quality and Control
- Personal Protective Equipment
- Deactivating, Decontamination, Cleaning and Disinfecting
- Spill Control
- Documentation and Standard Operating Procedures
- and more....

2019

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USP General Chapter <800>
*Hazardous Drugs –
Handling in Healthcare Settings*

Reprinted from USP 42—NF 37

Links for Supplemental Resources

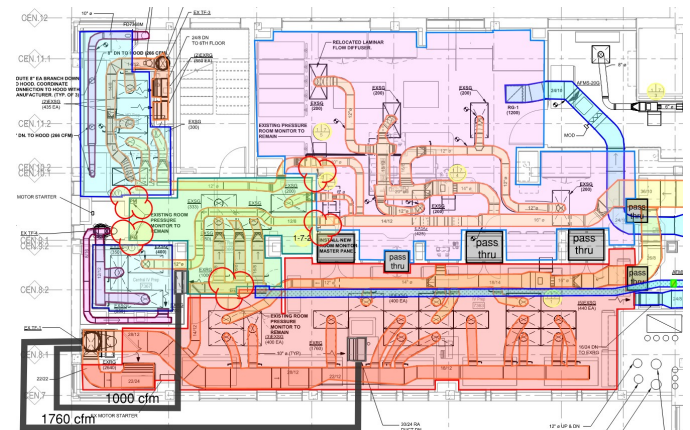
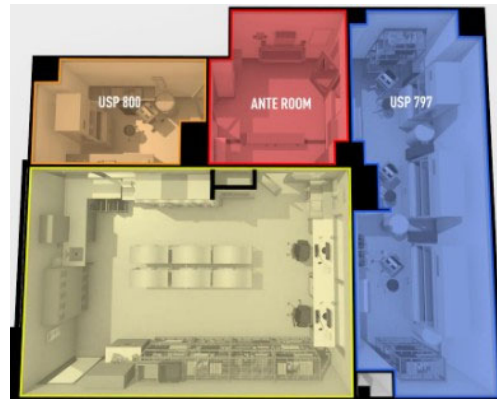
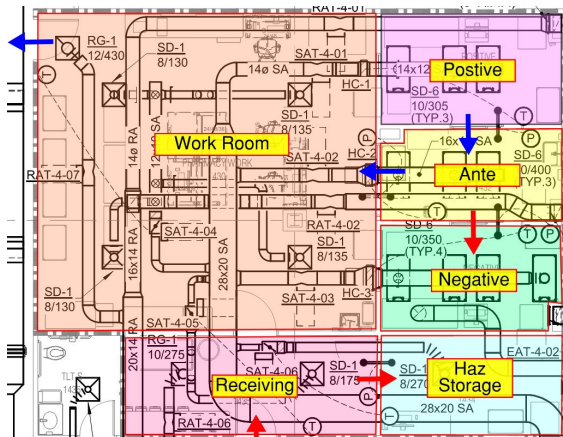
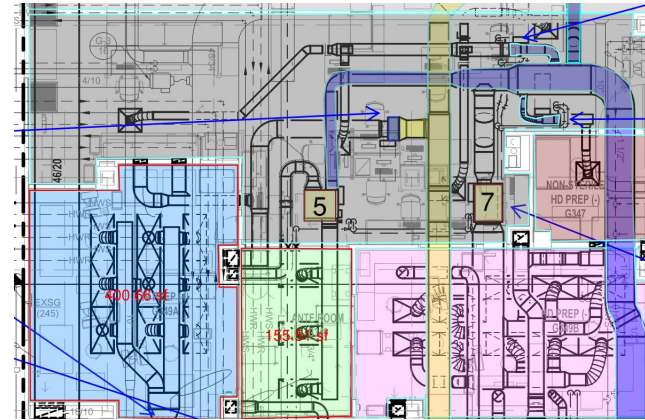
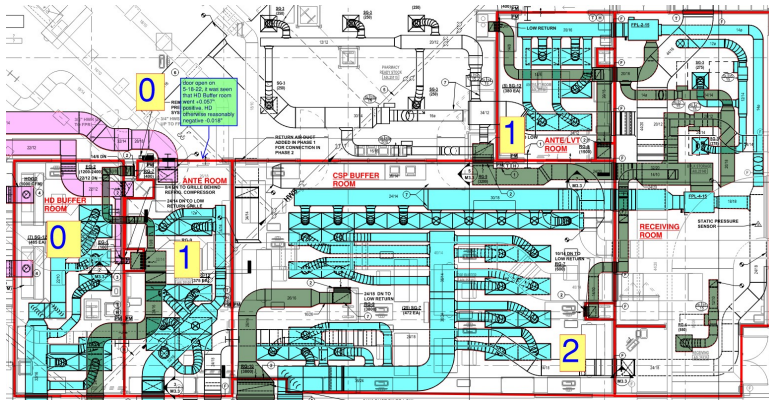
- [Information on USP General Chapter <800>](#)
- [USP General Chapter <800> FAQs](#)
- [USP General Chapter <800> Education Courses](#)
- [Sign up for USP updates](#)

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This text is a courtesy copy of General Chapter <800> Hazardous Drugs – Handling in Healthcare Settings, intended to be used as an informational tool and resource only. Please refer to the current edition of the USP-NF for official text.

This chapter alone is not sufficient for a comprehensive approach to safe handling of hazardous drugs. Additional chapters are required for complete implementation; see [USP Compounding Compendium](#) or [USP-NF](#).

LET'S GET OUR FEET WET... DESIGN



NAVIGATING USP 797/800

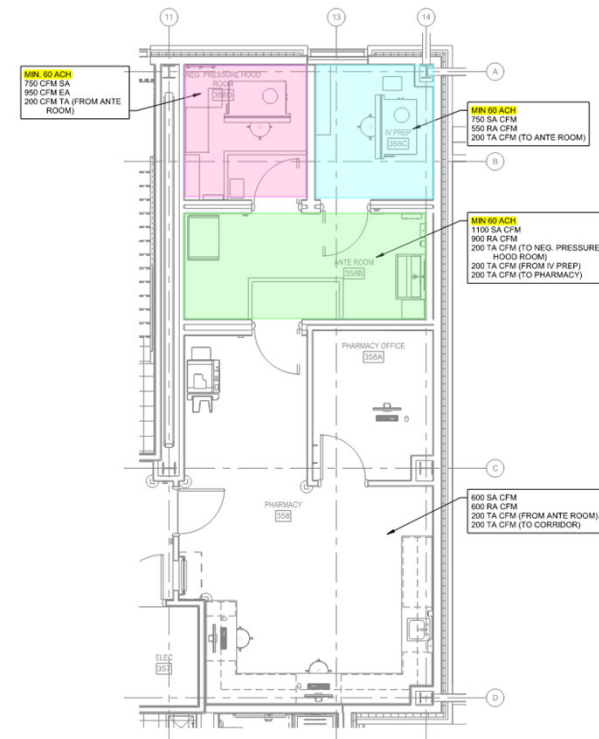
HVAC Requirements

USP Minimum Air Changes per Hour (ACH)

- Ante Room = 30 ACH
- Sterile Prep (IV Prep) = 30 ACH
- Hazard Drug (Chemo Prep) = 30 ACH

Best Practice Recommended Air Changes per Hour

- Ante Room = 60 ACH
- Sterile Prep (IV Prep) = 60 ACH
- Hazard Drug (Chemo Prep) = 60 ACH



NAVIGATING USP 797/800

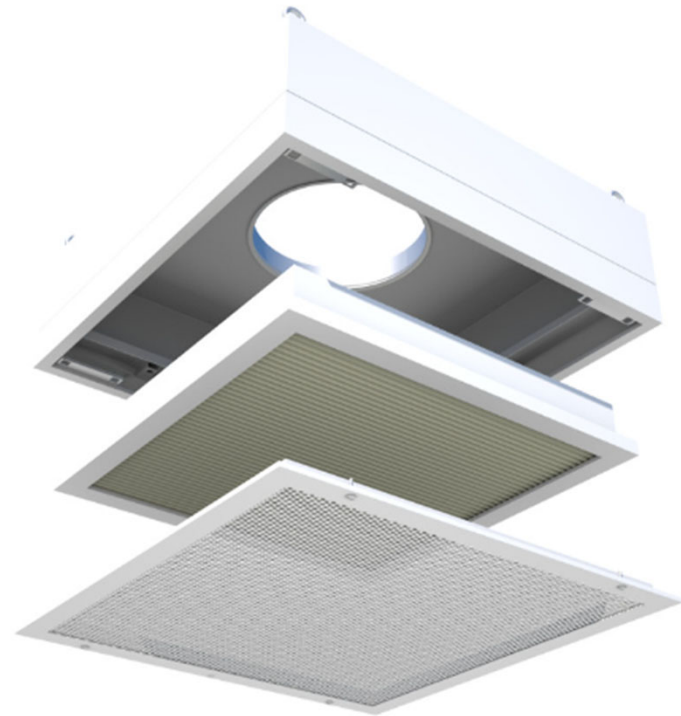
HVAC Requirements

Filtration Requirements

USP requires all air being supplied to pharmacy clean rooms to pass through a HEPA filtered supply diffuser.

The supply diffuser shall be sealed to ensure all air passes through the filter to avoid any contaminants from entering the room through the air stream.

HEPA filtered diffusers shall be leak tested on a regular basis as part of the room recertification process.



NAVIGATING USP 797/800

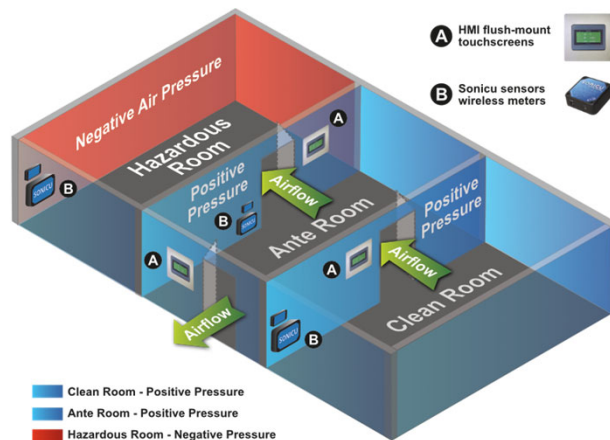
HVAC Requirements

Room Pressurization

Ante Room – positive to surrounding hospital.

Sterile Processing (IV Prep) – positive to Ante room and other surrounding spaces.

Hazardous Drug (Chemo Prep) – negative to Ante room and other surrounding spaces.



USP 797

ESTABLISHING AND MAINTAINING PRESSURE DIFFERENTIALS

Continuous differential positive pressure is required to minimize airflow from an area with lower air-quality classification to an area of higher air-quality classification. In a cleanroom suite, a minimum differential positive pressure of 0.020-inch water column is required between each ISO classified area (e.g., between the buffer room and ante-room). The pressure differential between the ante-room and the unclassified area must not be less than 0.020-inch water column. No pressure differential is required between the SCA and the surrounding area. See (800) for pressure requirements for compounding HD CSPs.

Where pressure differentials are required, a pressure differential monitoring device must be used to continuously monitor the pressure differentials. The quantitative results from the pressure monitoring device must be reviewed and documented at least daily on the days when compounding is occurring.

USP 800

Table 3. Engineering Controls for Sterile HD Compounding

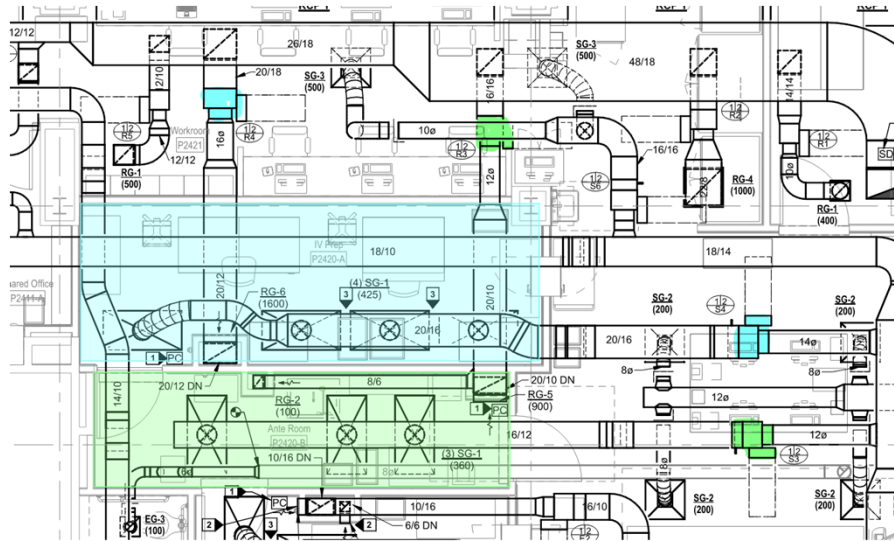
Configuration	C-PEC	C-SEC	Maximum BUD
ISO Class 7 buffer room with an ISO Class 7 ante-room	- Externally vented - Examples: Class II BSC or CACI	- Externally vented 30 ACPH - Negative pressure between 0.01 and 0.03 inches of water column relative to adjacent areas	As described in (797)
Unclassified C-SCA	- Externally vented - Examples: Class II BSC or CACI	- Externally vented 12 ACPH - Negative pressure between 0.01 and 0.03 inches of water column relative to adjacent areas	As described in (797) for CSPs prepared in a segregated compounding area

NAVIGATING USP 797/800

Design of Clean Room

Utilize air terminal boxes on supply and return/exhaust sides of any clean room. Boxes need to be located outside clean rooms.

Use dedicated air terminal boxes for each individual room.



Design of Clean Room

Locate room return/exhaust grilles low in walls to help maintain unidirectional airflow at work areas.

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GROSS FACT #1

- We are the biggest “particle generators”
- We shed about 9 pounds of dead skin cells each year¹
- Particles act as transport vehicles for microorganisms and introduce them into the compounding process

¹Facts Legend. Baidya, S. [50 Interesting Human Skin Facts](#). 2015. Retrieved 12/27/2018.



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GROSS FACT #2

- Each of us carries 3 to 5 pounds of bacteria
- Bacterial cells outnumber human cells 10 to 1
- Bacterial cells are much smaller than human cells so they only account for 1 to 2% of our body mass

The bacteria in our body would fill a large soup can like this one

Source: Lita Proctor, National Institutes of Health's Human Microbiome Project



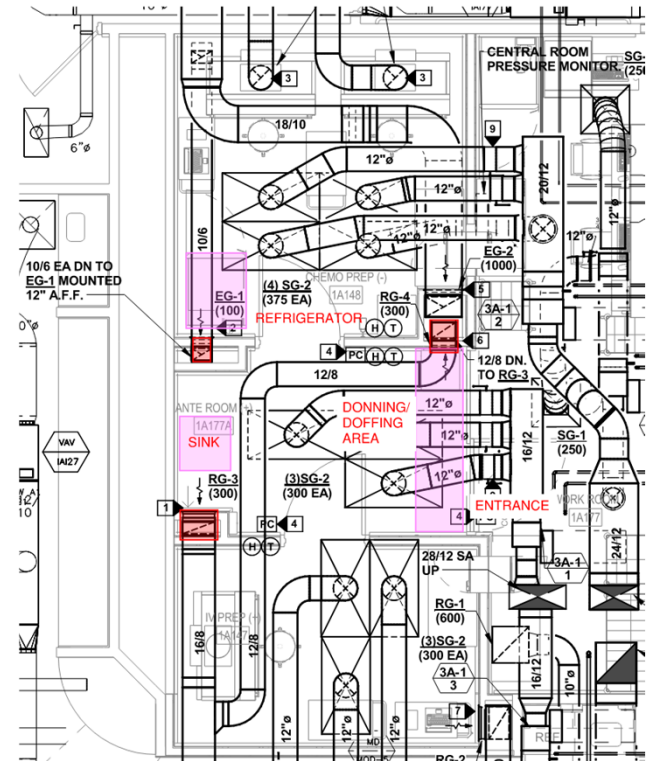
NAVIGATING USP 797/800

Design of Clean Room

Locate room return/exhaust grilles near entrance.

Locate return/exhaust grilles at the compressor height on all refrigerators and freezers.

Locate return/exhaust grilles at other potential sources of air contamination.



JUMPING IN THE *DEEP END*...CERTIFICATION



September 2026

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POSITIVE BUFFER ROOM

Positive pressure to adjacent space

Fixed walls and doors

Accessed through an Anteroom

An ISO Class 7 or cleaner room

PEC(s) are located within these rooms and those PEC(s) are ISO Class 5

Pressure minimum requirement of 0.020"

Minimum of 30ACH (*Best Practice recommendation 60 ACH*)

This can be achieved by:

- Minimum of 15ACH that is provided by the HEPA filtered air HVAC
- Minimum of 15ACH from the PEC(s)

Viable Sampling action levels

Air Sampling: >10 CFU/1000L of air

Surface Sampling: >5 CFU/plate

HD BUFFER ROOM

Negative pressure to adjacent space

Fixed walls and doors

Accessed through an Anteroom

An ISO Class 7 or cleaner room

PEC(s) are located within these rooms and those PEC(s) are ISO Class 5 and exhausted directly to outside

Pressure requirement of -0.010" to -0.030"

Minimum of 30ACH that is provided by the HEPA filtered air HVAC (*Best Practice recommendation 60 ACH*)

Viable Sampling action levels

- Air Sampling: >10 CFU/1000L of air
- Surface Sampling: >5 CFU/plate

HD RECEIVING/STORAGE ROOM

HDs are shipped from the distributor in totes and wrapped in plastic

Receiving

- Must be unpacked in an area that is neutral/normal or negative pressure relative to surrounding area

Storage

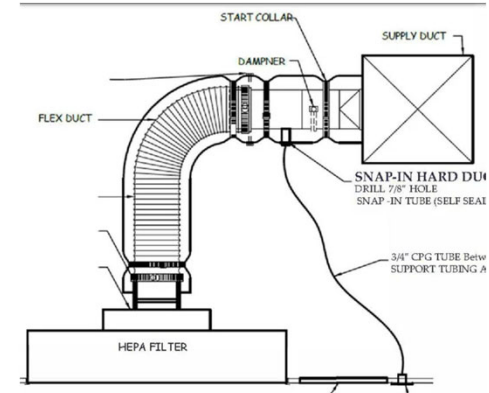
- Negative pressure to adjacent space
- Must be stored separate from non-HDs
- Externally vented
- Minimum of 12 ACH, can be from exhaust or supply-explain
- Minimum room pressure of -0.010" to adjacent space

PHARMACY CERTIFICATION PROCESS

- Testing equipment used for EM testing is wiped down and cleaned prior to being staged in Anteroom
- Testing is completed with a Pharmacy staff member conducting activities as expected during normal mixing operations to ensure EM testing is completed under dynamic conditions
- Samples are sealed and packaged to be processed by Laboratory
- Airflow at the HEPA filters in ceiling are measured and considered “First Air”. Adjustments to airflow are made to the supply system as needed to ensure ACH requirements are satisfied and airflow measuring devices are calibrated
- Laminar Airflow Workbench (LAFW) and Biosafety Cabinet (BSC) airflow will be measured. Adjustments are made during this process, if needed to ensure airflow is within spec.

PHARMACY CERTIFICATION PROCESS

- HEPA integrity testing of all associated HEPA filters (LAFW, BSC, ceiling mounted HEPAs) will be challenged. This will be done through manufacture installed ports or externally installed ports
- AVS testing is completed with a pharmacy staff member as this needs to be completed under dynamic conditions
- Pressure measurements within Sterile Compounding Suite are measured and calibrated
- HEPA pass throughs will be measured for airflow and HEPA integrity tested



ENVIRONMENTAL SAMPLING

Particle Counts (Non-viable)

- ISO 14644-1 and 14644-2 Standards
- Exclusively in terms of concentration of airborne particles
- Sampling numbers are based on square meters of the room
- Sampling time is 1 minute and sampling volume is 2 liters
- Only particles based on lower limit size ranging from 0.1 to 5 μm
 - Report particle count of $\geq 0.5\mu\text{m}$

Class	Maximum Particles/m ³					
	$\geq 0.1 \mu\text{m}$	$\geq 0.2 \mu\text{m}$	$\geq 0.3 \mu\text{m}$	$\geq 0.5 \mu\text{m}$	$\geq 1 \mu\text{m}$	$\geq 5 \mu\text{m}$
ISO 1	10	-	-	-	-	-
ISO 2	100	24	10	-	-	-
ISO 3	1,000	237	102	35	-	-
ISO 4	10,000	2,370	1,020	352	83	-
ISO 5	100,000	23,700	10,200	3,520	832	-
ISO 6	1,000,000	237,00	102,000	35,200	8,320	293
ISO 7	-	-	-	352,000	83,200	2,930
ISO 8	-	-	-	3,520,000	832,000	29,300
ISO 9	-	-	-	35,200,000	8,320,000	293,000

Table A.1: Sampling locations related to cleanroom area

Area of cleanroom (m ²) less than or equal to	Minimum number of sampling locations to be tested (N_L)
2	1
4	2
6	3
8	4
10	5
24	6
28	7
32	8
36	9
52	10
56	11
64	12
68	13
72	14
76	15
104	16
108	17
116	18
148	19
156	20
192	21
232	22
276	23
352	24
436	25
636	26
1 000	27
> 1 000	See Formula (A.1)

NOTE 1 If the considered area falls between two values in the table, the greater of the two should be selected

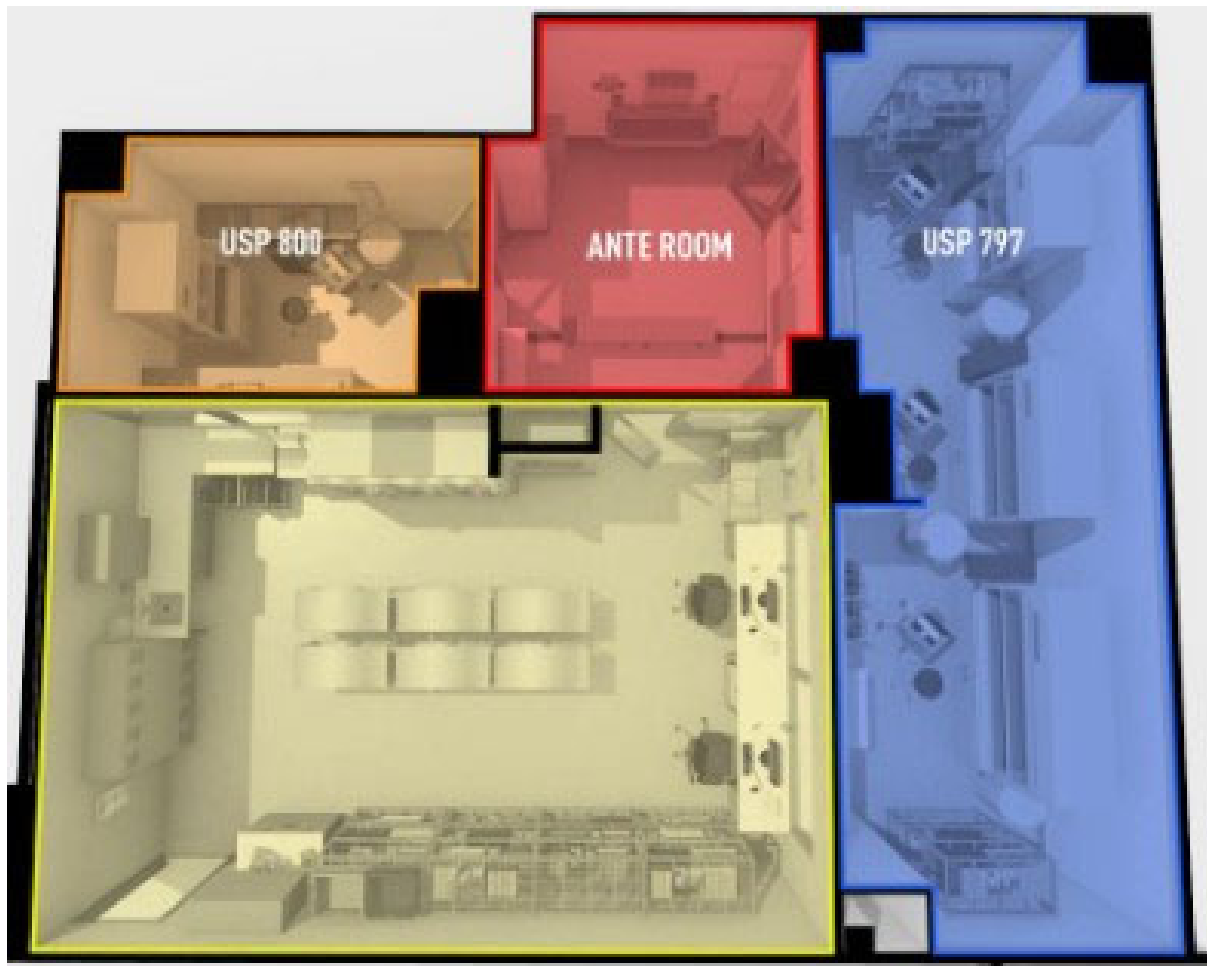
NOTE 2 In the case of unidirectional airflow, the area may be considered as the cross section of the of the moving air perpendicular to the direction of the airflow. In all other cases the area may be considered as the horizontal plan area of the cleanroom or clean zone

ENVIRONMENTAL SAMPLING

Viability Sampling

- Viable sampling programs should be designed to provide information which demonstrates that:
 - The engineering controls, sanitization practices, and processes as a whole provide a “state of control” which means an environment that is consistently capable of maintaining microbial organisms at an acceptable level
- Sampling plates can either be TSA or SDA media
- Sampling is done by surface sampling or air samples
- Lab incubates samples
 - First incubation is at least 48 hours at 30°C to 35°C (microbial growth)
 - Second incubation is at least 5 days at 20°C to 25°C (fungal growth)





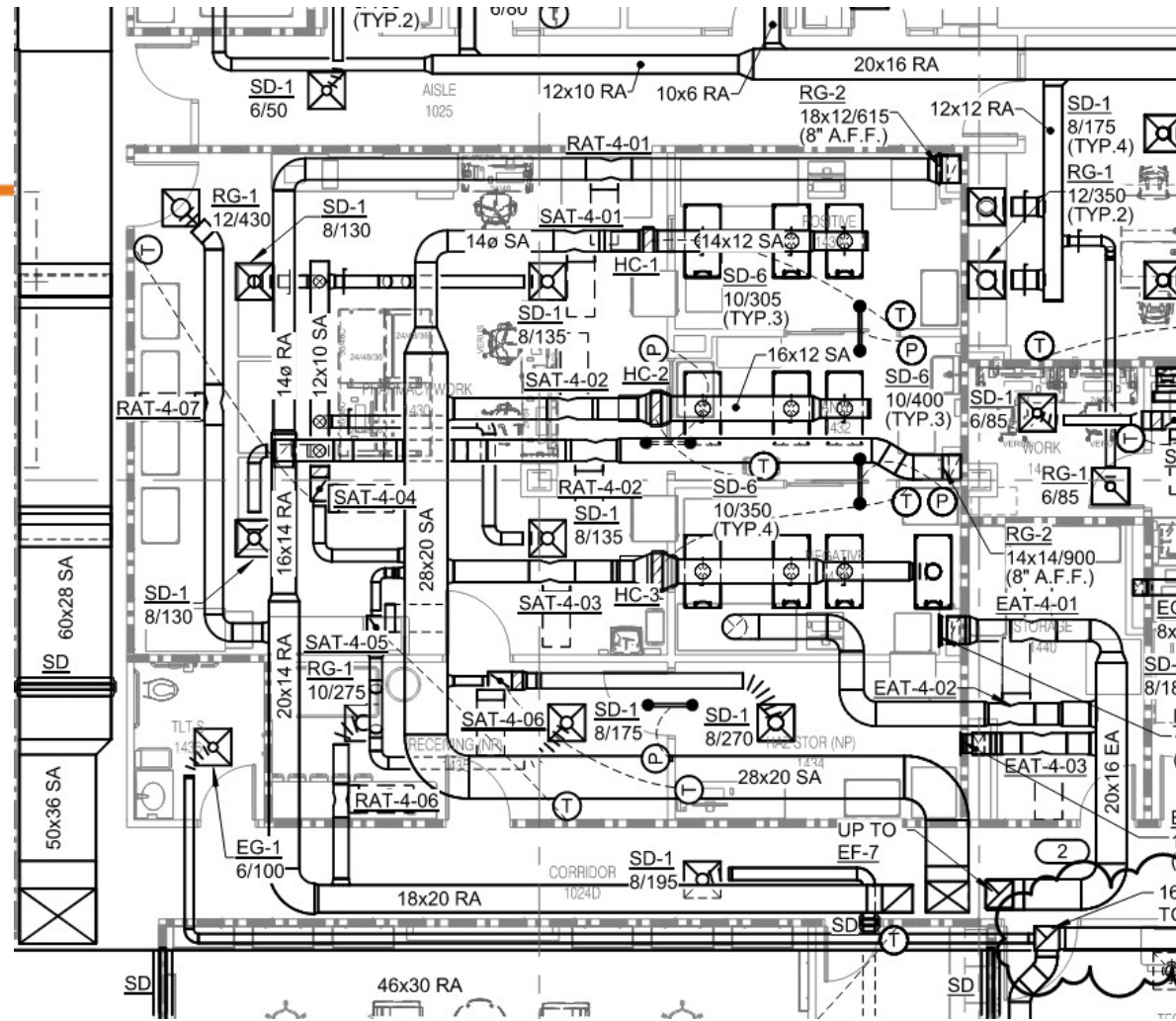
DISSECTING A PHARMACY

**Pressure
Requirements**

DISSECTION

Review what we have:

- Generally, a lot going on in a relatively small space
- Consider using the power of Blue-Beam to gain a better understanding

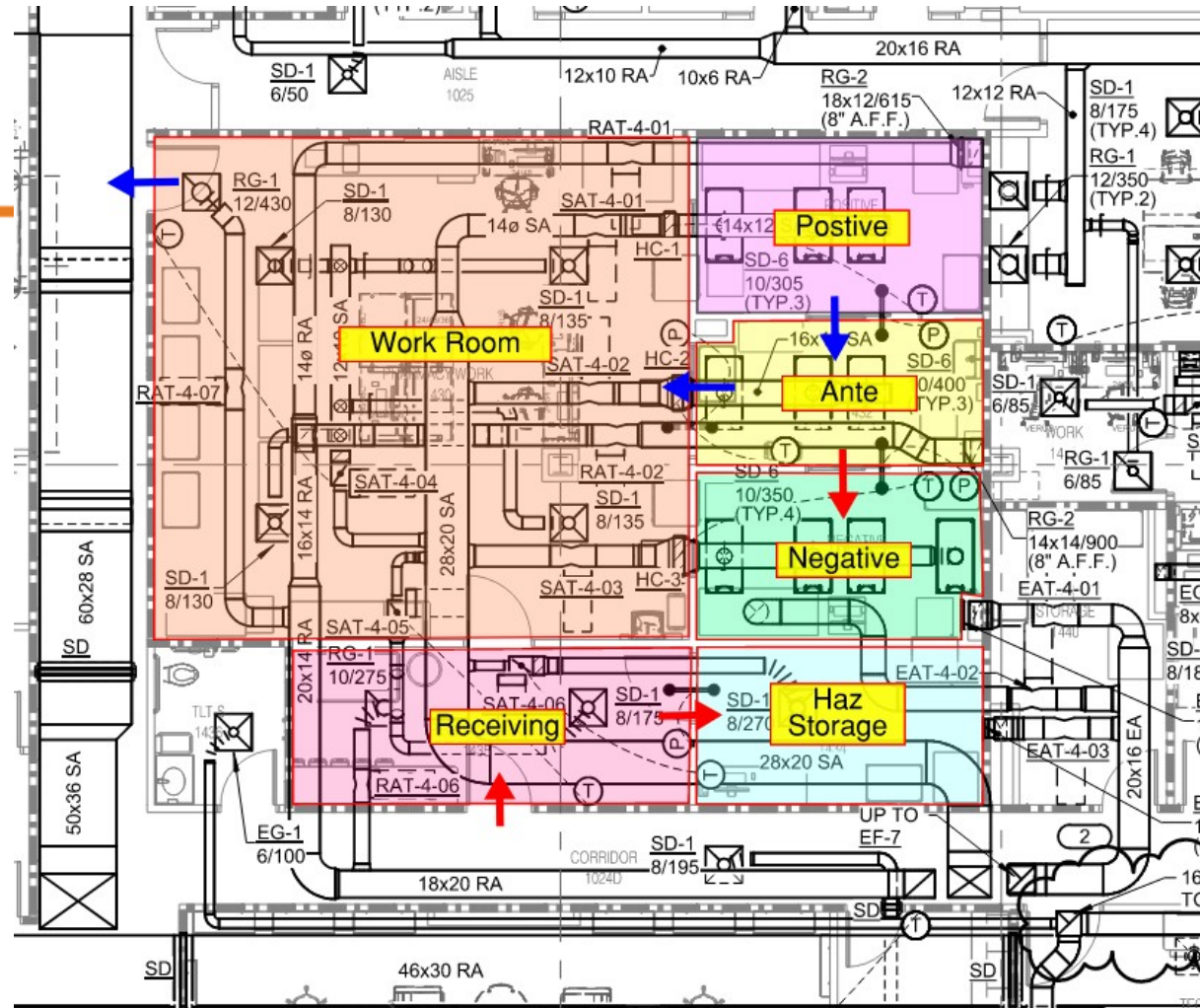


DISSECTION

Identify Zones

Typical layout:

- Work room
- Ante Room
- Haz Compounding
- Sterile Compounding
- Receiving
- Haz Storage

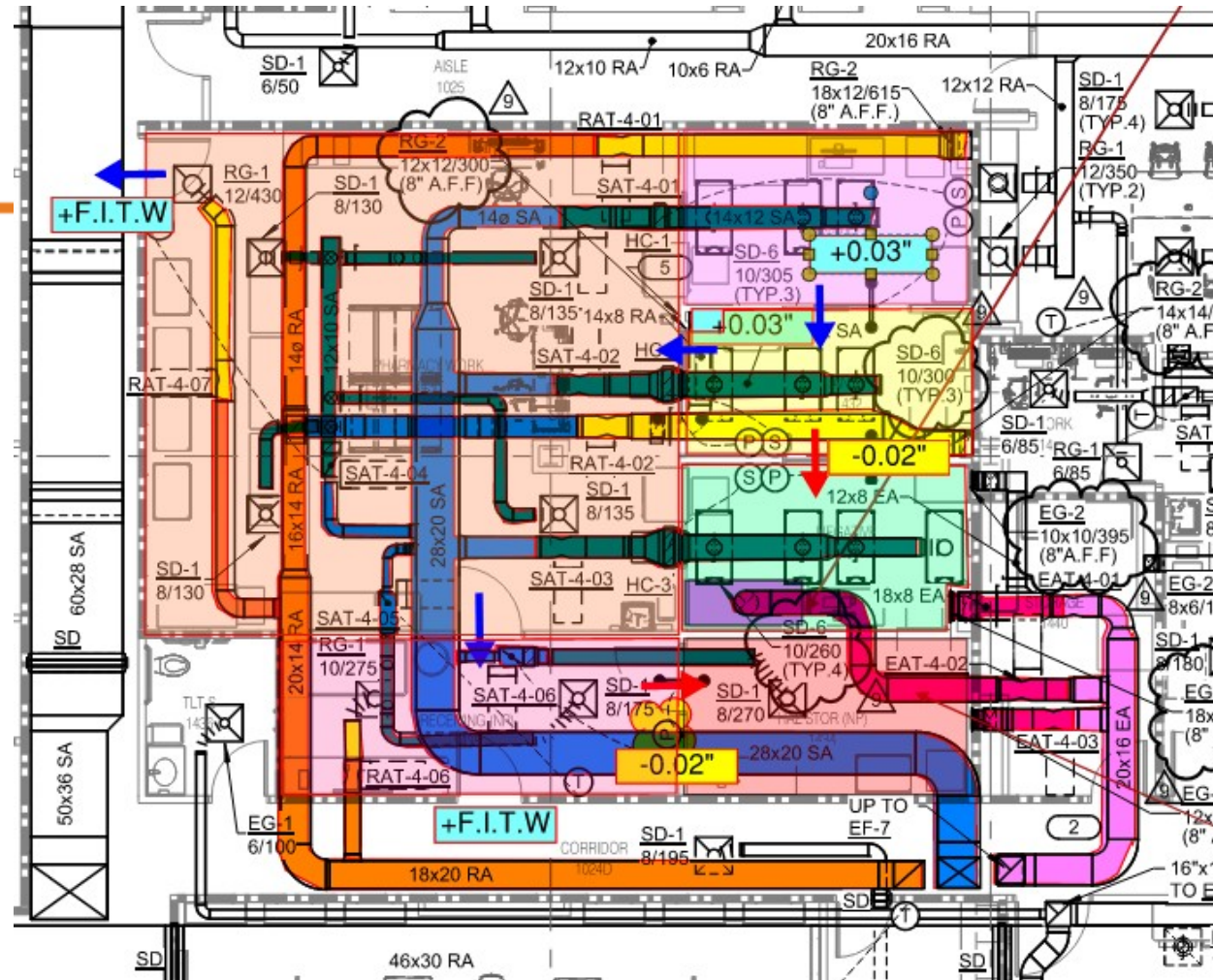


DISSECTION

Review Ductwork

Types of Terminals:

- Venturi Type of exhaust and return
- Butterfly on supply



Operations of Terminal Devices

- Supply constant
- Returns modulate for pressure

- Exhaust constant
- Supply modulates for pressure



Preparation

Dedicated 2N Exhaust System

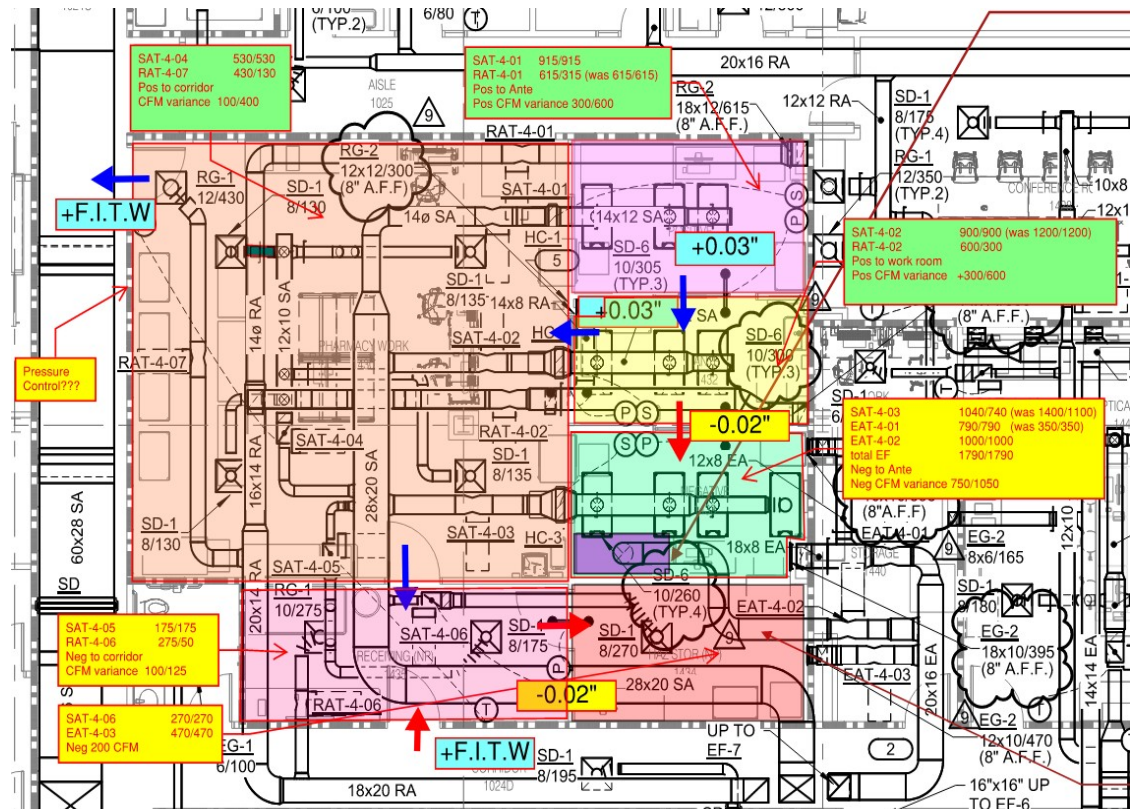
Every air terminal device (supply, return and/or exhaust) is controllable



WILL IT WORK FOR?

- Temperature control
- Humidity
- Dehumidification
- Pressure
- Air Changes

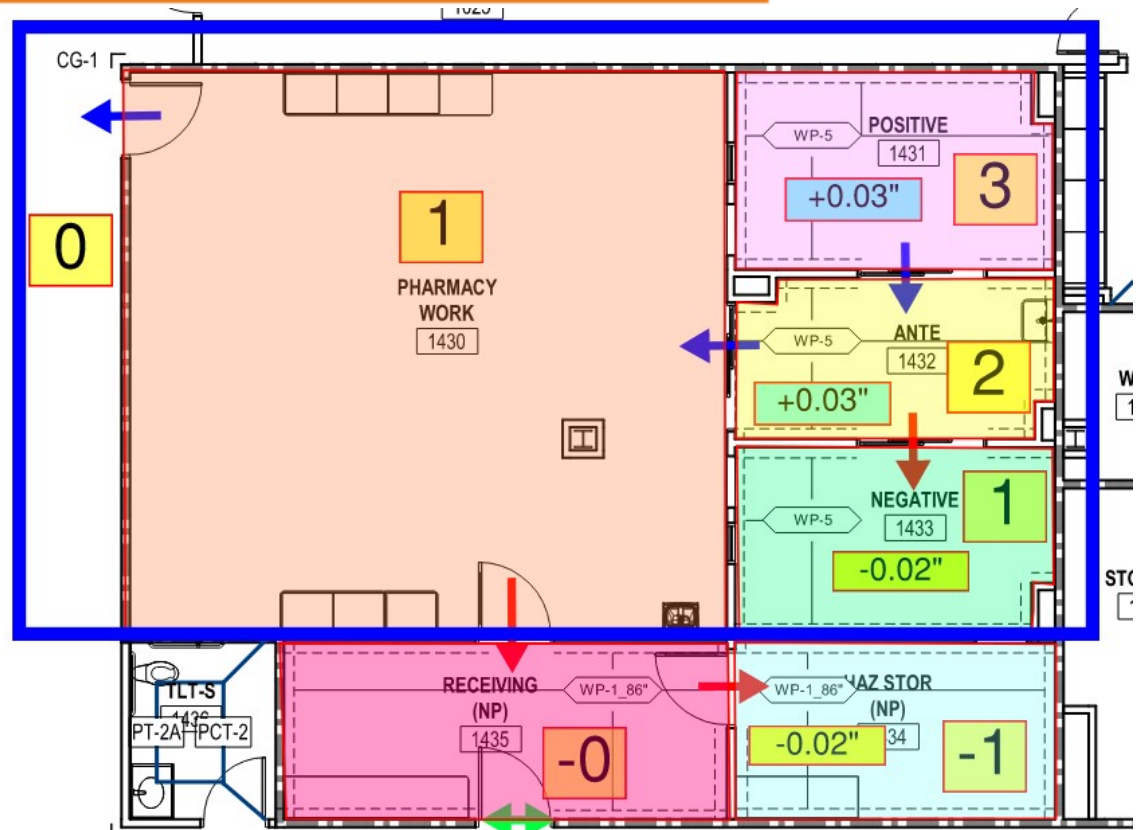
The general means to make the overall system work are all present, but there is always a 'but'... lets dig into one of the 'buts'...room pressure control.



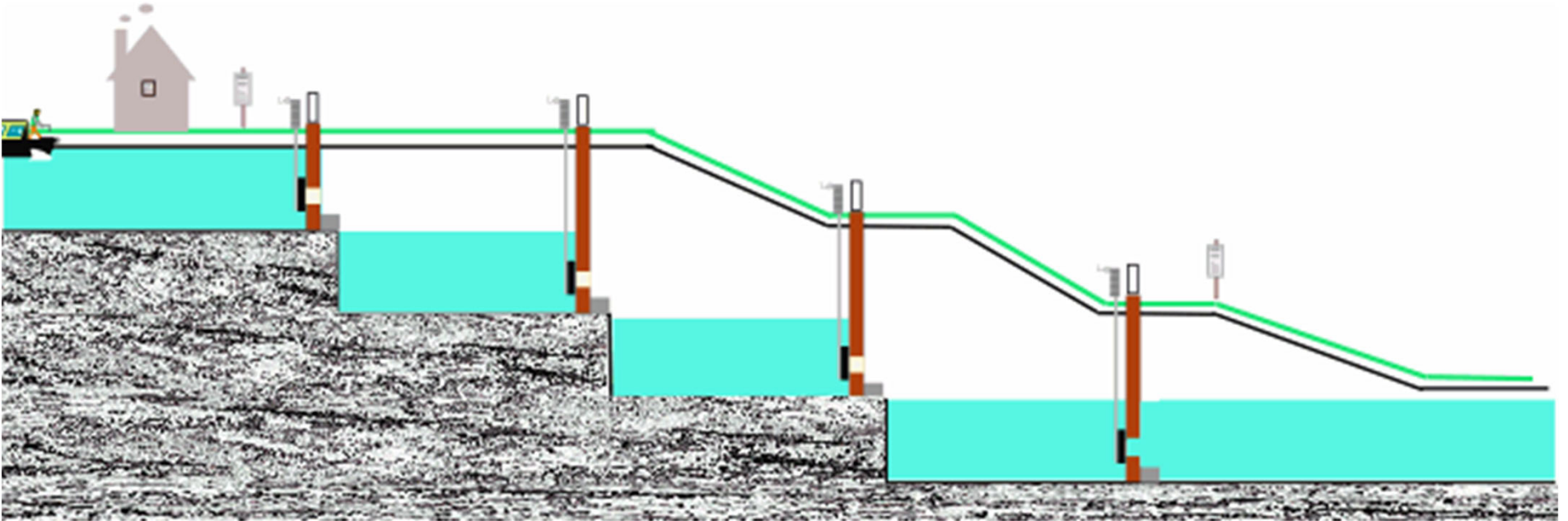
FOR EXAMPLE

- Pressure control
 - Without door switches
 - Per door, use of door switches
 - ORTRTA, use of door switches
- Volumetric control
- Hybrid

I like using a unit-less scale to show pressure relationships between space.



CASCADING PRESSURE RELATIONSHIP ANALOGY: LOCKS



PRESSURE CONTROL

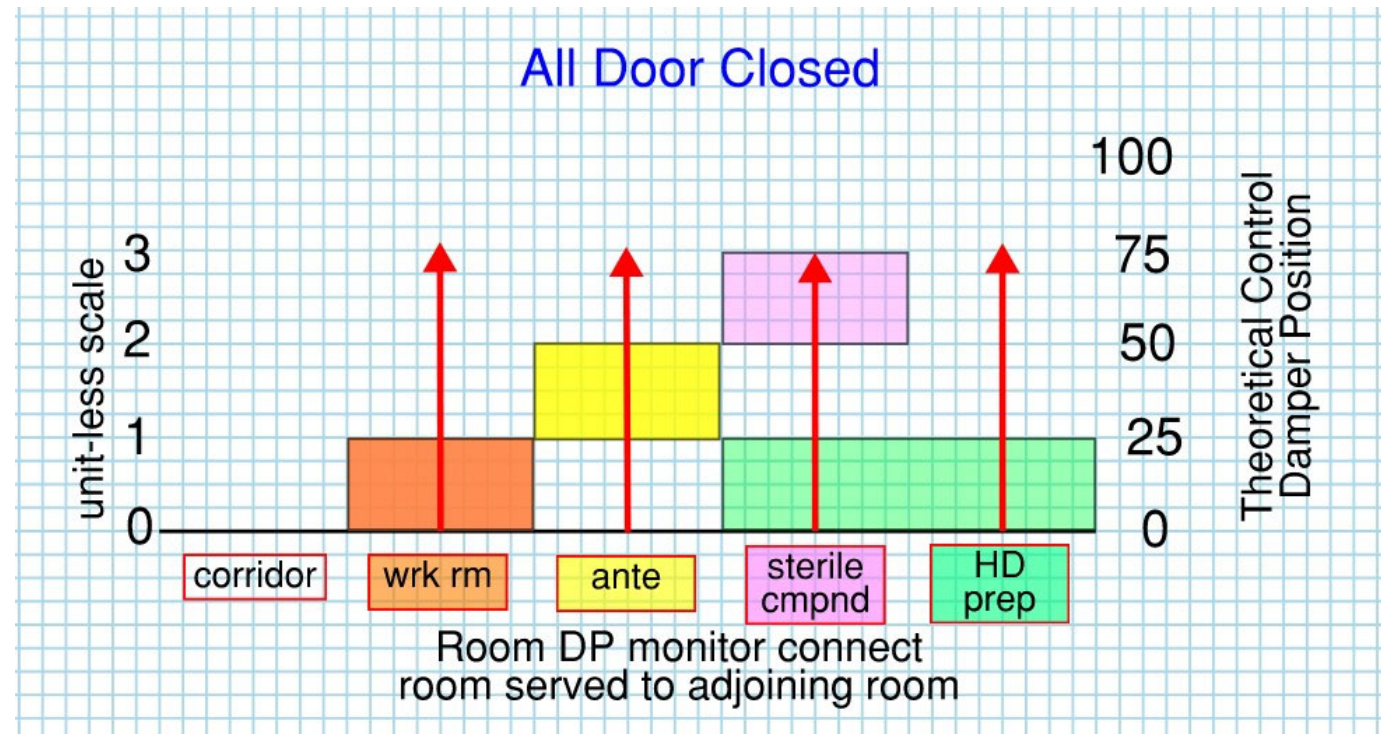
- Do you use a pressure monitor to then allow the BAS to control the controlling damper?
- Do you use a pressure controller to directly control of the controlling damper?
- Location of the pressure controller or monitor:
 - Outside the room served showing space is OK to work in before entry (but no reference within the space itself)
 - Inside the room itself where use might not know room is safe to enter to do work, but once inside a person can see and hear if there is an issue.
- The use (need) for door 'in use' switches indicating an open or closed door to allow for control interlocks.
- Sally Port operation is also beneficial

PRESSURE CONTROL

Consider the following...

No door switches:

- With all doors closed, system can achieve steady state
- For sake of discussion lets show all pressure control dampers sitting at approximately 75% open (good sizing by designer)

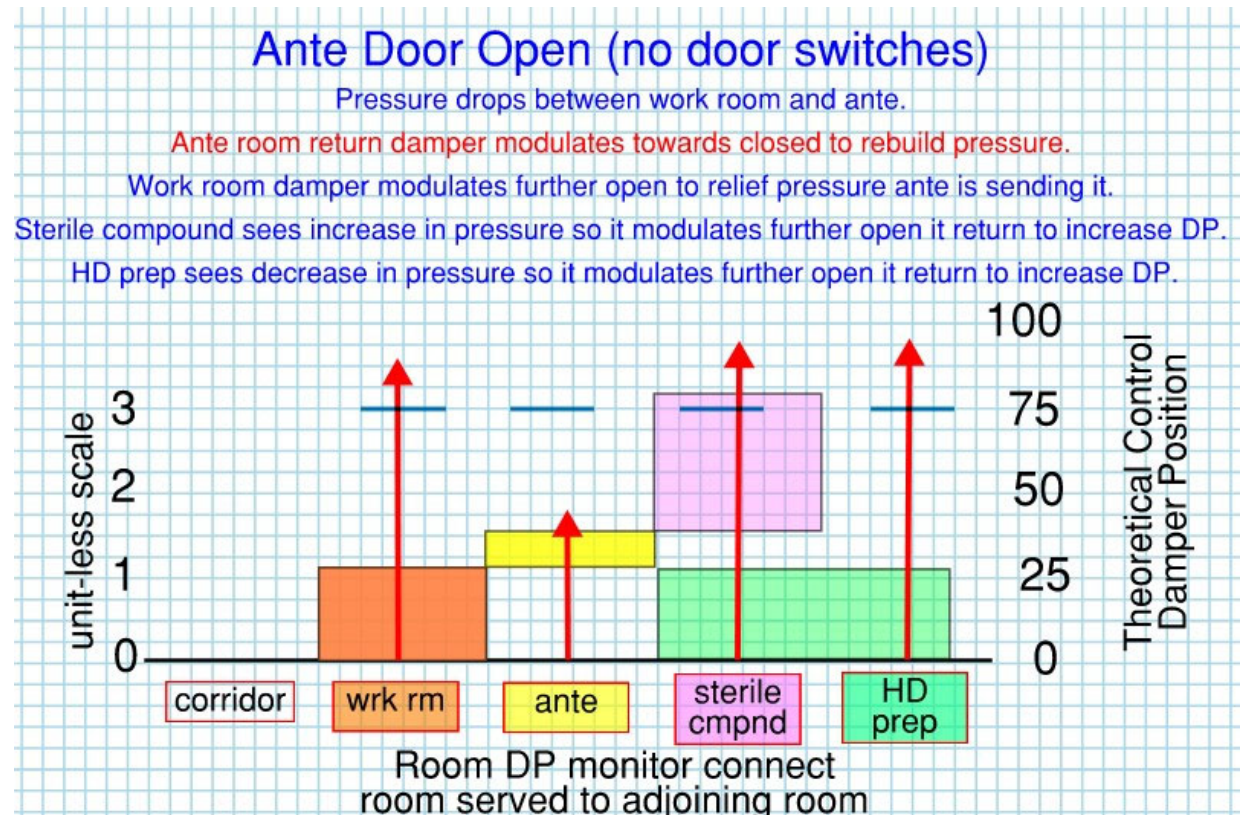


PRESSURE CONTROL

Consider the following...

No door switches:

- Pressure collapses between spaces between open door
- Pressure changes at all other control points as ante room touches all
- All the pressure control dampers react to the respective changed pressures

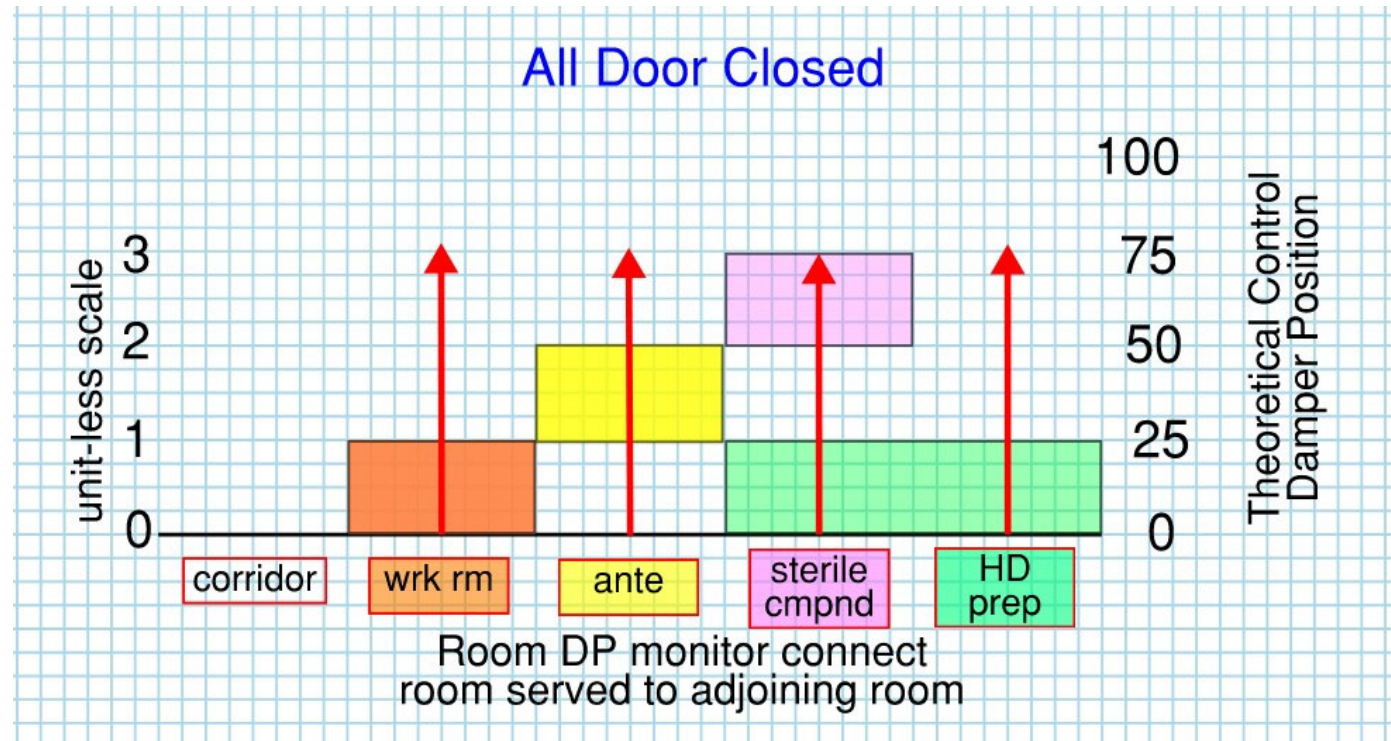


PRESSURE CONTROL

Consider the following...

Door switches:

- Consider this a typically door switch install, one door switch to an assigned pressure controller
- Starting from a steady state



PRESSURE CONTROL

Consider the following...

Door switches:

- The door that is open holds, but all other controllers are reacting the pressure changes
- Depending on damper speeds choose (I advocate for slow, except for a fume hood), the whole system is moving devices

Ante Door Open (door switch @ ea. door (controls own door))

Pressure drops between work and ante.

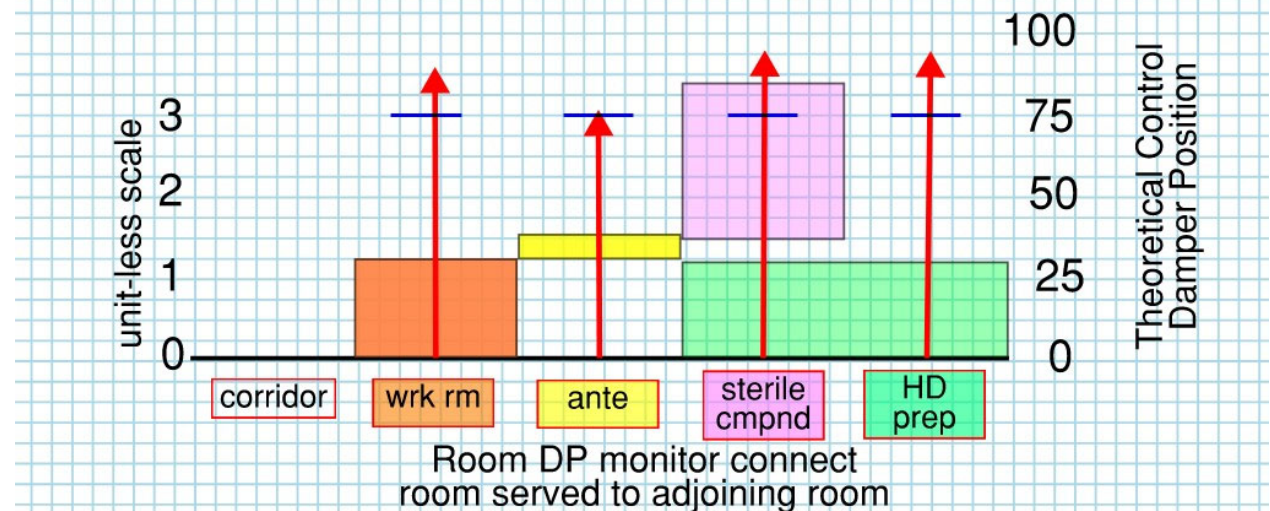
Ante room return damper HOLD's its position via door switch.

Other rooms still react to the DP changes due to ante room door open

Work room damper modulates open to relief pressure ante is sending it.

Sterile compound sees increase in pressure so it modulates open its return to increase DP.

HD prep sees decrease in pressure so it modulates open its supply to increase DP

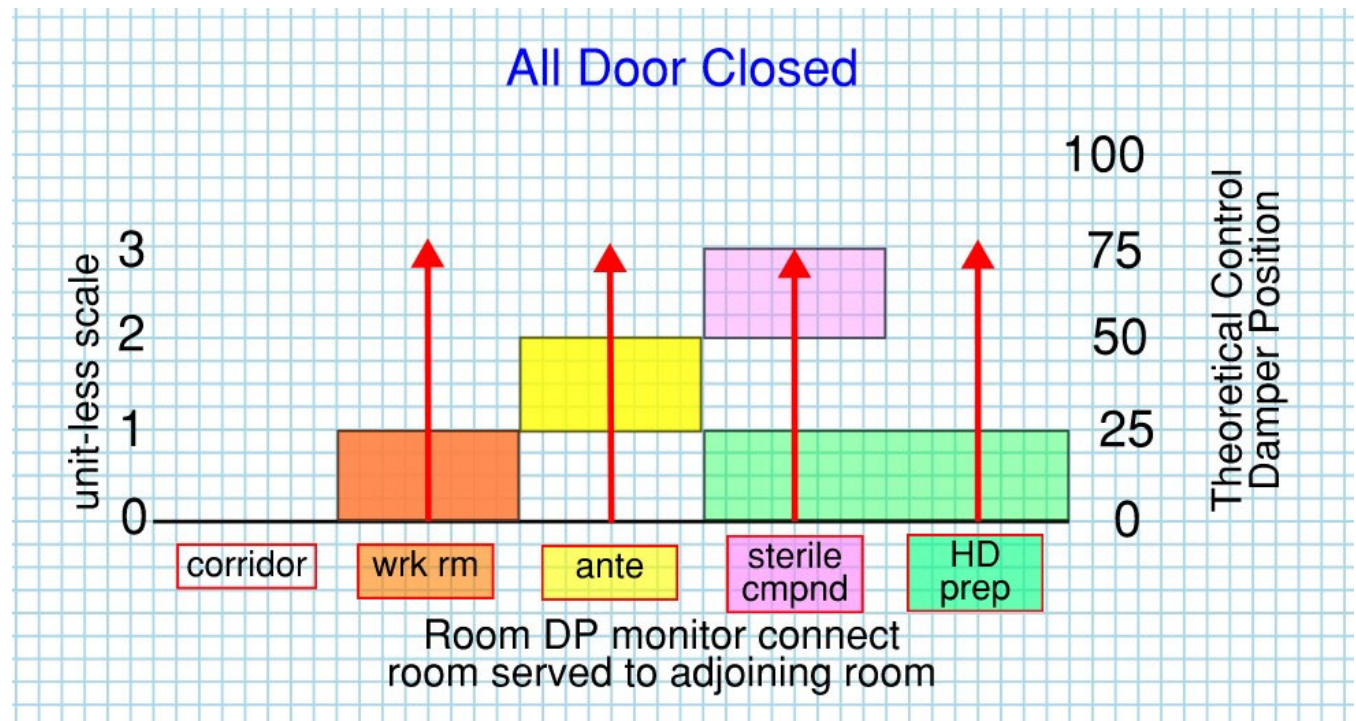


PRESSURE CONTROL

Consider the following...

Door switches:

- This control scenario has all door switches wired to a central panel to then incorporating wiring that any one door being open signal would go to each pressure controller (ORTRTA)
- Starting for steady state





ORTRTA

One ring to rule them all...

PRESSURE CONTROL

Consider the following...

Door switches:

- With ORTRTA strategy all the dampers hold, the pressures change, but the pressure relationships stay the same (like volumetric)
- When active door closes, systems resume as if time stood still
- Create a more stable AHU

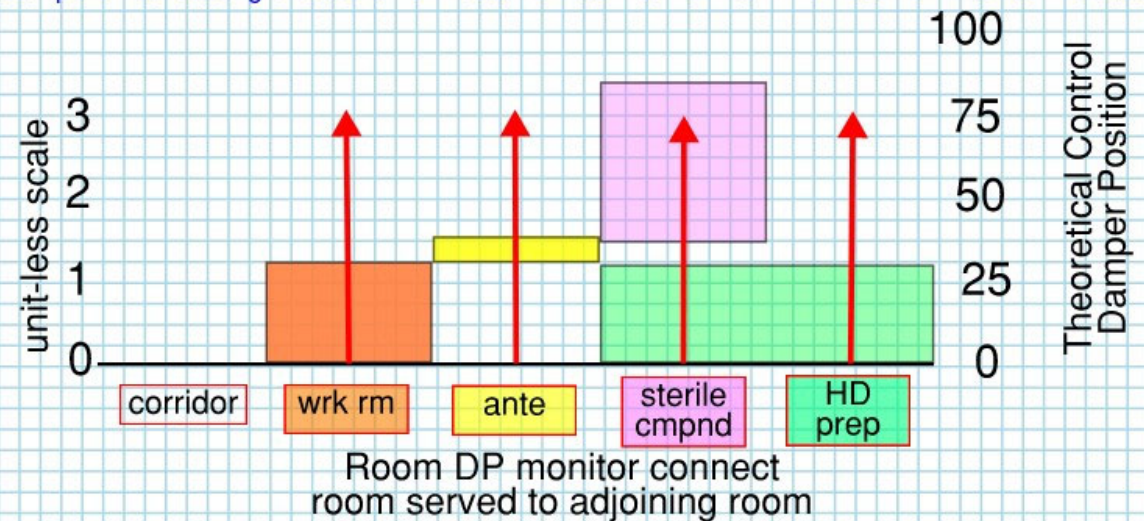
Ante Door Open (door switch @ each door, (any one holds all))

Pressure drops between work and ante.

Ante room return damper HOLD's its position via door switch, DP does change

Other rooms DP's also change due to ante room door open, but dampers do not react (hold)

The dampers not reacting creates a non-reactive 'return to normal' when door sw interlock releases



VOLUMETRIC CONTROL

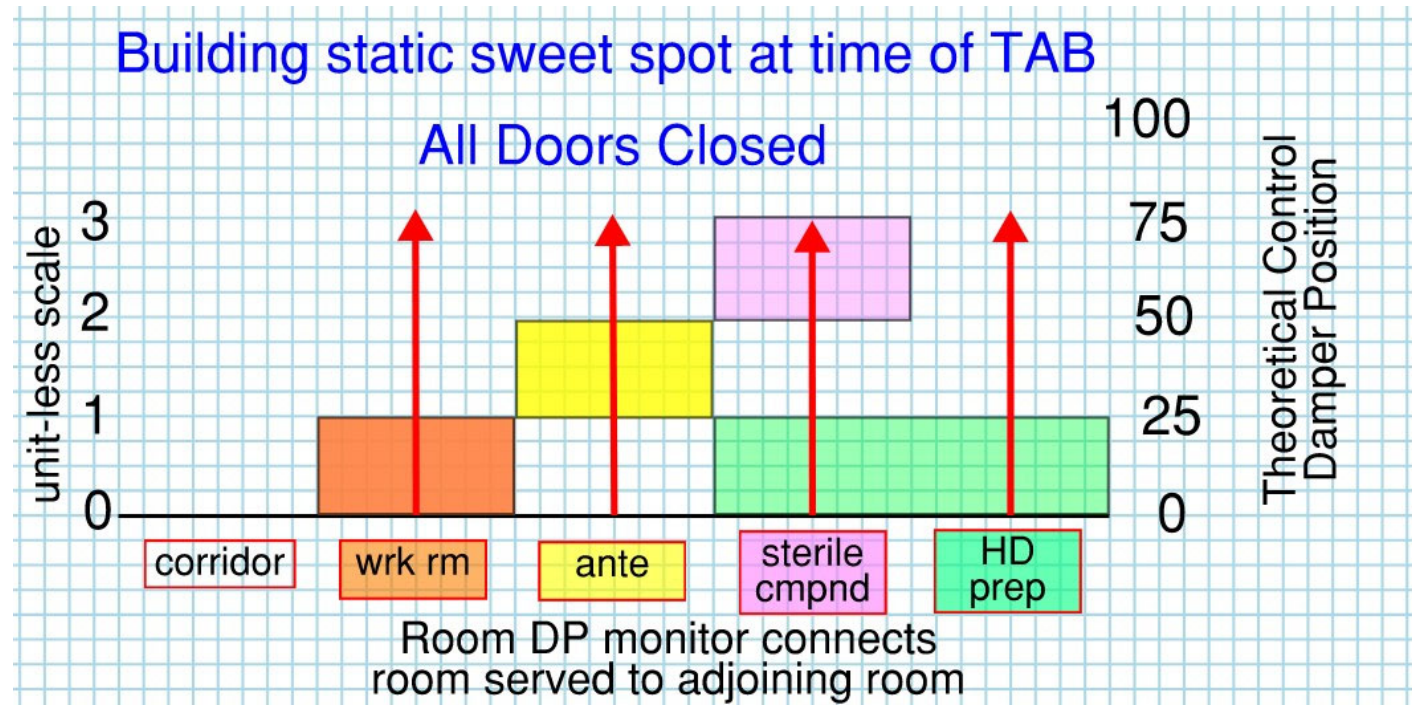
- Only a pressure monitor is used
- A Device Tracking control strategy is used, examples:
 - For the clean room (IV prep/compounding) and ante room, and possibly work room the supply VAV is constant volume and the return VAV varies its position to track the supply CFM actual to maintain a fixed offset that provides prescribed positive differential between adjoining spaces
 - For the hazardous side typical exhaust is boss, where the sum of the exhaust VAV's actual air flow (one for each fume hood (many times 2) and one for low room exhaust) is used to determine the position of the supply VAV by tracking the exhaust CFM actual to maintain a fixed offset that provides prescribed negative differential between adjoining spaces
- Some owners prefer on the hazardous side that air changes are still based on supply and not exhaust volumes.

VOLUMETRIC CONTROL

Consider the following...

No door switches required (with a qualifier):

- System continually operates in a steady state
- Potential Achilles heal, doesn't compensate for filter loading and building pressure changes



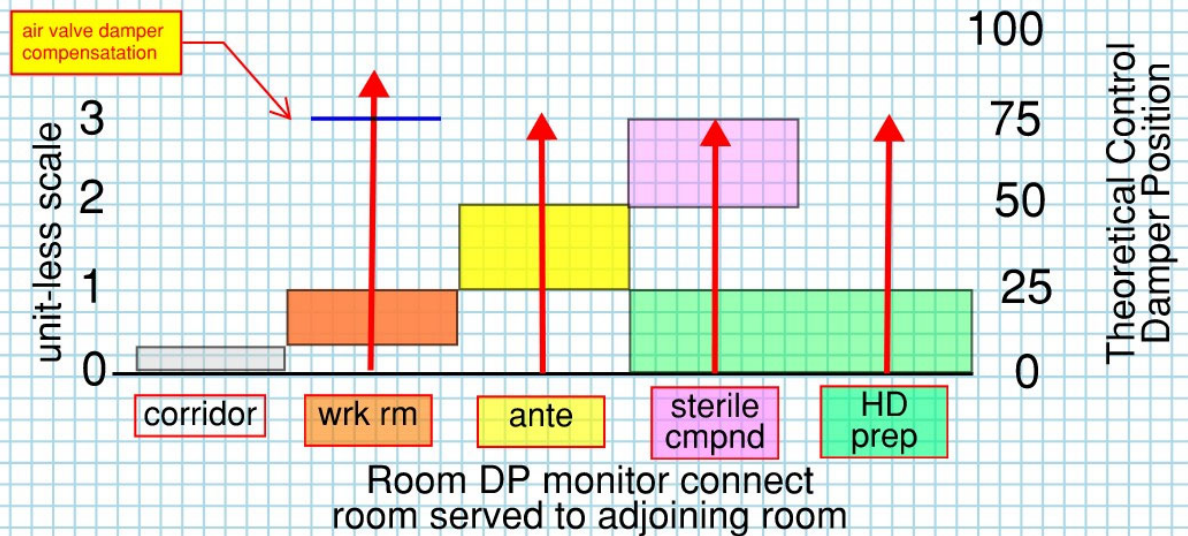
VOLUMETRIC CONTROL

Consider the following...

No door switches required (with a qualifier):

- System continually operates in a steady state
- Potential Achilles heal, doesn't compensate for filter loading and building pressure changes

Volumetric, Compensating for Building Static
The work room is the buffer between the building and the pharmacy proper, consider pressure control to adjust for building static pressure fluctuation. Controlling work room constant supply and adjusting return VAV for work room pressure (with possible door switch to corridor), to ante room can compensate for BSP changes



TAKEAWAYS

- Design details are key to a successful and stable compounding pharmacy.
- Pharmacy Certifications
 - Rooms are certified every 6 months
 - LAFWs and BSC's are certified every 6 months
 - Certifications are to USP797/800, CETA CAG's, NSF/ANSI, IEST RP's and ISO-14644
 - Advocate for HEPA Filter testing connections
- Pharmacy Pressure Control
 - Pressure, Volumetric, Hybrid can all work, but they need the appropriate accessories/programming to make them work.
 - Consider the location of the monitor/controller... inside the room or outside





Where do you want to go next?





Thank you!