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PHARMACEUTICAL INDUSTRY SET UP BY USING THERMOREGULATORY PARAMETERS

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ABSTRACT

Heating, Ventilation, and Air Conditioning (HVAC) systems play an important role in the pharmaceutical industry, ensuring the maintenance of optimal environmental conditions for the production, storage, and distribution of pharmaceutical products. This dissertation provides a comprehensive study of HVAC systems in the pharmaceutical sector, focusing on their design, operation, validation, and regulatory compliance. Through an comprehensive review of industry standards, this paper elucidates the critical parameters influencing HVAC system performance, such as temperature control, humidity control, air cleanliness, and airflow patterns. Filters are a vital component of HVAC systems, playing an important role in maintaining indoor air quality and protecting equipment. This review article includes different types of filters used in HVAC systems, materials, efficiency, and applications in pharmaceutical facilities. It examines compatibility with cleanroom classifications and also discusses emerging trends and advancements in filter technology, such as High-Efficiency Particulate Air (HEPA) filters, Ultra-Low Penetration Air (ULPA) filters. This review article may focus on the valuable resource in the field of pharmacy regarding HVAC system design implementation and maintainence.

KEYWORDS: HVAC system, pharmaceutical industry, temperature control, humidity control, air cleanliness, filters, HEPA filters, ULPA filters.

INTRODUCTION

Pharmaceutical plants are one of the most sensitive types of manufacturing facilities. As various products are being made, it is important to maintain control of the environments they are being produced to ensure the quality of the product. These products vary from simple pills to complex medications in different doses form. The primary goal in pharmaceutical manufacturing is to maintain the consistency of the product in quality, safety, and efficacy. With so many factors influencing the result of a product, pharmaceutical companies have to be especially stringent when it comes to the design of the facilities they are manufactured in. It is common for a company to design the facility around the production of a new product. A critical component of the pharmaceutical industry is HVAC (Heating, ventilation, and air conditioning system). The many components of HVAC aid in providing proper humidity and temperature in the production environment. The HVAC system manages the ambient temperature and humidity in the manufacturing and storage units of the pharmaceutical industry.

The HVAC system is used to regulate the humidity in the air, which in turn regulates the temperature of a certain area. It also regulates the amount of carbon dioxide and oxygen in the air, which brings in fresh air. By adjusting air circulation, it also manages the pollution of airborne particles.

Figure 1: HVAC.

- **IMPORTANCE OF HVAC SYSTEMS IN PHARMACEUTICAL INDUSTRY**

1. These systems retain the controlled environment that is essential to various biotechnological and medicinal products. These products are extremely sensitive to environmental factors, and any deviation from the

necessary environment could lead to product deterioration, health and safety concerns, compliance issues, investigations, remediations, product invalidation, and product loss. HVAC systems are also required in clean rooms for maintaining the desired room pressure, cleanliness and air change/ventilation rates. In these situations, excluding airborne pollution that can affect the product's quality is the goal. These factors are subject to incredibly high degrees of control and monitoring.

2. In order to preserve the integrity of both fluid and powdered reagents, modern diagnostic equipment must function under extremely tight temperature and humidity limits. The repercussions of a faulty reading or incorrect diagnosis brought on by the unexpected moisture introduction. An efficient diagnostic procedure requires customized HVAC units that guarantee consistent environmental conditions, regardless of temperature—cold, hot, or dry—and fit well into frequently constrained spaces.

3. One of the biggest threats to the manufacturing of contemporary pharmaceuticals is moisture. Excess moisture can impair the effectiveness of the medication, create manufacturing inefficiencies, or, in the worst case, damage a whole batch of product during every stage of the production process, from grinding to coating. There is virtually no chance that there will be too much moisture in the air to interfere with production thanks to specialized HVAC equipment that enforce a set dew point depending on the application.

▪ BASIC COMPONENTS OF HVAC SYSTEM

Furnace: This is the largest and main component of the HVAC system. It uses a heat pump, solar energy, or the combustion of natural gasses to heat the air that is delivered to the system. A heat exchanger located inside the furnace aids in turning it on when it is turned on. Through the vents, the heated and heated air is drawn in and the cold air is circulated.

Thermostat: The thermostat can be manually adjusted or pre-programmed to reach the ideal temperature. It is an easily visible and accessible system component. The heat exchanger or evaporator coil-condensing device can be set by the thermostat to circulate heated or cooled air across the room.

Evaporator Coil: It helps in cooling the hot air. It is attached to the refrigerant gas-filled condensing device. Usually, the equipment is mounted outside the space. The condensed liquid is pumped to the evaporator coil, where it evaporates and turns back into gas.

Refrigerant Lines: This unit transports the refrigerant to be vaporized in the condensing unit and then returns the liquid refrigerant to the evaporator. Usually made of small tubes, they are not easily heated or cooled.

Ductwork: The air that is heated or cooled in the room is circulated by this machine. The ducts are made of lightweight aluminium. Air that is heated or cooled and distributed to specific rooms is connected to the ductwork. They often have angled slats on the front and are situated close to the ceiling. The temperature of the area they are focused upon can be manually adjusted.

▪ THE CORE FUNCTIONS OF HVAC SYSTEM

1. Regulation of dust, airborne particles, and microorganisms. The main task of a functional HVAC system is to manage dust, which is removed by filtration. If dust is not managed, it may lead to contamination during the production process. Airborne particles can cause pollution and interfere with the manufacturing process. They are also present in the air. Microorganisms pose a possible risk to the pharmaceutical processing industry since the plant's atmosphere needs to be sterile. The HEPA systems get rid of all of these.

2. Preserving the manufacturing spaces at the proper temperature. In the pharmaceutical sector, temperature is a critical factor. Poor temperature regulation could lead to the growth of microbes on employees or in the premises, which could have a negative impact on their health.

3. Preserving the appropriate pressure in the space. Certain spaces and surfaces in the pharmaceutical business need to be kept spotless at all times. As a result, these regions need to always be under positive pressure. There should be more air at the opening regions in these areas. By allowing more air to enter the clear areas than to leave at the same time, the HVAC system makes sure that positive pressurization is accomplished. This guarantees that microorganisms cannot develop or have the opportunity to do so.

4. Maintaining the proper ratio of humidity. Desiccant dehumidifiers are installed to control the moisture in the manufacturing facilities. The production of stable medications depends on the room having the proper humidity levels. In most cases, proper relative humidity is required to guarantee high-quality tablet manufacturing.

Functions of Pharmaceutical HVAC

1.Temperature Control

2.Maintaining Humidity

3.Handling air inside an area

4.Regulation of pressure

Temperature Control: The fundamental and essential role of HVAC in the pharmaceutical sector is temperature management. This is required because unregulated temperature environments can promote the growth of microorganisms. Additionally, it may raise the local water activity, which serves as the foundation for microbial development. The right temperature conditions are provided by pharmaceutical HVAC for a safe pharmaceutical product. By improving the process of regulating temperature, it also avoids wasting energy.

HVAC monitors the space continuously to regulate the temperature. The AHU cools the area by supplying cool air when the temperature rises above the necessary level. In a similar vein, when the temperature drops below the

intended level, the supply air temperature increases. The HVAC system maintains the area's temperature in this manner.

Maintaining Humidity: Another essential component of a pharmaceutical HVAC system is humidity management. Similar to temperature, humidity raises contamination and encourages the growth of microorganisms. HVAC systems need to keep humidity levels appropriate for pharmaceutical procedures and products. In the absence of a product or method, human comfort is taken into account.

Cooling air is often applied to a specific region to control humidity. This method involves supplying chilled water to the AHU's cooling coils. The supply air cools and becomes less humid as it moves through the cooling coil. This air lowers the relative and absolute humidity as well as the dew point when it is exposed to a particular location. **Handling the air inside an area:** In order to maintain a consistent airflow, pharmaceutical HVAC also controls the airflow inside a specified space. It is required because uncontrolled air flow can lead to the re-entry of dust particles or other foreign objects into the air stream.

The air handling unit's airflow is maintained by the blower. The primary HVAC control receives the necessary airflow, and many sensors continuously track the airflow in a given space. To adjust the blower speed, the main controller controls the blower motor driver, such as the Variable Frequency Drive, or VFD. By opening or shutting the air dampers positioned at the supply air, airflow can also be changed.

Regulation of pressure: Another essential role of pharmaceutical HVAC is pressure regulation. Air from uncontrolled locations cannot enter a clean or controlled area due to pressure regulation. By delivering air at higher amounts than nearby places, pressure can be regulated. It stops air infiltration from non-critical or uncontrolled locations and increases the area's pressure relative to other areas.

▪ DESIGN CONSIDERATION

System Design: Meetings with process engineers, architects, and representatives of the facility user or owner initiate the HVAC design process. All interested parties are given a general overview of the process and the process and instrument diagrams are examined. The facility's operation is examined, and any plans for upcoming additions or adjustments are talked about. Following the initial meeting, the rules and codes guiding the design are outlined in a formal basis of design. Function defines spaces, and criteria for humidity and temperature are established. In addition to documenting pressure relationships and space adjacency, room classifications are recorded. At this point, the HVAC system must also be built to accommodate any special or uncommon facility requirements, including emergency backup for HVAC systems.

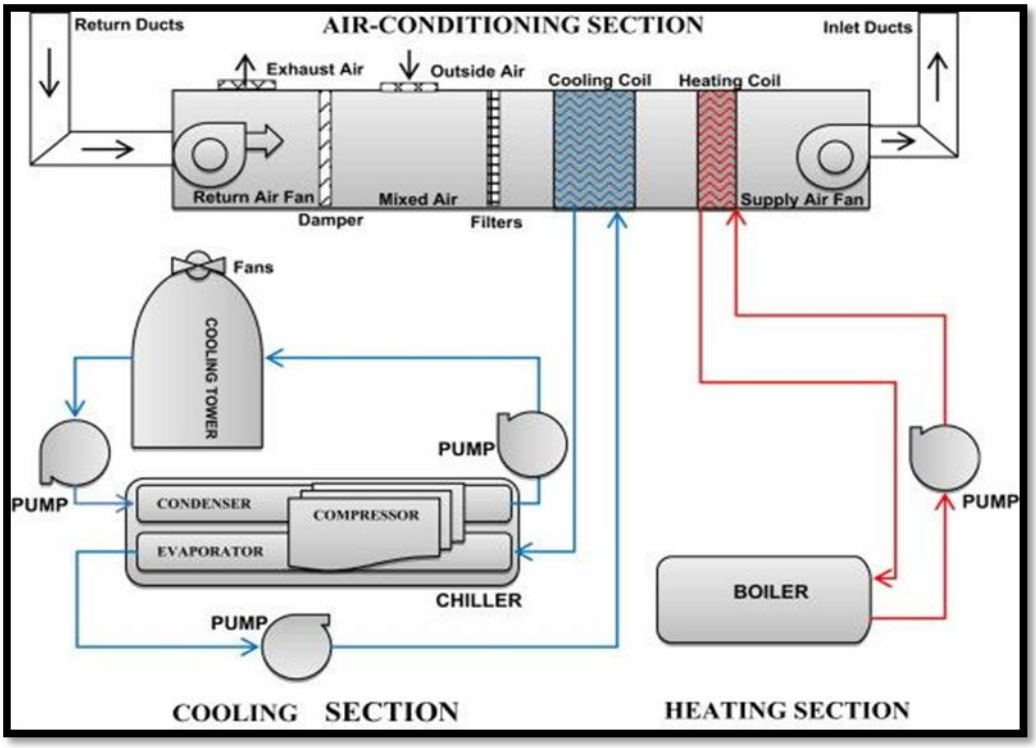
During this phase of the design process, alternative studies are carried out to evaluate HVAC system possibilities. Should airflow or temperatures exceed specifications, the cost of a redundant or backup HVAC supply system might be contrasted to the cost of lost product or experimentation. Other possible research topics include thermal storage and heat recovery from exhaust systems. Airflow diagrams are created to display the supply, return, exhaust, and transfer air between places that are supplied by a certain air handling system. The main pieces of equipment to be employed, as well as the quality of the building materials and components, are all described in the design basis.

Building Design: Achieving and sustaining the planned levels of cleanliness and pressure gradients requires careful building design as well as planning for the movement of people, materials, and equipment. The ability of an air conditioning system architect to meet end-user needs will be restricted if the building's construction and layout are substandard.

Building Layout: In order to connect similarly classed regions to the same air handling system and minimize duct lengths, costs, and air system complexity, it is ideal from an HVAC perspective to keep them physically close to one another. Additionally, it is essential that areas be set up so that people can move around them without compromising their containment or cleanliness. Combining unclean and clean systems or suites is not a good idea since it could lead to cross-contamination between the suites. It is possible for leaks to occur in filters, or for a contaminant to enter the air supply or return systems and cause cross-contamination.

Sterile zones are normally divided into three sub zones.

i. Main sterile zone or white zone.
ii. Cooling zone which is also a white zone.
iii. Set of three change rooms: black, grey and white in ascending order of cleanliness.



HVAC LAYOUT

Building Construction: In every cleanroom design, internal particle creation is the primary consideration. The internal generation is made up of those from equipment, operators, and most crucially, building materials including floors, ceilings, and walls. A "tight" building construction is one that has as few uncontrolled leaks and infiltrations as possible. In the case of formulation and sterile production buildings, this is crucial. Hard-surfaced materials have to be utilized in the building of the pharmaceutical facilities.

There are some special points of interest.

i. Every material used in building needs to be cleanable and non-chipping. Finishes for walls and floors should have self-cleaning surfaces and not release particles.
ii. Every visible surface needs to be flawless, undamaged, and impenetrable.
iii. There should be no dirty nooks and as few protruding ledges, shelves, cabinets, and equipment as possible.
iv. Avoid having sharp corners between the ceiling, walls, and floors.
v. Complete sealing should be applied to false ceilings and floor tile joints.
vi. Installing pipes, ducts, and other utilities should prevent recesses from being formed.
vii. In locations designated as grade Class 100, sinks and drains must be prohibited.
viii. In the sterile area, every door should be constructed with airtight integrity. If required, drop seals should be installed at the bottom of the door and special gaskets on the door frame.
ix. These regions need to be painted with epoxy.

Areas Without False Ceiling: The type of ceiling needs to be taken into particular consideration. The approach that is most frequently adopted is doing away with false ceilings and replacing them with a concrete slab that accommodates the ducting and air handling systems. The terminal filters are concealed in cut-outs in this slab. These filters are accessible from the slab's top. It is important to properly reinforce this slab in order to support the weight of the pipes, ducting, and air handling devices.

In the case of NO false ceiling is considered, the air-conditioning system is required to be designed before slab construction is started.

i. To accurately determine the size and location of the terminal filter cutouts. Grouting should be applied to terminal filter mounting frames and terminal filter boxes at the time the slab is cast.
ii. To accurately determine the size and placement of the slab's cutouts for return air risers and inserts.
iii. To accurately determine the extra cutouts needed for additional MEP services.
iv. To accurately ascertain the size and placement of the air handling equipment in relation to the cut-out position and size.
v. Must install curbing around the cutout edges to stop water from seeping into the work area.
vi. To accurately specify where air handling units floor drains are located.
vii. Should think about installing water proofing where air handling devices are situated.

Areas With False Ceiling

In the case of a false ceiling in the sterile area, the following points should be considered:

i. Filter mounting and false ceiling support should be accommodated with inserts.
ii. In order to stop the formation of fungus and remove air leaks, the false ceiling should be made of non-shedding materials, including CRCA sheet covered in PVC or aluminium.
iii. A portion of the weight of terminal filters should be supported by false ceiling elements by design.
iv. It is necessary to have adequate sealing between panels and between filters and panels in order to prevent leakage of air.

Ceiling Construction

A possible entry point for pollutants into the clean zone is the cleanroom ceiling. Although pressurization of the cleanroom helps to prevent this, it also has the potential to drive pollutants from the operations inside the cleanroom into the surrounding region. Sealing the cleanroom ceiling lowers the likelihood of this occurring. The cleanroom's cleanliness class dictates the kind of seal that should be used. For Class 1,000 and higher (less clean), the ceiling grid can be gasketed aluminium T-bar with a 1" face tee. A Class 100 cleanroom should have a gasketed aluminium T-bar grid with 2" face tees and Class 10 and cleaner should have a modular / T-bar ceiling grid with a gel seal.

The cleanliness class of a space influences the type of ceiling panels that are utilized in it. Class 100 and cleaner can only have blank aluminium panels, while Class 1,000 and above can have vinyl covered, cleanroom approved panels or blank aluminium panels. Cleaning class also determines ceiling grid support. Class 1,000 and above should have 10 ga hanger wires to the filters and 12 ga hanger wires to the grid. Class 100 and cleaner should have an all-thread rod with strut and turnbuckles. The grid intersections are where the hanger wires need to be installed.

▪ CLEANROOM CLASSIFICATION

Cleanroom: A cleanroom is characterized as having controlled airborne particle concentration. The construction, upkeep, and use of the clean rooms minimize the introduction, creation, and retention of contaminants. They also feature a defined environmental control of particle and microbial contamination. The amount of particles 0.5 microns and larger found in $1ft^3$ of measured air is used to determine the classification of cleanrooms. In the pharmaceutical sector, class 100 to 100,000 rooms are commonly utilized.

The strictest categorization level is Grade-A. During filling and closing operations, air in close proximity to exposed sterilization processes must have no more than 3500 particulates per cubic meter, with particles sized 0.5 microns and larger, measured no more than one foot from the work site and upstream of the air flow. This holds true for both "in-operation" and "at rest" situations. In both "at rest" and "in-operation" states, Grade-A areas must be totally free of particles larger than or equal to 5 microns.

In addition to "at-rest" and "in-operation" cleanroom states, HVAC contractors also frequently utilize "As – Built" condition. Cleanrooms that are "as built" are fully operational and connected to all services, but they lack staff and equipment. The "as built" or "at rest" cleanroom stages are often the HVAC contractor's responsibility, and pharmaceutical companies frequently request higher cleanliness levels for these stages than for the "operational" stage.

Facility Classification: A pharmaceutical facility usually comprises of several interconnected rooms that are arranged according to the requirements of the manufacturing process. To ensure that the air in the sterile rooms is suitable for the activities associated with the manufacturing process, a few fundamental requirements must be met. Every sterile space that is created by "aseptic" processing needs to be clinically isolated from the surrounding region. The process of creating a sterile (devoid of live things) product is known as aseptic processing. Assembling previously sterilized goods, containers, and closures in specifically created, controlled conditions with the aim of reducing the risk of microbiological or particle contamination is the goal of aseptic processing techniques.

Cleanrooms classifications differ for sterile and non-sterile areas.

- Non-sterilized operation = controlled area = non-aseptic application
- Sterilized operation = critical Area = aseptic application

Controlled Area (Non-Sterilized Operation): The preparation spaces for non-sterilized items are classified as "controlled areas" according to US standards. This covers compounding areas, locations exposed to the plant environment for components, in-process materials, medication products, and equipment, container, and closure contact surfaces.

Requirement: When measured in the proximity of the exposed articles during periods of activity, air in "controlled areas" is generally considered to have acceptable particulate quality if the particle count per cubic foot is not more than 100,000 in the size range of 0.5 micron and bigger (Class 100,000). An incidence of no more than 2.5 colony forming units per cubic foot is considered acceptable in terms of microbiological purity. To preserve the quality of the air in regions under controlled areas. In general, a pressure differential of at least 0.05 inches of water gauge is advised, as well as airflow adequate to achieve at least 20 air changes per hour.

Critical Area (Sterilized Operation): According to US guidelines, "Critical Areas" are locations where sterilized

procedures are performed. There will be aseptic clean rooms for these.

Requirement: When measured in the vicinity of the exposed articles during periods of activity, air in "critical areas" is generally considered to have acceptable particulate quality if the particle count per cubic foot is not greater than 100 in the size range of 0.5 micron and bigger (Class 100). An incidence of no more than 0.1 colony forming units per cubic foot is considered acceptable in terms of microbiological purity. Laminar airflow at a speed of 90 feet per minute ± 20 and, generally, a pressure differential of at least 0.05 inch of water gauge is advised in order to maintain air quality in sterile environments. The Fed and EEU rules do not specify any particular air change rate.

Types Of Cleanrooms

Cleanrooms are also categorized by the way supply air is distributed. There are generally two air supply configurations used in cleanroom design.

1. **Multi-Directional**
2. **Unidirectional.**

Multi-directional Air Flow: This airflow pattern can be utilized in spaces when significant external contamination, such as makeup air, is anticipated because it will create a significant quantity of turbulence. By improving the mixing of high and low particle concentrations, this turbulent flow creates a homogenous particle concentration that is suitable for the process.

One of two ways is usually used to supply air to the area. HEPA filters and supply diffusers are used in the first. The HEPA filter can be found upstream in the ductwork or air handler, or it can be built right into the supply diffuser. In the second approach, work stations with HEPA filters are used to provide pre-filtered supply air into the cleanroom, which is located upstream of the area. Non-unidirectional airflow may provide satisfactory control for cleanliness levels of Class 1000 to Class 100,000.

Unidirectional Air Flow: A single pass, single direction air flow of parallel streams is known as a unidirectional air flow pattern. Since there is only an 18 - 20 degree divergence between the parallel streams, it is also known as "laminar" airflow. Federal Standard 209 version B specifies that the air flow velocity must be maintained at 90 feet per minute ±20; however, version E does not include any velocity standards. When low levels of airborne contaminants are necessary and interior contamination are the primary concern, unidirectional cleanrooms are utilized.

They are generally of two types.

i. Vertical down-flow cleanrooms where the air flow is vertical 'laminar' in direction.
ii. Horizontal flow where the air flow is horizontal 'laminar' in direction.

Clean make-up air is normally injected at the ceiling and returned through an elevated floor or at the base of the side walls in a vertical downflow arrangement. Similar principles are applied in horizontal flow cleanrooms, which have a supply wall on one side and a return wall on the other. A down-flow cleanroom usually has ceiling-mounted HEPA filtration units. More HEPA units are installed in the ceiling as the cleanroom's class decreases, and at Class 100, HEPA filtration is needed throughout the ceiling. A downflow cleanroom's airflow provides the space with a downward stream of pure air. Generally, the room's contaminants are swept down and out through the return. Similar to a downflow cleanroom, a horizontal flow cleanroom uses filtering airflow, but air moves from the supply wall to the return wall.

Cleanroom Requirements: Temperature, relative humidity, particle counts in separate rooms, air flow pattern, and pressure difference between different clean air system rooms must all be strictly regulated in a cleanroom.

The requirements are.

i. **Increased Air Supply:** Whereas comfort air conditioning would require about 2-10 air changes/hr, 50 to 100 air changes would be needed in a standard cleanroom for Class 10,000. By providing more air, the pollutants are diluted to a manageable concentration.
ii. **High Efficiency Filters:** Cleanrooms are further distinguished by the use of HEPA filters, which have a filtration effectiveness of 99.97% down to 0.3 microns.
iii. **Terminal Filtration and Air Flow Pattern:** In addition to using high efficiency filters, a laminar flow is desired.
iv. **Room Pressurization:** The cleanrooms experience gradient pressure due to the increased intake of fresh air. In order to prevent outside particles from entering clean areas, this is crucial.

Cleanroom Classification

Area	Parameter	US FED STD 209E	EEC (European)	ISO 14644-1
Non-Aseptic Operations (Non-Sterile)	Clean Room Class	Class 100,000 (M 6.5)	Grade C	ISO 8
	Maximum Allowable Particles (≥ 0.5 and < 1) per m^3	3,530,000	3,500,000 (During Operation)	3,520,000
Aseptic Operations (Sterile)	Clean Room Class	Class 100 (M 3.5) followed by Class 10,000 (M 5.5)	Grade A followed by Grade B (During Operation)	ISO 5 followed by ISO 7
	Maximum Allowable Particles (≥ 0.5 and < 1) per m^3	Class 100 – 3,530 Class 10,000 – 353,000	Grade A – 3,500 Grade B – 350,000	ISO 5 – 3520 ISO 7 – 352,000

- **HVAC REQUIREMENTS**

Room Temperature: As long as it creates comfortable surroundings, room temperature (T) is not critical. Areas are typically built with a control point of 72°F and room temperatures between 67 and 77°F. When people are extremely well-groomed and would feel uncomfortable in a "normal" environment, it may be necessary to have lower space temperatures.

Relative Humidity: On the other side, relative humidity (RH) is more significant in every production region. Facilities intended for processing hygroscopic powders must have a RH of 30 ± 5%, even though the majority of the regions may have a RH of 50 ± 5%. To ensure that product quality is maintained, automatic RH control is necessary. Humidity regulation is essential for maintaining personal comfort, preventing corrosion, managing microbiological growth, and lowering the risk of static electricity. In the parts that follow, we shall go into further detail regarding the relative humidity control.

Cooling Loads: Pharmaceutical buildings typically have no windows and are completely enclosed. This keeps the building "tight" and reduces uninvited intrusion. Because of this, process equipment, lighting, and staff all contribute to the room sensible loads. In clean environments, fan heat from recirculating fans can potentially be a significant heat source. With the exception of the tablet manufacturing plant, which covers granulation, drying, and tabletting, there is a low density of equipment loads.

To calculate heat loss through the walls, roof, and floor, heat-loss calculations are also required. Since the process may be inactive and the area would still require temperature maintenance, process heat gain should not be taken into account in this computation.

Airflow Sheets: The dehumidified airflow must then be calculated using computer analysis or psychometric analysis once the cooling demand has been established. These findings are contrasted with the airflow quantities necessary to determine the minimal amount of air necessary to meet the standards for air purity and space cooling load.

Air quantities supplied, returned, and exhausted from each place should be displayed on the airflow sheets, which should be created on full-size drawings. In addition, they have to display the airflow into and out of the areas. Although the quantities should be displayed, pressurization will probably need to be achieved by field modification. Information dissemination to the owner or user, agency evaluations, HVAC designers, and other engineering disciplines can all benefit from the use of the airflow sheet.

Return Air System: Another essential part of the cleanroom air distribution system is the air return system. The return points must be placed in the walls low, close to the floor, and as evenly apart as the design of the structure permits. Return grilles should be constructed for as long as practical in order to gather more dust particles over a greater surface area.

To prevent dead air pockets, return air grilles should be positioned in the primary sterile zones. The return grille should be placed with caution so that it is not next to a door leading into a lower pressure chamber that is adjacent. This is done to prevent creation of a low

pressure zone near the door, thus preventing air leakage from the low pressure to high pressure room at the time of door opening.

Mixed Areas: It is possible to create Class 100 space within Class 10,000 areas at background. Install "localized laminar flow workstations" in these locations. These are commercially available and typically have a vertical or horizontal flow pattern that circulates within the clean space.

It is crucial to remember that larger airflows and higher energy consumption are associated with higher air change rates (ACR). Human occupants are the main source of contamination in most cleanrooms. Lower air changes per hour to preserve cleanliness after a cleanroom is vacated may be feasible, allowing the air handling systems to set back. All recirculation air systems should use variable speed drives (VSD), which enable air flow modifications to enhance airflow or take filter loading into consideration. If mild turn downs are combined with VSD, which can be installed in places where they are not currently existent, they can yield exceptional returns. Optimized airflow rates can be attained by designing a flexible system with changeable air flow. Current systems should be carefully monitored for their impact on cleanroom procedures and changed to operate at the lower end of the recommended ACR range.

Pressurization: The process of pressurization inhibits infiltration from adjacent areas. Pressurization of clean areas is necessary to prevent particle contamination of products and/or to shield individuals from inhaling or coming into physical touch with dangerous materials. Providing more air than is cumulatively returned, exhausted, or leaked from the room will easily accomplish this. Magnahelic gauges or 'U' tube manometers are used to track the pressure gradients. When there is a disturbance in the pressure gradients, alarm and warning systems could also be offered.

Pressure Gradient: Aseptic rooms and non-aseptic spaces must to have a net airflow. Only in the event that there is a pressure gradient between two nearby rooms is this feasible. Air always moves from an area of high pressure to one of low pressure. The term "DP" refers to the differential pressure between two rooms. The following pressures between different zones are often achievable and maintained with moderately excellent building construction and airtight doors and windows.

Air locks are utilized when significant pressure demarcations are necessary. These are tiny rooms that serve as partitions between spaces thanks to carefully managed airflows. It reduces the amount of polluted air that enters the cleaner chamber when the door is opened. Recall that the whole volume of the dirtier room may finally make its way to the cleaner room if there is ZERO pressure differential and the door is open.

- Doors open/close FAST (to minimize time of contamination).
- Both airlock doors should not be opened simultaneously.
- High air changes to permit faster “recovery”.
- People use smaller airlock.

The pressure differential exerts a force on the door. The force (0.15 in water/36 Pa) may be excessively high, causing the door to partially close or become difficult to open. This is especially crucial in big, complicated buildings where multiple pressurization levels could be needed. Sliding doors are used in many facilities these days, and it is crucial that the seals be properly engineered to allow minimum leakage and appropriate confinement or pressurization. In the HVAC design of vital locations, alarms that ring to warn a loss of pressurization are invaluable elements.

Room Seals and Doors: The majority of facilities experience leaks as a result of pressure differences between rooms around the doors. All room openings must be sealed with an appropriate sealant that is readily cleaned and won't encourage the growth of organisms in order to create tight spaces. The ceiling tiles, light fixtures, pipe penetrations, phone outlet penetrations, and any fractures or openings that show up in the structure are among the areas that need to be sealed. A normal door would be the following size, with a crack space around the edge: The door is 3 feet wide by 7 feet high, with 1/8-inch cracks on top and sides and a 1/4-inch undercut. The area around the door, as determined, is 0.24 ft^2.In order to attain a water pressure differential of 0.05 across the door, airflow through the cracks must be around 215 CFM. Closed cell neoprene door seals, which typically encircle the top and sides of the door, are intended to minimize the area where cracks appear. A drop type seal should be utilized to lessen the undercut. Calculations for the system must take pressurization air into consideration. The HVAC room balance table records air that enters through gaps or openings as transfer air.

Filtration System: Air filtration needs to be done correctly for cleanroom controls. Filters are used in industrial areas including granulation, coating, tabletting, and grinding because they retain particulates produced internally as well as regulate atmospheric pollution.

A variety of dry particles, fibres, mist, smoke, odours, and living or dead organisms can be found in atmospheric dust. Particles in the air can range in size from 0.01 microns to 100 microns. Particles larger than 2.5 microns are referred to as "coarse," while those smaller than 2.5 microns are considered fine. Long-lasting in the air, fine particles have the potential to settle on vertical surfaces. Particles that are coarse in nature, resulting from mechanical abrasion in settings such as granulation and grinding departments, have a shorter lifetime in the air and are prone to gravitational settling.

Air Filters

- Solid materials are captured by air filters.
- Can be used as a "roughing" filter to collect thirty percent of the overall mass.
- A higher percentage of mass and some of the "weightless" tiny particles (85%–95%) may be captured with "high efficiency."
- "High efficiency particulate" can eliminate 99.97% or more of all particles and nearly 100% of the material weight.

Types of filtration system

- **HEPA Filters:** A specific type of mechanical air filter with pleats is called HEPA (high efficiency particulate air) filter. At least 99.97% of dust, pollen, mold, bacteria, and other airborne particles larger than 0.3 microns (µm) should be theoretically removed by this kind of air filter. The diameter parameter of 0.3 microns represents the most invasive particle size, or worst-case scenario. Larger or smaller particles are even more effectively trapped.
- **ULPA Filters:** One kind of air filter is ultra-low particulate air (ULPA). At least 99.999% of dust, pollen, germs, and other airborne particles with a minimum particle penetration size of 0.12 µm, (ultrafine particles) may be removed from the air by a ULPA filter. To a considerable degree, but not completely, ULPA filters may eliminate oil smoke, tobacco smoke, pollution, and pesticide dust. To some extent, carbon black can also be eliminated by it. ULPA filters are included in several fan filter systems.

Difference between HEPA and ULPA Filters

The size of the particles that industrial HEPA filters and ULPA filters can remove is one of their main distinctions. ULPA filters can remove 99.99% of particulates with a diameter of 0.12 microns or greater, whereas HEPA filters can remove up to 99.97% of pollutants as small as 0.3 microns. 99.99% of particles between 0.2 and 0.3 microns are supposedly removed by standard HEPA filters like HEPA C and HEPA J. On the other hand, it is claimed that 99.999% of particles between 0.1 and 0.3 microns are removed using conventional ULPA filters. More and smaller particles can be captured by ULPA filters than by HEPA filters.

The ability of HEPA and ULPA filters to circulate air through them is another distinct difference between them. Air flow in ULPA filters is 20% to 50% less than in HEPA filters with the same dimensions because the ULPA filter's filter material is denser. Because of this, there is less air circulation and the blower uses more energy to push air through ULPA filters in rooms or biosafety cabinets.

The cost difference between HEPA and ULPA filters is approximately 35%. ULPA filters tend to be more expensive than their HEPA filters since they are more effective at screening pollutants.

The typical lifespan of HEPA and ULPA filters is another significant distinction. HEPA filters typically have a 10-year lifespan, but ULPA filters only have a 5- to 8-year lifespan. Theoretically, HEPA filters will take longer to reach their full filtering capacity because they permit better airflow. Improved lifespan of the HEPA filters is implied by this. Therefore, compared to ULPA filters, industrial HEPA filters are less expensive and have a longer lifespan, which means that they require less continuous maintenance.

Hence, ULPA filters are more costly than HEPA filters despite being more effective at removing tiny particles from the air. To enhance airflow in the room, a stronger blower is also required because the fiber material in ULPA filters is denser. Together, these increase the initial and operational expenses of ULPA filters, thereby making HEPA filters a more economical option in the pharmaceutical industry.

Terminal HEPA Filters: When it comes to 0.3µ particles, HEPA (High effectiveness Particulate Air) filters have a removal effectiveness of 99.97% to 99.997%. Put otherwise, a filter of this kind can only allow fewer than 0.03% of all particles that are 0.3 microns or larger to pass through. Therefore, after passing through the filter, the concentration of the return air would drop to three particles per foot square if it originally contained 10,000 particles. With a 99.9997% removal effectiveness on 0.12µ particles, ultra low particulate air (ULPA) filters are normally advised for cleanliness levels of Class 10 and lower, mainly for the semi-conductor sector.

HEPA filters use sub-micron glass fibre media housed in an aluminium framework and are available in two types of constructions.

i. Box type
ii. Flanged type.

Box-style filters work well inside ceiling slab cutouts where the filter is removed from above. In order to enable filter mounting and transfer the load to false ceiling members, additional housing is also needed for flanged filters. Under the terminal filters, protective grilles with slots made of stainless steel or aluminium can be installed. Epoxy or stove enamel paint should be applied to the housing and grilles. The ideal way to handle the installation issue of sealing filters to frames is to use a filter frame that has a gel-like seal that the filter fits into. The chosen sealant should be easily cleaned and should not encourage the growth of organisms.

Filter Testing: A filter's efficiency is extremely important and needs to be measured properly. The DOP and dust spot tests are two frequently performed tests on filters. The filter's capacity to lessen discolouration and

soiling is gauged by the dust spot test. Using the Di-octyl Phthalate (DOP) technique, high efficiency filters are tested.

Using a light scattering photometer or another type of particle counter, the DOP test counts the particles both upstream and downstream. Test particles are formed by condensation of DOP vapor (dioctyl phthalate or bis-2 ethylexyl) and have a consistent 0.3 micron diameter and density of 80 mg/cum. Essentially, just three particles will be able to pass through a HEPA air filter when ten thousand (10,000) 0.3 micron-sized particles are blown through it. As a result, the rating at.3 micron is 99.97%. All of the filters are glass and synthetic fibre dry types. The final filters are disposable, but the pre-filters could potentially be cleansed.

- **HVAC SYSTEM COMPONENTS**

Air Handling Unit: It is the central nervous system of Pharmaceutical HVAC, the air handling unit handles all important area conditioning tasks. It has a single casing that houses the fan portion, coils, and filter. Leakage into and out of the AHU is prevented by the insulated and sealed enclosure. In addition, it has view apertures and access doors for upkeep and inspection. One of the most crucial components of an HVAC (heating, ventilation, and air conditioning) system is the air handling unit (AHU), which is especially useful in large buildings where several zones need to be heated and cooled. AHU operations have a major impact on the energy used for heating, cooling, and ventilation in addition to the temperature and humidity levels of the supply air. Implementing regulations in place to cut energy use is crucial.

An AHU has two different kinds of coils: heating and cooling. Cooling coils often circulate chilled water, whereas heating coils circulate heated water. The serving area's temperature drops as a result of the supply air temperature dropping as it moves through the cooling coils. Similar to this, the serving area's temperature rises when supply air travels through the heating coil, heating the air in the process. Air purification filters are also included in the Air Handling Unit. Various filter categories may exist based on the required area. The AHU uses blowers to provide airflow. Their operating rates can be adjusted to produce the required airflow. Via the primary controller, these blowers can be operated automatically or manually. The airflow in the region is continuously monitored by sensors positioned throughout the AHU. Any variation in the needed airflow is promptly made up for by the main controller.

Via the ductwork, the HVAC conditioned air is delivered to the desired location. In addition to contaminating the conditioned air, poorly built ducting will disrupt the properties of airflow. The ducting's design and profile are determined by the features and hygienic standards of a certain area. AHU operations have a major impact on the energy used for heating, cooling, and ventilation in addition to the temperature and humidity levels of the supply air. AHU operations have a significant impact on occupant health, thermal comfort, and building energy consumption. Furthermore, AHUS integrates building zones to primary heating and cooling facilities in order to regulate the intake of ventilation in buildings. Different dampers are available to connect to air ducts, such as supply, exhaust, return, and fresh air ducts, in order to carry out ventilation functions.

Components Of AHU

Filters: In order to provide clean, dust-free air to building inhabitants as well as to the central operations and manufacturing areas of pharmaceutical companies, air filtration is virtually always present. In order to maintain the cleanliness of all the downstream components, filtration is usually positioned first in the AHU. The types of filters utilized include G-4, F-6, F-9, and H-13, depending on the needed filtration grade. Because G-4 filters are less expensive to maintain and replace, they avoid having to replace other costly filters too soon. By keeping an eye on the pressure drop across the filter medium at the design air volume flow rate, one may determine the span of a filter. A pressure gauge is used to create a visual display for this purpose. When a filter fails to be replaced, the forces of the fan may eventually cause it to collapse. This will contaminate the downstream ductwork and air handler as well as cause pollution.

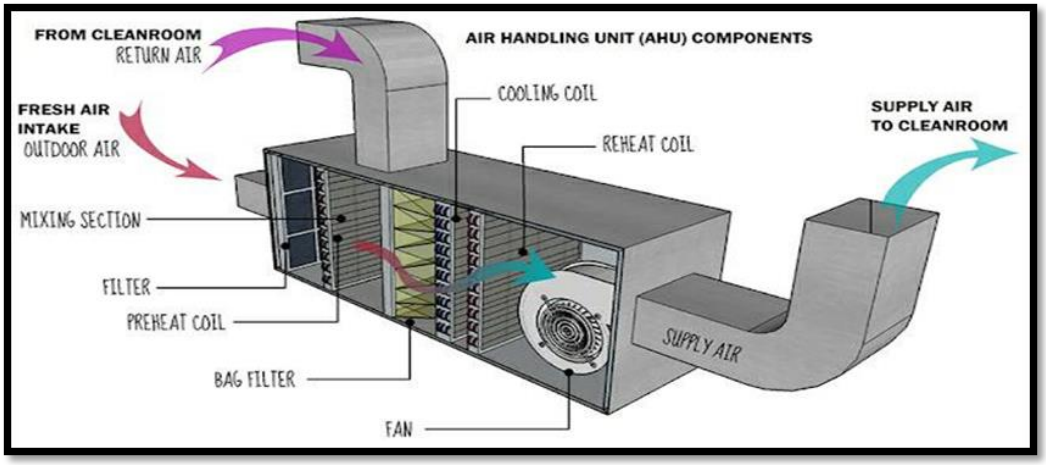
Heating and Cooling Coils: Depending on the place of operation and the application, air handling systems must provide heating, cooling, or both to alter the supply air temperature and humidity level. Heating and cooling coils in the air stream of the air handling unit provide this conditioning; the coils' actions are directly controlled by the medium that produces the heating or cooling effect. Usually, copper is used to make the coil's tubes, and aluminium or copper fins are added to help in heat transfer. Eliminator plates are also used by cooling coils to remove and drain condensate water. A chiller provides chilled water, and a hot water generator produces hot water. Temperatures are normally monitored and controlled using downstream temperature sensors in conjunction with a suitable motorized control valve prior to the coil. It is necessary to use a dehumidifier before using the cooling coil to overcool the area until the dew point is achieved and condensation forms. Air is reheated to the appropriate supply temperature using a heater coil that is positioned after the cooling coil. As a result, the supply air's relative humidity level decreases. Heating coils are frequently employed as the initial step of air treatment in colder climates where winter temperatures frequently drop below freezing, protecting chilled water coils or downstream filters from freezing.

Humidifier: Humidification is frequently required in colder climates because constant heating causes the air to become drier, which leads to poor air quality and a rise in static electricity. Moisture may need to be added to

makeup air in drier areas in order to control relative humidity. Although there are various humidifiers on the market, "steam grid" humidifiers are the most widely utilized type. These have a chamber to stop condensation and water droplets in the duct and are operated by modulating a steam valve at the humidifier. A signal from a room humidistat or from the return or exhaust airstream controls the valve. After the humidifier, a high-limit stat is installed in the duct to override the controlling stat and stop condensation from forming in the duct. It is imperative to adhere to the manufacturer's recommendations while positioning the humidifier in the duct to avoid condensation and ensure adequate dispersion area.

Blower Fan: To suction air, air handling machines typically use an enormous squirrel cage blower powered by an AC induction electric motor. A variable frequency motor powers the blower, enabling a broad range of air flow rates. The fan's outlet dampers or intake vanes regulate the flow rate.

Vibration Isolators: The occupants of the building located in the manufacturing and central parts of the pharmacy plant would be subjected to noise and vibration from the huge duct system caused by the blowers in the air handling unit. Vibration isolators or damper blocks are typically installed into the duct just before and after the air handler, as well as frequently between the fan compartment and the remainder of the AHU, to prevent this. These sections' rubberized canvas-like material permits vibrations in the air handler components without passing along the motion to the connected ducts. By supporting the fan compartment on a spring suspension, which will lessen vibration transmission through the floor, the fan compartment is more separated.



AHU

Filters

HEPA Filters: HEPA Filter is an abbreviation for High-efficiency particulate air filter. HEPA filters are defined as the filter that removes 99.95% or 99.97% particulate of size less than equal to or greater than 0.3 microns. The pharmaceutical industry uses HEPA filters a lot to filter the air. HEPA filters are utilized in HVAC systems in the pharmaceutical industry to provide clean air in clean rooms. Although AHUs can be equipped with HEPA filters, terminal diffusers that send air directly into clean rooms are a more efficient use of these filters. In addition to several other pollutants, air from the outside world contains pollens, fibers, dust, bacteria, and viruses. Thus, before providing to the clean rooms, these should be filtered and eliminated from the air.

The HEPA filter functions differently from other popular filters. It is sometimes asked how it filters particles that are 0.3 microns or smaller because the space between fibers may be greater than that. In HEPA filters there are three different mechanisms used to remove the contaminants.

- Straining/Impaction/Sieving
- Interception
- Diffusion

Straining/Impaction/Sieving: This mechanism removes large particles of size 1 micron. As we know HEPA pore size is 0.3 micron so the large particles are stuck inside the glass fibres and it is called impaction or straining or sieving.

Interception: The intercepting mechanism removes particles from the air that range in size from 0.3 to 1 micron. Particles move following the airflow pattern during interception, but because of their large size and sluggish speed, they stick to fibers and are drawn out of the atmosphere.

Diffusion: By using the diffusion process, particles smaller than 0.3 microns are eliminated. Because they travel in a zigzag pattern in air streams, particles smaller than 0.3 microns become stuck in fibers as a result of the arrangement of the fibers.

Ductwork Design

Duct Pressures: As pharmaceutical facilities require a lot of filters, volume control devices, and physically complicated arrangements, their ductwork typically has greater system pressure. To enable the fabricator to supply the appropriate metal thickness and construction techniques for the necessary system pressures, the duct system pressures must be computed and explicitly mentioned on the contract documents. Because the system is run with filters that become dirty or because space pressure conditions fluctuate, system pressures will likewise change. The fans may need speed controls, inlet vanes, or variable pitch blades to match the changing flow and pressure conditions. Duct systems must accommodate these pressure changes.

Duct Materials: Most systems use rectangular, round, or elliptical layouts of unlined galvanized steel, stainless steel, or aluminium ducting. Whenever available space allows, round ducting is a logical choice because of its self-cleaning form. Galvanized duct should not be utilized downstream of the HEPA filters to prevent contamination from the duct system itself since it can rust or flake off. Stainless steel is the preferred duct material when the HEPA filter is situated upstream of the room terminal and there is a lengthy duct run; nevertheless, because of its high cost, its use should be restricted. Numerous systems can also be cleaned or fumigated while still in place, and the cleaning chemical should not have an impact on the duct material that is utilized.

Cleanability: It's critical that duct systems be able to be cleaned in case an installed system becomes polluted or soiled. Access doors in the duct should be placed where they can be readily accessed without interfering with operations or going against designated areas during the design phase. Only the end seals on any sealed duct that is transported to the installation site should be broken and promptly resealed during the last installation. Before being shipped to the location, the duct is factory cleaned and sealed in extremely important applications. Although it is costly, this procedure eliminates the oil and other contaminants that were present during duct installation. Finding sheet-metal fabricators who are ready to perform this work could be challenging because they aren't usually prepared for such operations.

The following precautions should be taken.

i. To ensure that the system is airtight, longitudinal connections in ducts should be sealed with silicone sealant. Transverse joints should employ rubber gaskets.
ii. Angle iron flanged joints or pocket slips should be utilized in place of GI flanged joints.
iii. The ducts shouldn't contain any acoustic insulation.
iv. The dampers provided should have an extended handle to accommodate the thickness of the insulation and be made of compatible duct materials.
v. In order to transport particulate matter along with return air, return air risers should be engineered at velocities not to exceed 1800 fpm, with a minimum velocity of 1200 fpm at the highest point. On the other hand, the return grille's inlet velocity should be progressively increased from 300 to 400 fpm to 1200 to 1800 fpm.
vi. Diffusers and grilles should be flush mounted into walls, ceilings, or ductwork. They should all be made of stainless steel or have stove enamel or epoxy coatings applied to them.

Chillers: Chillers are advanced machinery used in absorption refrigeration or vapor-compression refrigeration systems to extract heat from liquids. Commercial cooling applications, industrial processes, and air conditioning systems all frequently use these devices. A chiller's main job is to cool liquids like water or other refrigerants. The cooled liquid is then pumped via heat exchangers to release the heat that has been absorbed into the surrounding air.

Chillers come in various types.

i. Air-cooled chillers: Air-cooled chillers utilize ambient air to dissipate heat from the refrigerant, making them suitable for applications where water availability is limited.
ii. Water-cooled chillers: Water-cooled chillers employ water as a cooling medium, offering higher efficiency and better temperature control.

Cooling Towers: Cooling towers are large, open-topped structures used to remove excess heat from industrial processes and HVAC systems. They help cool water by letting some of it evaporate, which takes away some of the heat and cools the water that's still there. Power stations, refineries, petrochemical facilities, and many other businesses requiring large heat dissipation frequently employ cooling towers.

There are different types of cooling towers.

i. Natural Draft Cooling Towers: These towers use the natural convection of air to cool the water. They are massive structures typically seen in power plants.
ii. Mechanical Draft Cooling Towers: This type uses fans to draw air through the tower, enhancing the cooling process and making them more versatile for various applications.

- **TESTING AND BALANCING**

In pharmaceutical facilities, the most crucial and toughest to balance aspect is creating pressure differentials between adjacent rooms. By modifying airflows, performing smoke tests, measuring pressure, and tweaking controls, these differentials can be found. Because every facility is unique and every room has different leakage factors that affect pressurization, this work may take some time to complete.

In order to achieve the necessary pressure differentials, you can discover throughout the balancing process that the duct systems or rooms are not as tight as intended and that more sealing is needed. Remember that airflows depicted in drawings are design values, and in most cases, they need to be slightly adjusted in order to provide the necessary pressure differentials. Keep adding more external air to the system as a straightforward fix for many pressurization issues. When heating or cooling coils fail to meet this requirement and design values are exceeded, it can cause issues with off-design humidity and room temperature levels. The room supply temperature will be greater than intended because the AHU coils will employ the cooling capacity that is available to condition an excessive amount of outdoor air. Tightening the spacing is therefore the recommended course of action initially. When there aren't many facility employees or construction workers around, it's best to balance the areas. All doors should be closed when balancing because opening and closing them disturbs system pressure and makes balancing difficult.

In general, testing and pre-commissioning test procedures cover the following parameters.

i. HEPA filter integrity via DOP testing for pinhole leaks across sealants and frame gaskets, supporting the wall and frame, and in the filter media.
ii. Velocity of air flow beneath every filter panel. To ensure correct flows and record patterns, airflow measurements should be taken at supply, return, and exhaust outlets in addition to traverses across the face of hoods.
iii. Create a particle spectrum using suitable air sample data.
iv. If feasible, smoke testing should be done to determine flow patterns. If not, comparable tests should be conducted both when the cleanroom is operating and while it is not in use to ensure thorough validation.
v. Pressure changes when moving from one room to another.
vi. Relative humidity and room temperature. At this point, accuracy of temperature and humidity sensors at crucial regions should also be verified by physically reading space conditions and comparing results with those given by the BMS.
vii. The facility is prepared for production only when a thorough documentation of the test readings and procedures has been completed.

- **SEQUENCE OF OPERATIONS**

The establishment of a sequence of operation, or a documented description of how the HVAC system and related systems operate, is the first step in the system design process. Every air handling system often has its own sequence established outlining every step of the process, from controlling humidifiers and coils to regulating humidity and temperature in the space. The functioning of the air handling unit fans is described, including how to turn on and off the fans. It also describes how to interlock the return or exhaust fans with the main air system fans. The normal operation of all fans is simultaneous, which keeps pressurization constant. The procedure also handles anomalous events like an exhaust fan malfunctioning or a smoke detector going off.

The sequence explains the actions taken by system elements when an anomalous event takes place. If a large exhaust fan fails to stop or reduce pressurization loss, it could be essential to turn off a supply fan. The sequence also outlines any energy-saving techniques that should be implemented in the system, such lowering the temperature at night or reducing ventilation and exhaust rates while the space is empty.

- **DOCUMENTATION**

Good manufacturing practices control the degree of control over different aspects of quality assurance, including validation of the facility, acceptance criteria, and operation and maintenance documentation. The system's operation, design, and performance requirements should all be covered in the documentation.

Documenting the HVAC system is crucial for several reasons as it provides a detailed record of your system's installation, maintenance, and repairs. This information can be invaluable for troubleshooting issues, improving system performance, and ensuring compliance with industry regulations.

Additionally, having thorough documentation of the HVAC system can streamline communication between contractors, technicians, and building owners. By keeping all relevant information in one place, you can avoid confusion and minimize downtime during maintenance or repair activities.

- **VALIDATION**

Commercial production cannot employ HVAC systems without validation and qualification. Documentary proof that the system is built, configured, and operating as planned is provided via validation.
The exercise starts with a methodology or approach that questions every component of the system's design. Every piece of documentation evidence, including mappings of temperature, pressure, and humidity as well as other regulated parameters, is captured and stored. Before any parameters are tested, the calibrations of all the instruments are double-checked. After the PQ report is published, HVAC systems can be utilized in commercial production settings.

The validating agency will review the HVAC paperwork and should get in touch with the design engineers to determine the HVAC system validation methodology when a pharmaceutical facility needs to be certified. The systems should be simple to validate if the components function as intended, the design is sound, and the system is installed correctly. In order to confirm that the actual

system installation and operation adhere to the design principles and intent, the validator will follow a master plan and protocols. Accuracy of the physical characteristics supplied by the BMS system must be confirmed through measurements made with calibrated instruments.

Air flow pattern or smoke pattern, air flow velocity and changes per hour, filter leak test, particle count, viable monitoring, filter integrity test (dioctyl phthalate (DOP)/polyalphaolefin (PAO) test, pressure difference, recovery test (temperature and humidity), temperature and humidity uniformity test, and fresh air determination are generally the various parameters to be evaluated for the validation of HVAC systems.

- **QUALIFICATION**

Design Qualification: The design qualification is a validation process of design requirements. This is proof, supported by documentation, that the system's design complies with the specifications tied to production processes. These design requirements must be properly taken into account and adhered to firmly. Three important steps are included in the design qualification process.

User Requirement Specifications: It is essential to look for the user requirement specifications based on the purchase request, known as the purchase order. These specifications are taken into account by the vendor who finalises the material supply that meets the technical and financial needs. It is important to check each section of the equipment to ensure the standards of the material in the purchase order.

Verification Process: This stage includes a detailed audit of the design specifications including the tracing and drawing of the products. The deviation in the design is drafted and is submitted to the vendor.

Final Check: The last phase is crucial since there is no room for error. Focused on the end product are the comprehensive design specifications. After taking into account the deviation reports, the outcome is compiled, and the necessary remedial action is taken.

Installation Qualification: Newly installed or updated equipment must first undergo Design Qualification (DQ), a technique that is defined as the documented verification of a proposed design's capacity to meet the requirements it must complete, in order to ascertain whether it can yield the intended outcomes.

However, the installation process determines how a certain piece of hardware or software functions in practical situations. Installation Qualification (IQ) is the process of confirming that an instrument or piece of equipment is installed and configured in compliance with the installation checklist or manufacturer's standards. The FDA's IQ definition provides a helpful summary of the overarching objective, regardless of whether software or a physical unit is being tested: it documents that the "system has the necessary prerequisite conditions to function as expected."

The Validation Master Plan (VMP) also needs to include a detailed documentation of all CGMP standards that are pertinent to the IQ and the technique used for IQ. Re-qualification is required after the first IQ, after any significant maintenance, and whenever equipment is updated. Regular quality assurance procedures should include re-qualification as well.

Successful IQ is typically measured by how well the installation process followed the manufacturer's guidelines and met their requirements.
This often includes the following areas of focus.

- Location of install and necessary floor space
- Documentation of any and all computer-controlled instrumentation
- Gathering all manuals and certifications
- Properly unpacking and cross-checking instruments
- Examining instruments and components for damage
- Ensuring correct power supply
- Installing ancillary instruments
- Documenting firmware versions and serial numbers
- Environmental and operating conditions
- Checking software system installation and accessibility
- Recording calibration and validation dates of tools used for IQ
- Verifying connections and communication with peripheral units

Essential Installation Qualification Documentation
The IQ Protocol: The IQ Protocol is a detailed strategy that describes the parameters, approach, and requirements for carrying out the IQ. It should contain.

- Details for identifying the equipment (manufacturer, model, and serial number).
- A list of systems and equipment that need to be qualified.
- Installation standards in accordance with manufacturer guidelines.
- Requirements for environmental conditions (such as temperature and humidity).
- A checklist of installation requirements that need to be confirmed.

IQ Checklist: An extensive list of items covering every facet of the installation that needs to be confirmed, generated from the IQ protocol. This covers environmental factors, software installation, calibration, electrical connections, and physical installation inspections.

IQ Report: This report summarizes the observations, conclusions, and outcomes of the IQ procedure and chronicles its execution. If the equipment installation

satisfies the predetermined standards, it should be made visible.

Operational Qualification: Meeting each IQ protocol is the first step towards completing operational qualification, or OQ. The goal of OQ is to ascertain whether, within the operating ranges indicated by the manufacturer, the equipment's performance is consistent with the user requirement specification. This entails locating and examining equipment components that may have an effect on the quality of the finished product.

Every item in the test plan is tested during OQ, and every test result is meticulously recorded. This can only be done once the IQ has been completed, as it is a requirement for the acceptance of the facility and the equipment. OQ generally functions as a thorough examination of the starting, operation, maintenance, cleaning, and safety protocols of hardware or software. It must be demonstrated that every piece of software and hardware is functioning within the allotted parameters. The action items of OQ are identifying and inspecting the components of equipment that impact product quality and ensuring they're operating within specific limits these often include the following.

- Temperature control and variations
- Servo motors and air flaps
- Temperature protection systems
- Card readers and access systems
- Pressure and vacuum controllers
- Temperature distribution
- Display units and signalling LEDs
- CO2 controls
- Humidity-measuring and control
- Fan and fan-speed controllers

Essential Operational Qualification Documentation

The OQ protocol: It is a detailed document that describes the goals, parameters, approach, and standards for carrying out the OQ. It should contain.

- Objectives: Give a clear explanation of the objectives of the OQ, together with the operational characteristics and functions that will be tested.
- Methodology: Outline the precise steps needed to carry out the operational testing, together with any setups or special circumstances that may be required.
- Acceptance Criteria: Specify the quantifiable requirements that each test must be passed by the device. The needs of the user, legal requirements, and manufacturer specifications should serve as the foundation for these standards.

  The OQ Report: The OQ report documents the execution and outcomes of the OQ testing. It includes:
- A brief overview of the OQ objectives and scope.
- A summary of the testing methodology used.
- Detailed results of each test, including any measurements or observations made. This section should clearly indicate whether the equipment met the defined acceptance criteria.
- Any deviations from the protocol, including unexpected results or failures, should be documented along with an analysis of their impact and any corrective actions taken.
- A summary of the OQ findings, stating whether the equipment has successfully passed the operational qualification based on the predefined criteria.

Performance Qualification: Performance Qualification is the last stage of qualifying equipment. The certification and validation team confirms and records that the user requirements have been confirmed to be met during this step. The usual operating range that is necessary should be part of these user requirements (as defined, approved by QA, and confirmed in the DQ). After the equipment has been qualified, you can create each process needed for every product. Each procedure can then be validated after it has been fully developed. PQ tests all of the instruments and components as a partial or entire process, as opposed to testing each one separately.

However, the team needs to develop a thorough test strategy based on the process description before they begin qualifying. It is noteworthy that the quality of the test plan has a direct impact on the quality of the qualification. To ensure accuracy and thoroughness, it is generally advisable to involve a third-party specialist in this particular area.

▪ CONCLUSION

The primary goal of every pharmaceutical company is to maintain a functional HVAC system in order to guarantee that the items they produce are of the highest quality. Additionally, during the production process, hazardous byproducts such gasses can occasionally be released and these systems regulate this by ensuring appropriate ventilation. In light of this, proper HVAC systems is essential to maintain the health and safety of the operator.

The HVAC system, which circulates and purifies outside air, is the backbone of the pharmaceutical industry. HVAC systems offer a certain set of environmental conditions that are necessary to produce high-quality goods and the comfort of operator, hence they need to be verified periodically.

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