USP 800 Compounding Pharmacies

Best Practices for Designing Safe, Compliant, Compounding Facilities

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Regulations

Designers are tasked with creating built environments that are safer and more resilient than yesterday.

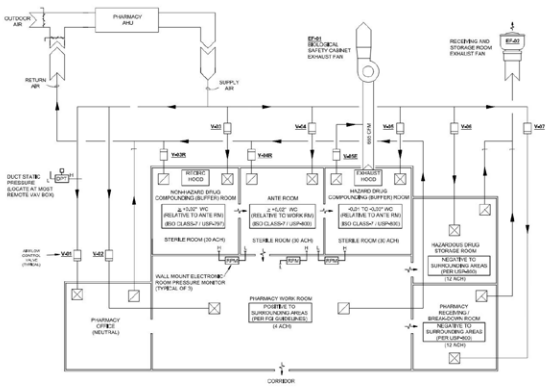
Some of these choices are evident to a casual observer — clearer access to emergency exits, for example — but many are unseen and vitally important.

That includes the technologies and systems used in buildings for preventing the escape of dangerous particles, including hazardous materials, pathogens, or allergens. The work may require room pressurization controls, improved ventilation, and proper protective barriers.

But as straightforward as it sounds, the natural (and invisible) airflows of a building constantly in use and reacting to its environment can be incredibly tricky. That's what many designers are learning as they seek to help pharmacies handling hazardous drugs comply with new regulations.

AIRFLOW DIAGRAM

Typical Layout



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When USP 800 was incorporated — seen largely as a supplement to USP 797, which covers requirements for pharmacy cleanrooms — it could be easily mistaken as tighter rules that could actually simplify cleanroom design.

But while more specifics leave little room for misinterpretation, they also leave little room for error.

Regulations

The most complex aspect turned out to be maintaining the room's pressure according to the new USP 800 guidance. In what seemed like a straightforward solution on paper — better control room pressure, reorganize the room layout and so forth — these newly implemented systems were failing under real-world conditions.

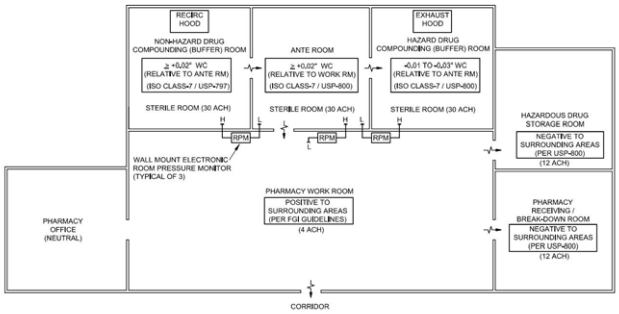
Even prefabricated compounding rooms were experiencing pressure leakages and weren't sufficient to meet the new standard. Existing spaces proved to be particularly challenging because of seemingly benign surrounding factors, such as proximity to a kitchen outside the construction scope.

The new regulations affect the following aspects of controlled, noncommercial prescription production facilities:

- **Room pressure:** USP 800 specifies the space's pressure range, which also affects facility exhaust requirements.
- **Space:** Ensuring there's enough room to adequately operate as it relates to equipment clearances, staff mobility, and donning and doffing personal protective equipment (PPE).
- **Ease of use:** Staff must be able to easily function based on their workflow, which includes communication between cleanrooms versus general areas. Staff should also be able to easily check the room's compliance by way of pressure gauges and other system tools.
- **Ease of cleaning:** Staff must clean the space routinely, making it essential that the room's materials and design can assist them in the maintenance.
- **Comfort:** The design of the room needs to be responsive to both human temperature requirements — especially as staff will likely be wearing layers of PPE — as well as the temperature needs for drug stability.
- **Primary engineering control:** The hood where the compounding occurs needs to meet certain requirements to ensure proper containment and cleanliness.

PHARMACY CLEAN ROOM DESIGN

Typical Layout



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Whole-Building Solutions

Careful review of the conditions that caused errors showed what mechanical design tweaks are needed to maintain the room pressures, which often means fighting against the surrounding building pressures. This included learning how to exhaust the "bad air" out of the building safely — while also maintaining the appropriate room pressure. The idea is to avoid exposing people in the building to, for example, chemotherapy drug particles that become airborne. The work is similar to efforts undertaken to keep air from COVID-19 patients' rooms from circulating into other parts of the healthcare facility. For example, such rooms often expel "bad air" by way of the roof, away from potential infiltration areas. Using a whole-building approach provides opportunities to identify how certain pressure needs can tax the existing infrastructure and have trickle-down influence elsewhere in the facility.

Although the regulations apply to all facilities that handle hazardous drugs, how those rules are met can vary widely from location to location. Each project — from remodels to new builds — required unique solutions to bring the facility up to code. Cushing Terrell's multidisciplinary healthcare design team used its past experiences and extensive knowledge of health care facilities to tackle each challenge.

> *Quality is never an accident: It is always the result of high intention, sincere effort, intelligent direction, and skillful execution. It represents the wise choice of many alternatives.*
>
> **- William A. Foster**

USP 800

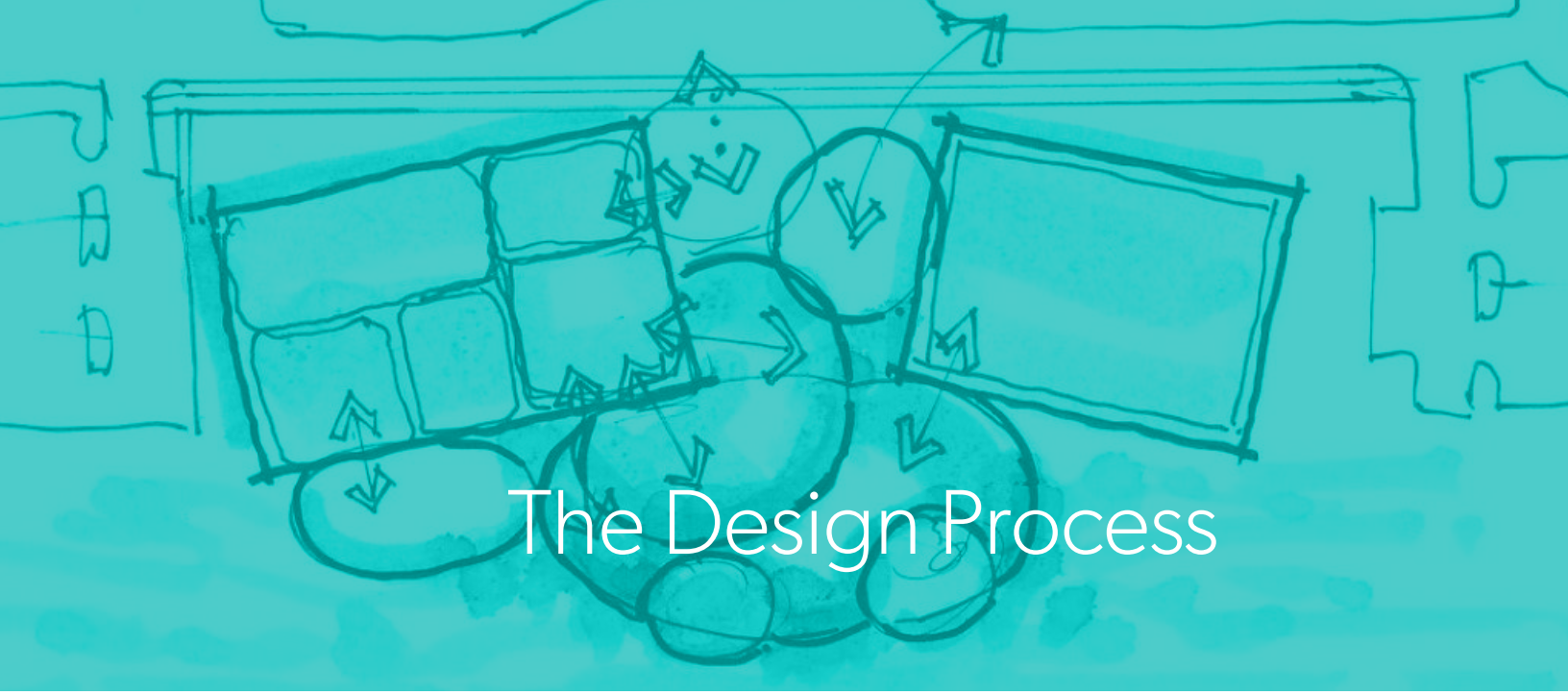
USP 800 establishes practice and quality standards for the handling of hazardous drugs as it relates to their receipt, storage, compounding, dispensing, administration, disposal, and more. Compliance with USP 800 can assure that any personnel who may be exposed to hazardous drugs are doing so in a manner that keeps staff safe and the drugs stable. This often means increased requirements for room pressures, filtration, and segmentation.

Other design considerations for the handling of hazardous drugs:

- **Receipt:** Breakdown areas are designated for the unpackaging of hazardous drugs from a distributor. The intent is to limit personnel exposure should the containers that hold hazardous materials potentially break during transit. To mitigate this, the breakdown area is enclosed and pressured at negative to neutral — compare this to a typical pharmacy, which is positively pressured to a corridor.
- **Compounded sterile product transfers between the sterile compounding rooms and general work areas:** Pass-throughs can be beneficial in that they facilitate material transfer without opening doors and without people entering or exiting clean rooms. But because these areas can cause pressure changes, the correct application of pass-throughs is vital.
- **Communication:** Hands-free intercoms and vision panels for staff, particularly working in compounding areas, can create efficiencies and avoid the transfer of hazardous materials to surfaces or the introduction of foreign matter to drugs.
- **Refrigerator storage:** To avoid unforeseen hazardous drug contamination being spread within the drug storage room by the refrigerator temperature requirements — especially as staff will likely be wearing layers of PPE — as well as the temperature needs for drug stability.

Setting the Scene

USP 797/800 sets out guidance that a compounding suite's buffer room must be negatively pressured to the ante room. The ante room is positively pressured to the adjacent pharmacy workspace, with lines of demarcation further separating the ante room into "clean" and "dirty" sides. Staff enters the ante room on the "dirty" side" and begins their donning of PPE. The "clean" side is where acceptable sanitation and hygiene are required for compounding sterile products. By understanding such staff protocols, these restrictions can be integrated into the space's design.



The Design Process

To guarantee the compounding pharmacy meets the new regulations, the design team carefully follows a list of steps to ensure they're catching any potential issues.

The process begins with programming:

The team establishes early goals and coordinates with the facility owners on the level of environmental quality as it relates to the compounding segregated area, compounding suite, and any necessary buffer zones and ante rooms.

The team then sets a project budget and goals, verifies any existing systems can meet the new requirements, and determines any phasing requirements and impacts. At this point, a preliminary design plan is set, which includes a verification of storage requirements, location of hazardous drugs throughout their lifecycle, maximizing the room volume, determining communication requirements, and establishing a site certifier.

Next, the team determines the schematic design, which establishes a baseline of the existing facilities, a refining of the preliminary design, establishing pressure control zones, and ensuring buy-in from all stakeholders. The team engages the owner, architect, mechanical engineer, electrical engineer, plumbing engineer, and vendors. When working with a multidisciplinary design firm like Cushing Terrell, this coordination is built into the process.

As the process moves forward, the team will refine its design, develop construction documents, engage in bidding and permitting, and handle construction administration.

CASE STUDIES

PROJECT #1

Trouble with the neighbors

The problem: The pharmacy clean rooms were experiencing pressurization issues. In particular, the rooms had a difficult time returning to their correct pressure relationships whenever there was a disruption in the rooms or mechanical systems. The issue often required technicians to pause their work and focus on returning the space to its correct pressure relationships.

Observations: The clean rooms struggled to maintain adequate supply airflows and weren't being actively controlled based on room pressure readings. The air handling unit (AHU) return fan was not controlled correctly, either, and there was no building pressure control. Upon installation and testing of a building static pressure sensor, the team found the pharmacy compartment was unable to build positive building static pressure. Further investigation revealed the nearby kitchen area was in a severe negative pressure condition caused by a lack of make-up air — affecting the adjacent pharmacy because of leaky walls. Lastly, the team noted the exhaust fan serving the hazardous compounding room hood was not performing adequately. Its configuration was atypical for exhausting air from hazardous spaces.

Specifically, external static pressure losses through the damper and rain cap negatively affected the fan's performance, and the rain cap eliminated the stack exit velocity for optimal plume rise and jet dilution.

Lessons and solutions: The AHU should have a minimum duct static pressure setpoint and the ability to increase duct static in response to terminal unit airflow requirements. Terminal units serving pharmacy clean rooms should have a fixed minimum cubic feet per minute (CFM) to satisfy the required air change rates, and each room should have a modulating controlled device responding to the current room pressure. The team also found that proper building pressure controls are essential both inside and outside the pharmacy compartment, with walls adequately sealed to ensure room pressures inside the pharmacy compartment are minimally impacted by adjacent pressure conditions.

Finally, exhaust fans serving hazardous compounding rooms should be designed with a straight, unimpeded upblast with high exit velocities. Facility Guidelines Institute requires a minimum 10-foot exhaust stack height.

PROJECT #2

New build, old problems

The problem: When this completed pharmacy's clean rooms were operating within design parameters, the rooms' pressure readings would shift out of compliance. Although the pharmacy had a dedicated air handling unit, the building's existing systems and pressures were strong enough to overcome the pharmacy's new design.

Observations: The pharmacy's clean rooms were served by variable air volume (VAV), which required a significant amount of setup and calibration to achieve adequate control. The VAV controls would periodically drive the VAV damper closed to calibrate the velocity pressure sensor, causing the room pressure sensors to go into alarm.

Significant swings in building pressure were causing pressure issues within the pharmacy compartment, which correlated with the existing system entering economizer mode. The existing AHU return air ducts within the pharmacy compartment also caused pressure issues.

Lessons and solutions: High-accuracy air valves are recommended for clean rooms. The precise flow requirements required to maintain the room pressures push the limits of standard VAV boxes for airflow accuracy. Proper building pressure control outside the Pharmacy compartment is essential. Pharmacy compartment walls must be adequately sealed to ensure room pressures inside are minimally impacted by the adjacent building pressure conditions. As a good practice the pharmacy compartment should have a dedicated AHU.

Alternative designs using HEPA fan filters can also be successful. Ceiling heights must be coordinated with all required accessories and options of the equipment to be used within the cleansuite, and typical equipment cut sheets may miss items such as accessory table/caster heights and hood canopy exhaust.

At this pharmacy, the building pressure controls were updated to resolve the issues. A vestibule was constructed at the entrance of the pharmacy from the corridor with door interlocks which minimized building pressure influence on the pharmacy general areas. The return air connections were also removed to resolve the AHU air ducts issue.

PROJECT #3

Reeling It In

The problem: The pharmacy clean rooms at this location would go out of compliance and into alarm, requiring service and/or adjustments to bring the rooms back into compliance.

Observations: On one occasion when the rooms went into alarm, an investigation revealed the sequence of operation to modulate the return air dampers in the ante room and non-hazardous compounding room had been inadvertently removed. This caused the rooms to drift out of compliance over time in response to gradual system changes due to normal operation, such as filter loading or duct static pressure variations.

On another occasion when the clean rooms went into alarm, the filters on the AHU were found to be past due for service. The resulting excess filter air pressure drop caused the supply fan to be starved for air, causing the clean rooms to be low on airflow.

Lessons and solutions: Mechanical systems gradually change over time due to normal operation. Each room should have a modulating controlled device responding to the current room pressure.

Proper service for the AHU serving the pharmacy compartment is critical and should include service notifications, with acknowledgement sent to the facility operator.

Other key learnings

Best Practices

With these lessons and best practices taking shape, designers and pharmacy managers not only better comply with new regulations, but they keep vital medical materials secure and stable, keep staff safe, and improve efficiencies.

Cushing Terrell's pharmacy design team works closely with facilities representatives and staff members to ensure the best possible USP 797 and 800 compliance. Some of the most important design insights are gained by listening to the needs of those occupying the space and observing the environments in action.

Those insights gained thus far include:

- **Scrutinize pharmacy staff workflow procedures:** The design should facilitate or even improve the organization's standard practices.
- **Verify cleaning agents used and compatibility with desired finishes:** Note that ammonia-based cleaners will remove certain epoxy paints.
- **Verify finish resilience and cleaning procedures:** Some facilities use UV lighting to assist in cleaning. UV light may require a blackout curtain on the outside of the compounding room to account for staff safety from exposure across vision panels.
- **Do not overlook air pressure influences on the clean room suite:** Something as simple as a transaction window opening into a corridor can have major air pressure impacts.
- **Verify the storage needs of the compounding suite.**
- **Keep staff comfort and drug stability in mind:** Multiple layers of PPE require a cool working environment, but this can conflict with the drug storage requirements.
- **Engage staff feedback:** Speak with employees prior to installing mirrors, sinks, and lines of demarcation.
- **Avoid the use of pass-through refrigerators:** It is difficult to seal such refrigerators, which can affect room pressure.
- **Limit the amount of built-in furnishing:** Dirt and pathogens can accumulate on such surfaces, and they're often enclosed with impervious finishes but use porous substrates.
- **Existing building controls and systems can affect pharmacy pressure.**
- **Do ample research and be aware of any state-specific requirements.**

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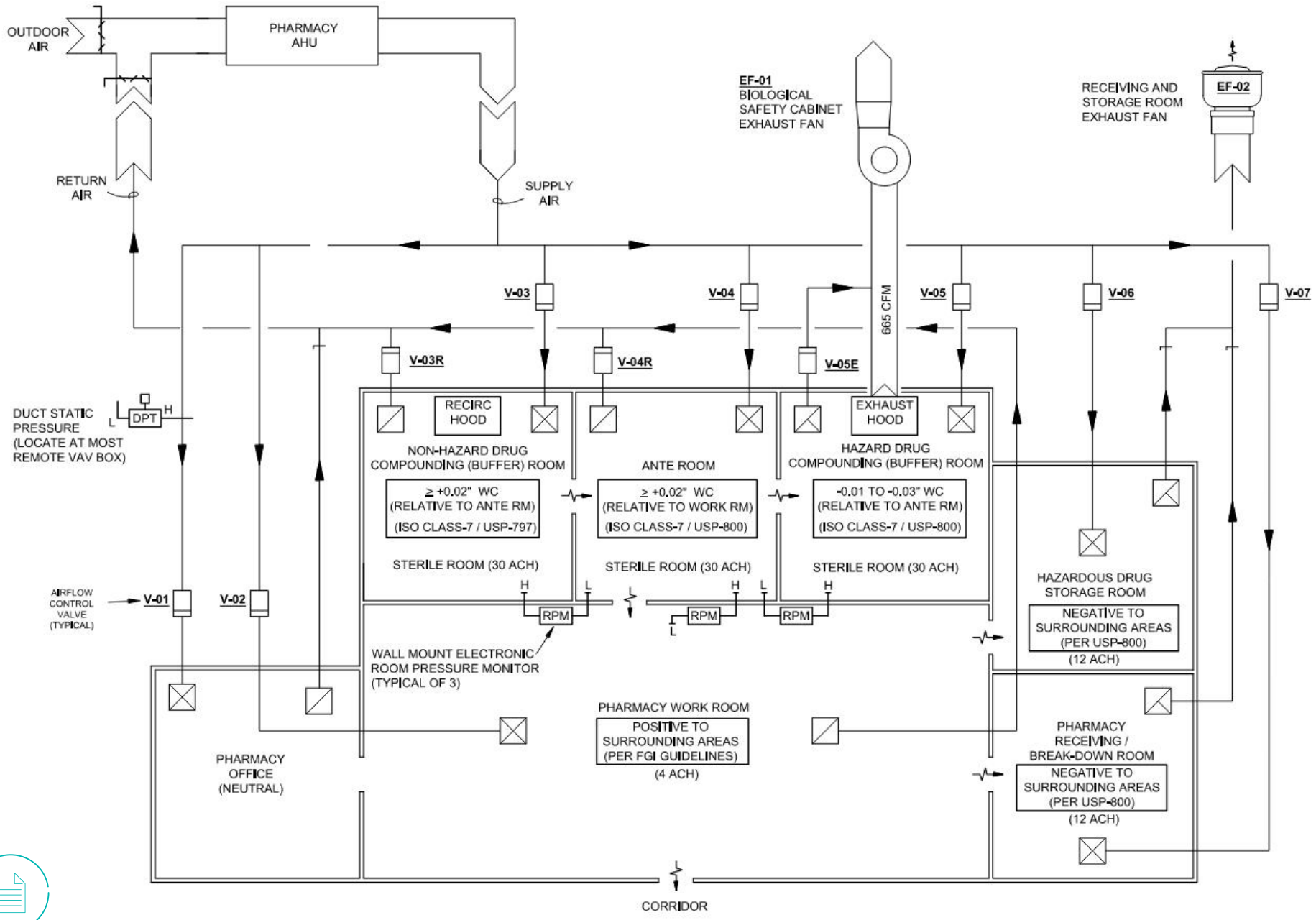

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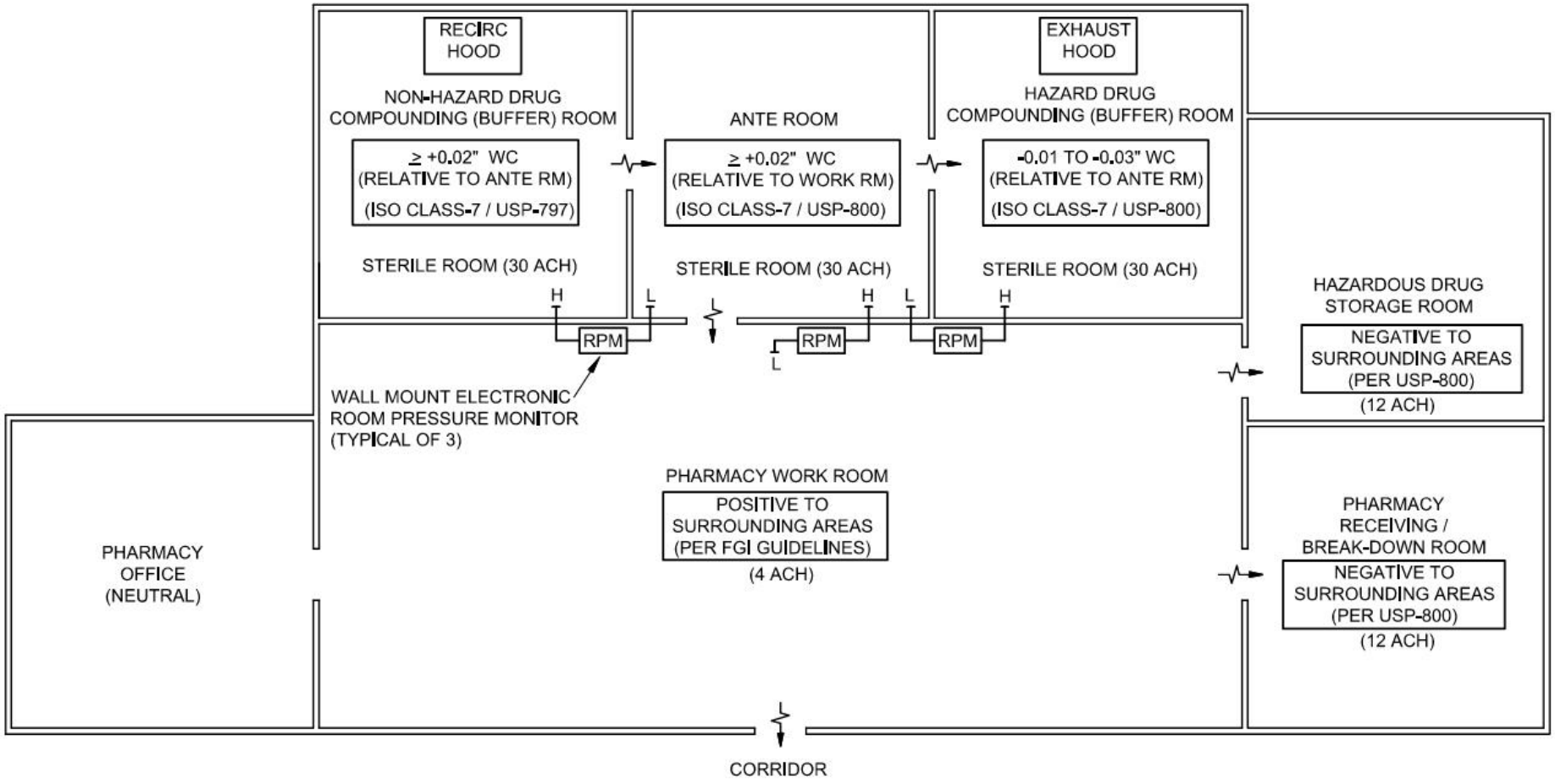

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