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Cleanroom Pressurization Methodology

Prime Consideration for Pharmaceutical Facilities

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Establishing an enclosed environment that requires pressurization control and monitoring of other environmental parameters such as temperature, humidity and airflow depends on several factors, including building architecture, traffic movement, and requisite control levels. This article discusses methods of pressurization and explains how, why, and when other environmental parameters are required and how to implement their control and monitoring to meet precise and repeatable conditions.

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Virtually all pharmaceutical research and manufacturing organizations must maintain facilities with rigidly controlled environmental parameters such as pressurization, airflow, temperature, and humidity. Whether they are implemented in a cleanroom, research laboratory, or sterile manufacturing area, precisely controlled environmental conditions determine the outcome of a research project or the final product of a processing-production cycle. To establish and maintain these conditions, pressurization control of a room or workspace is mandatory. Without it, accurate and repeatable control of the other critical environmental characteristics in an enclosed area cannot be maintained.

Airflow tracking versus differential pressure control

Airflow tracking and differential pressure control are the two most-popular methods of pressurization control. Controlling room pressurization by means of airflow tracking methods uses the principle of measuring and controlling airflow in and out of a confined space. This method maintains desired cubic feet per minute (CFM) differential (i.e., offset) between supply and exhaust air and permits precise airflow control, which results in either positive or negative pressure, depending upon the requirements. Differential pressure directly measures the pressure difference from an enclosed workspace to a reference space—usually an adjacent corridor. Variable airflow control into the pressurized workspace maintains a fixed level of differential pressure between a controlled space and the adjacent area.

Advanced instrumentation permits precise control

As with most technologies, airflow tracking and differential pressure control have certain advantages and disadvantages depending upon their application. Each of these technologies is practical and easily achievable because new instrumentation exists that can measure extraordinarily low levels of differential pressure, typically ~0.001 in./wc with a high degree of repeatability and reliability. In the past, the lack of accurate instrumentation prevented the possibility of achieving space pressurization at desired levels (typically ~0.02-0.05 in. wc). Then, pressurization levels were almost one order of magnitude higher mainly because of limitations in measurement devices and display instruments. Advancements in materials and mi-

Figure 1: Many pharmaceutical facilities incorporate controlled environment cleanrooms for research involving cryogenics. To ensure accuracy and repeatability of all tests, the control and monitoring of critical environmental parameters such as pressure, temperature, and humidity must be precisely maintained.

cromanufacturing technologies have resulted in pressure-sensing elements capable of measuring changes in thousandths (0.001) or even ten-thousandths (0.0001) of an inch water column of pressure. Improvements in temperature compensation circuitry provide greater stability and repeatability. Signal drift caused by temperature changes is the most significant challenge facing both manufacturers and users of low-pressure transducers. The combined effect of these developments is the availability of transducers in low ranges—as low as ± 0.1 in. full scale—and with greater repeatability and accuracy—as precise as ± 0.25% of scale.

Low levels of differential pressure are desirable for several reasons. First, safety considerations dictate that reasonable levels of differential pressure be maintained so that doors can be operated properly and safely. For example, if a door is designed to open inward and the space is maintained at a high positive pressure, it may not be possible to open the door. Conversely, if that space were maintained at a high negative pressure, releasing the latch may cause the door to fling open, possibly injuring the person attempting to exit. Second, depending upon construction, it is possible for the pressurized space to implode, blasting ceiling panels downward where employee injury or equipment damage could occur. Third, to maintain accurate temperature control it is desirable to minimize the quantity of air being infiltrated to or exfiltrated from the space. From a basic technology standpoint, either airflow tracking or differential pressure control will achieve the same objective—to maintain the desired direction of airflow into or out of a space. On the other hand, some factors must be considered to help determine which method is best for an application, and the most important of these are architectural details and access to and from the controlled spaces.

Table I: Considerations that affect pressure control and airflow tracking.

Architectural/Access Considerations	Differential Pressure Control	Airflow Tracking
Open architecture	N/A	Yes
Corridors open to lobby	N/A	Yes
High-traffic patterns (personnel & equipment)	N/A	Yes
Common ceiling space (not necessarily plenum)	N/A	Yes
Air locks	Yes	Yes
Limited access	Yes	Yes
Tight construction	Yes	Yes

Traffic flow and building architecture

The first consideration is access to and traffic flow in the workspace. How accessible is the area or series of areas to general spaces and means of egress to the facility? For example, is the space located in a high- or low-traffic area? Will access to the pressurized space be limited? Will air locks be used? How many people will be using the space? Answers to these questions will help identify the most-suitable technology.

For instance, if the pressurized space is in a high-traffic area that is open to the active movement of many people, pressurization control would not be desirable because of the multiple upsets to the airflow in the workspace that would require too many pressurization variations. Remember, every change in the room or reference pressure causes the control system to respond and vary the airflow to or from the controlled space.

Considering some of the general construction details in the facility can help determine whether the walls that define the space are contiguous (e.g., from structure to structure, slab to slab, or floor to floor). As Table I shows, the more the controlled space can be isolated, the easier it will be to successfully implement differential pressure control methods instead of airflow tracking.

In summary, the two main considerations for determining which method is most suitable—as opposed to discrete methods for controlling pressurization—are architecture (building design and/or construction) and movement of personnel.

Cascaded pressure control

Cascaded pressure control is a variation that uses elements of both tracking and pressure control. This technique measures all supply flow and exhaust flow in and out of a workspace and maintains a fixed CFM differential between supply and exhaust air. Cascaded control also measures differential pressure in the space and uses that measurement as a reset point to the CFM offset. This capability allows the CFM differential to vary between minimum and maximum values to respond to any influences that might affect the pressure. This technology is advantageous in that it provides the stability of airflow tracking

Table II: Advantages and disadvantages of airflow tracking.

Airflow Tracking	
Advantages	**Disadvantages**
Leakage geometry not critical	May be more complex to implement
Defined value for sizing ductwork, fans and terminal boxes	Measurement probes in airstream
Stable environmental conditions	If pressure value is required for validation, must be added as separate measurement

Table III: Advantages and disadvantages of differential pressure control.

Differential Pressure Control	
Advantages	**Disadvantages**
Direct-process measurement	Requires tight construction
May be less complex to implement	Requires limited access to minimize upsets
Avoids placing measurement probes in airstream	Requires stable reference pressure
	Potentially unstable environmental conditions in the controlled space
	Leakage geometry determines quantity of airflow necessary to create desired ΔP
	Leakage geometry not defined until construction is complete, making it difficult to determine airflow quantities during design.

with the flexibility of variable CFM differentials for meeting temporary external conditions without disrupting the space.

Differential pressure monitoring

Tracking with differential pressure monitoring is another variation that can be applied in certain areas. In this technique, airflow tracking is used as the control method, and differential pressure monitoring is added as an alarm set point and as a maintenance-management point throughout the building's ventilation system.

For example, if a differential pressure measurement changes during a period of time (i.e., other than when a door is opened or closed), it usually indicates that one of two events occurred: Either airflow was degraded on one side of the system, thus eliminating desired differential pressure, or a change has occurred in the envelope. For example, someone may have opened a hole in a confining wall to install a new piece of ductwork and did not seal it properly, or perhaps a pipe was installed through a floor and the resultant gap was not sealed. Cascaded pressure control techniques can be handy in these applications because they don't add much complexity to an overall control scheme.

Each of these control methods offers distinct benefits and drawbacks depending upon individual applications, and each should be evaluated on the basis of criteria that include practicality for the circumstances (e.g., logical work flow, employee movement patterns, etc.) and cost effectiveness. Table II lists the advantages and disadvantages of airflow tracking. With regard to differential pressure control, one must consider the kind of measurements that are necessary and review the advantages and disadvantages of this technology as shown in Table III.

Other considerations

The method of pressurization control that a company selects directly affects the management of other parameters such as temperature and humidity (see Figure 1). For example, with airflow tracking one can achieve the desired temperature workspace to a very high degree of tolerance. However, if differential pressure is used, temperature control may be lost because the volume of air is being dictated by pressure requirements instead of temperature requirements. In essence, if pressurization control is the driving variable for the quantity of airflow into the space, all other control parameters may suffer as a result, and temperature is usually the first to be affected.

In most laboratory or manufacturing spaces one can expect to control temperatures to tolerances of ± 1-2 °F. Humidity is more difficult to control and usually has a wider tolerance parameter depending on environmental factors within the facility. Ideally a laboratory maintains humidity at 50% RH, but a reading between 40 and 60% RH is usually an acceptable deviation. On the other hand, for many manufacturing processes (e.g., tablet production) humidity control must be much more stringent, particularly if the processes involve materials such as powders or coatings, which are highly sensitive to ambient moisture content.

For example, if a space is to be maintained at a negative pressure using differential pressure control, then the supply airflow would vary to maintain pressurization. If a door were opened to that space, then the first response from the system would be to reduce the amount of supply air into the room to maintain a negative pressure. The system response would likely include closing or reducing the supply airflow to zero to maintain the space at a negative pressure. When that occurs, temperature control is lost immediately. Furthermore, if supply air is used to maintain humidity control, then control over humidity in the space also would be lost.

If airflow tracking is the control method used, then the system will not respond to a door being opened. Although pressurization is not maintained, the CFM differential remains the same. Consequently the direction of airflow for pressurization purposes will still be maintained while temperature and humidity control are maintained. In other words, overall environmental control will not be affected. This method is the only way to accomplish this level of control if maintaining temperature and humidity levels is critical. PT