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Pharmacies and HVAC:

The Mechanical Impact of USP 797 on Pharmacy Compounding Areas

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COMPLIANCE WITH PHARMACY REGULATIONS HAS BECOME MORE COMPLEX.

In 2004, *The United States Pharmacopeia – National Formulary – USP Chapter <797>, Pharmaceutical Compounding, Sterile Preparation* (herein designated USP 797), was issued. This document set a federally enforceable minimum standard for facilities that prepare or compound sterile preparations. Once voluntary, these facilities would now be monitored by the Food and Drug Administration (FDA), as well as local and state pharmacy boards. The main thrust of this document is to ensure patient safety.

Compounding is an integral procedure in any pharmacy. Improperly prepared or contaminated preparations are a danger to patients. The USP 797 set out to create a standard that would provide a minimum level of uniformity for pharmacy compounding areas, as well as to deal with the preparation and transport of the compounded materials. This text addresses the important provisions of USP 797 that affect the building systems with an emphasis on the area's ventilation and HVAC requirements.

Standard Hospital HVAC requirements are generally more stringent than the average use building. Not only does a Healthcare Facility need to comply with Building Codes, but also has to meet the requirements of the Joint Commission on Accreditation of Healthcare Organizations (JCAHO). Besides minimum code required ventilation air, the JCAHO requires minimum air change rates for certain specific areas within a Healthcare Facility, generally using the latest *AIA Guidelines for the Design and Construction of Hospital and Healthcare Facilities* and the *ASHRAE Healthcare Design Guide* as minimum requirements. Pharmacy compounding areas are no different in this regard, and now have additional requirements due to USP 797. JCAHO has indicated its intent to begin surveying facilities for compliance with USP 797, with a timeline discussed later in this text.

USP 797 divides the compounding space into three different areas. First is the critical area, which is where the actual compounding occurs. The second area is the buffer area, which is the room or space in which the critical area resides. The third area is the anteroom, which separates the buffer area from the rest of the suite. USP 797 requires that all these areas be 'clean rooms,' which means a room where the airborne particulates are limited and controlled. The actual level of cleanliness is determined by ISO 14644-1, which replaced the repealed US FS 209E standard.

Clean room classes are indicated on Table 1, below. It is common for the ISO Class and 209E Class to be used interchangeably. For instance, an ISO Class 8 room and a Class 100,000 space are the same thing. What this classification determines is the number of airborne particles that are present within a given volume (in this case, number of particles 0.5 micrometers within one cubic foot or meter) of the space. These particles can be generated by three sources: Supply air, infiltration from adjacent areas, and internally. This is where the Pharmacy HVAC system becomes very important.

The supply air particulate count is controlled by providing HEPA (High Efficiency Particulate Air) filtered air to the space. HEPA filters are 99.97% efficient at capturing particles 0.3 micrometers and larger. Therefore, with HEPA filters, the supply air can be considered practically particle free. In retrofit jobs, this can be a difficult task, as HEPA filters have air pressure drops reaching 1.5" w.g. – a considerable drop. There are HEPA filter supply modules on the market that have a booster fan to accommodate this added pressure drop. Please note that ULPA (Ultra Low Penetration Air) filters do not appreciably improve the particulate count of the supply air, as they are 99.999% efficient at removing particles 0.12 microns in diameter or larger, resulting in a very small difference in particle volume.

The infiltration from adjacent areas is controlled via positive air pressurization relationships with adjacent areas. The accepted minimum positive pressure relationship is 0.05" w.g. between the spaces. For a space with a standard three (continued…)

Table 1: **CLEANROOM CLASSES**

ISO CLASS	US FS 209E	PARTICLES PRESENT (0.5 Micrometer)	
		Per m^3	Per Ft^3
3	Class 1	35.2	1
4	Class 10	352	10
5	Class 100	3,520	100
6	Class 1,000	35,200	1,000
7	Class 10,000	352,000	10,000
8	Class 100,000	3,520,000	100,000

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foot wide by seven foot high door, with a 1/8" crack between the door and the frame, this would require 186 cubic feet per minute (CFM) of air. Also, to help control infiltration, all cracks or openings within the room need to be caulked and sealed.

Internal generation is the most difficult to control, as airborne particulates come from the individual workers clothes and own bodies. The generally accepted estimate from individuals within the space is 5000 particles per second per cubic foot, a high number considering the levels of particles that are trying to be maintained within the rooms. This is generally done though dilution of the room air with HEPA cleaned supply air by means of high air change rates.

USP 797, using ISO 14644-1, indicates the required clean room classes that must be maintained for the different spaces. For the critical area, this must be ISO Class 5. This is usually obtained by means of a hood where the compounding occurs which provides very high air change rates.

For the buffer area, the requirement is ISO Class 7. To this level of particles, 30 air changes per hour minimum are required. To put this in perspective, ASHRAE recommends 25 air changes per hour for operating rooms. Though the actual buffer areas are often relatively small rooms, this can still amount to very high air rates. (Please note that USP 797 currently calls for an ISO Class 8 room for the buffer area. This is being changed to ISO Class 7 for the next issue of USP 797, due sometime this year or next. Therefore, our recommendation is to design to ISO Class 7).

The ante room is to be ISO Class 8, requiring a minimum of 20 air changes per hour. The ante room is also affected by what risk level of sterile preparation the Pharmacy is performing. USP 797 separates this into 3 levels: low, medium, and high, but for mechanical purposes, only two levels need to be considered: low\medium and high. A low\medium risk area does not require a separate ante room, only a separate ante area. A high risk area requires an actual physical ante room. The risk level needs to be determined by licensed healthcare professional.

The buffer area pressurization is to be positive to the ante room\area, which is in turn to be positive to the rest of the suite to control infiltration, as discussed previously.

The ISO Class 5 hood for the critical area needs to be exhausted to the outdoors. Most manufacturers, the National Sanitation Federation, and ASHRAE all recommend doing this via a 'thimble' connection (also known as an exhaust canopy). This design has the air from the hood exhausted by terminating the exhaust duct with a 1" air gap directly above the hood exhaust outlet. The exhaust system inlet duct transitions out to the size of the outlet, thereby resembling the 'thimble' it is named for. Other recommendations for this exhaust inlet are to have an exhaust damper in the duct to balance the airflow, having the thimble be removable, and sizing the exhaust flow rate to 130% of the ISO 5 hood exhaust flow rate.

By implementing this design for the exhaust of the ISO Class 5 hood, the following will be accomplished. The system will completely capture the exhaust from the hood. The exhaust hood HEPA filter can be scanned for filter leaks and can be changed out easily. Also, a safety buffer will be maintained to make sure proper minimum exhaust airflows are maintained.

The termination of this exhaust is equally important. The exhaust should be in a location at least ten feet above any location where people might be located. Also, AIA Guidelines recommend a minimum of 25 feet be maintained between any exhaust and any operable windows or outside air intakes.

There are other requirements and good practice recommendations for compounding areas. Exhaust duct through occupied spaces (including the ceiling space above) should be welded to prevent leaks. Room pressure sensors should be installed to confirm proper air pressurization is maintained. Compounding areas and hoods need to be certified every six months. All components within the space need to be sealed and cleanable.

JCAHO has issued a recommended timeline for compliance with USP 797 requirements. Most imminent is that the facility has a written plan for compliance with compounding work area requirements for January, 2005, with renovations to these spaces being complete within three years of this date. Also, interim measures must be in place by July, 2005.

The advent of USP 797 has several ramifications for pharmaceutical facilities performing compounding. Generally, the items that USP 797 now requires are more stringent than the voluntary requirements of the past. The result of this is that pharmaceutical facilities need to assess their existing conditions and develop a plan to meet any deficiencies they might have.

(A list of references used in the development of this article is available from the author).