Clean Room Classification for Pharmaceutical Industry

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***Abstract*— A clean room is an environment, typically used in manufacturing or scientific research that has a low level of environmental pollutants such as dust, airborne microbes, aerosols particles and chemical vapors. More accurately, a clean room has a controlled level of contamination that is specified by the number of particles per cubic meter at a specified particle size.**

As per the regulations specified by regulating authority FOOD & DRUG ADMINISTRATION, it is necessary to implement specified norms for all pharmaceutical & food industries. For this reason, the air conditioning and ventilation system in the pharmaceutical industry is one of the most vital elements in the manufacturing process.

The working area is sensitive to airborne contamination which is why it is necessary to provide adequate protection from ingress of pollutants. The manufacturing process itself also generates fumes that need to be exhausted from the plant to prevent the contamination of areas in which the production takes place. Only the familiarity with all the specificities of the pharmaceutical industry guarantees successful designing and manufacturing of optimal HVAC solution. In this paper, the necessary classifications for clean air, air handling unit and its different components are discussed.

***Index Terms*—Clean Room Specification, Air filter, AHU**

I. INTRODUCTION

Terminology used for clean room systems:

1. Particle size: Micron = 10^{-6} m
2. Number of air changes: Integer number indicating ratio of blower capacity of air handling unit to the room volume.
3. Particle count: Number of particles of specified size per m^3 of air inside the clean room.
4. Quality standards for the clean rooms:
   a. US FED STD 209E clean room standards
   b. ISO 14644-1 clean room standards
   c. BS 5295 clean room standards
   d. GMP EU classification
5. AHU: Air handling units
6. HEPA: High-efficiency particulate air

II. INTRODUCTION

Industrial clean room is mainly applied in electronics industry for semiconductor manufacturing. Furthermore, it extends its application s in new material development and fine chemical Industry, pharmaceutical & food industry.

One of the industrial clean room criteria is that, its employment will get the investment capital returned with the improvement of quality and production yield of the products. In short, the investment for industrial clean room is profitable. What level of clean room is necessary for what kind of products is determine by the product requirement. It is important to design the higher clean room for more important production area and lower and economical clean room for other areas.

III. CLEAN ROOM CLASSIFICATION

Table No. (1) US FED STD 209E clean room standards

Class	Maximum particles / ft^3					ISO equivalent
	≥ 0.1 Mm	≥ 0.2 µm	≥ 0.3 µm	≥ 0.5 µm	≥ 5 µm	
1	35	7.5	3	1	0.007	ISO 3
10	350	75	30	10	0.07	ISO 4
100	3500	750	300	100	0.7	ISO 5
1000	35000	7500	3x 10^3	1x 10^3	7	ISO 6
10000	35x 10^4	75x 10^3	3x 10^4	1x 10^4	70	ISO 7
100000	35x 10^5	75x 10^4	3x 10^5	1x 10^5	700	ISO 8

Definition of Cleanroom: The definition of cleanroom has been expanded in the ISO 14644 compared to FS 209E, the definition has include the specific internal environmental conditions. The definitions for both FS 209E and ISO 14644 are as follow;

FS 209E Clause 3.5 Define cleanroom as 'A room in which the concentration of airborne particles is controlled and which contains one or more clean zones.'

ISO 14644-1 Clause 2.1.1 expanded the definition of a cleanroom to 'A room in which the concentration of airborne particles is controlled, and which is constructed and used in a manner to minimize the introduction, generation, and retention of particles inside the room and in which other relevant parameters, eg temperature, humidity and pressure are controlled as necessary.'

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Table No. (2) BS 5295 clean room standards

Class	Maximum particles / m^3				
	≥ 0.5 µm	≥ 1 µm	≥ 5 µm	≥ 10 µm	≥ 25 µm
Class 1	3000		0	0	0
Class 2	300000		2000	30	
Class 3		1000000	20000	4000	300
Class 4			200000	40000	4000

BS 5295 Class 1 also requires that the greatest particle present in any sample do not exceed 5µm.

Table No. (3) ISO 14644-1 clean room standards

Class	Maximum particles / m^3						FED STD 209E equivalent
	≥ 0.1 µm	≥ 0.2 µm	≥ 0.3 µm	≥ 0.5 µm	≥ 1 µm	≥ 5 µm	
ISO 1	10	2.37	1.02	0.35	0.083	0.0029	
ISO 2	100	23.7	10.2	3.5	0.83	0.029	
ISO 3	1000	237	102	35	8.3	0.29	Class 1
ISO 4	10000	2370	1020	352	83	2.9	Class 10
ISO 5	100000	23700	10200	3520	832	29	Class 100
ISO 6	$1x\ 10^6$	237000	102000	35200	8320	293	Class 1000
ISO 7	$1x\ 10^7$	$2.37x\ 10^6$	1020000	352000	83200	2930	Class 10000
ISO 8	$1x\ 10^8$	$2.37x\ 10^7$	$1.02x\ 10^7$	3520000	832000	29300	Class 100000
ISO 9	$1x\ 10^9$	$2.37x\ 10^8$	$1.02x\ 10^8$	35200000	8320000	293000	Room Air

Table No. (4) GMP EU classification

Class	Maximum particles / m^3			
	At Rest	At Rest	In Operation	In Operation
	0.5 µm	5 µm	0.5 µm	5 µm
Class A	3520	20	3500	20
Class B	3520	29	352000	2900
Class C	352000	2900	3520000	29000
Class D	3520000	29000	n/a	n/a

IV. Equipment Used in Pharmaceutical Industry

The definition of air handling unit from ANSI/AHRI Standard 430-2009 states that it is "A factory-made encased assembly consisting of a fan or fans and other necessary equipment to perform one or more of the functions of circulating, cleaning, heating, cooling, humidifying, dehumidifying and mixing of air...."

The AHU is used to control the following parameters of the space.

- Temperature
- Humidity
- Air Movement
- Air Cleanliness

Components of Air Handling Unit:

Here are some of the air handling unit components that may be contained in the equipment.

1. Housing: The housing that contains all the other components of an AHU is usually make of metal, some are painted to prevent corrosion. In sections where the fans and the coil are located, 1-2 inches of polyurethane foam or PU is used to insulate them to prevent the condensation on the panel. Drain pan is also used as a precaution in the event of condensation of water.

2. Blower Section: Centrifugal fan is used to circulate the air to the various parts of the sections in the building. The typical types of fan available are Backward Inclined, Backward Curved, Forward Curved and Airofoil. The selection of the fan will depend on the air volume and the static pressure required of the system. Usually, the designer of the system will use a specialized software to do this selection. In order to reduce the effect of vibration on the panel, the motor and the fan are usually installed on the vibration isolator except when the drive assembly is external to the fan casing.

In recent years, the use of variable air volume (VAV) system is becoming more popular as the volume of the air being discharged can be varied depending on the load condition. If the load is high, the fan speed will be higher and if the load is lower, the speed of the fan will be lower.

The speed of the fan is varied by using frequency inverter instead of conventional motor such as PSC motor. Frequency inverter provides better control of the fan speed as a whole range of fan speed from super low to super high can now be utilized based on the load conditions required. This technology has enabled better use of energy and is in tandem with the move to go for greener energy.

3. Cooling Coil: Cooling Coil is used to cool and dehumidify the air. Both DX (direct expansion) cooling and CW (chilled water) cooling coils are available for use depending on the system design. The coil diameter, no. of rows of copper tubes are calculated on the basis of surface area required for effective heat transfer.

These coils are arranged in rows with different fin spacing. Aluminium fins and copper tubes are used in the design of the coils. The corrosion resistance hydrophilic fins are also used due to its lower cost and lower resistance to the air velocity.

4. Filters: Filters are to remove particles and contaminants of various sizes from the air. The type of air filter being used will very much depend on the application of the system.

Panel Filter is a flat and rectangular in shape and provides a minimum low efficiency filtration which is acceptable to the air conditioning industry. The high velocity filter is arranged vertically whereas the low velocity filter is arranged in V shape. Typical air velocity that moves through the filters is in the range of 2-3 m/s.

Table No. (5) Pre- filter and fine filter efficiency

BSEN 7794/5	Efficiency	Filter Group
G1	-	Coarse filter
G2	-	Coarse filter
G3	-	Coarse filter
G4	-	Coarse filter
F5	40 – 60 %	Fine filter
F6	60 – 80 %	Fine filter
F7	80 – 90 %	Fine filter
F8	90 – 95 %	Very Fine filter
F9	95 – 98 %	Very Fine filter

HEPA Filter is very efficient and is able to achieve efficiencies up to 99.97%, removing minute particles and airborne bacteria from the air. It is usually used in clean room applications such as semiconductor production floor, operating theaters and critical processes.

Table No. (6) HEPA filter efficiency @ 0.3micron particle

BSEN 1822	Efficiency	Filter Group
H10	85%	HEPA
H11	95%	HEPA
H12	99.5%	HEPA
H13	99.95%	HEPA
H14	99.995%	HEPA
U15	99.9995%	ULPA
U16	99.99995%	ULPA
U17	99.999995%	ULPA

Electrostatic Filter is used to remove particles from the air by using highly charged electrodes that ionized the air. Bag Filter is able to remove dust particles and is thrown away after use. Roll Filter is used for high velocity filtration where the used part is rolled up automatically/manually.

5. Humidifiers: During winter, the humidity level of the air can be low hence causing discomfort to the occupants. The humidity of the air is increased by using the humidifiers. Here are the commonly used humidifiers:
Spray Type has a header and spray nozzles that spray water with a pressure of 15 psi or more.
Steam Pan Type has a pan and a heating coil to heat up the water of the pan. The evaporation of water caused by the heating will increase the humidity level of the surrounding air.
Steam Grid Type has tiny holes on the pipe to distribute the steam that flows through it. In this case, the water that is heated up to produce the steam to be supplied to the grid is conditioned to prevent odour being discharged to the room.

6. Mixing Box: This box has air inlets that is attached to the dampers. This is the place where the outside air and the return air are mixed to provide the correct proportion of air to be distributed to the space that is to be conditioned.
Other functional parts are supply & return ducts, supply air dampers, return air dampers & volume control dampers.

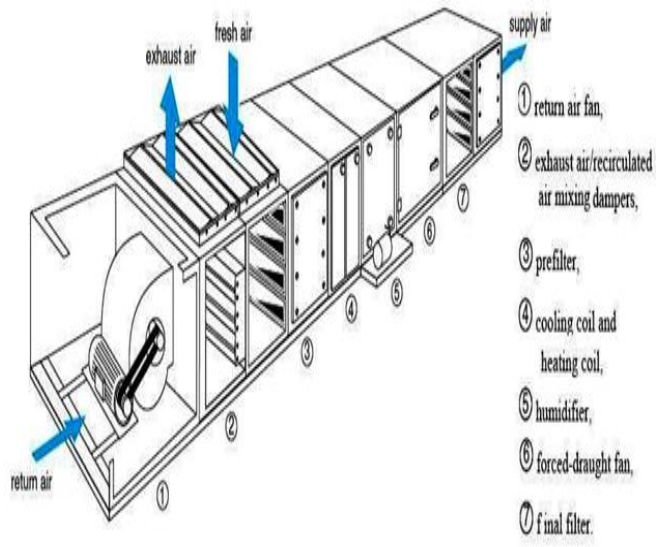

Figure No. (1) Different sections in air handling unit.

V. CLEAN ROOM REQUIREMENTS FOR VARIOUS INDUSTRIES

Globalization & growth have become key words in present scenario of an industrial development. Along with this various stringent conditions are l aid down on food, cosmetic & pharmaceutical industries. These norms are dependent on type of product manufactured and countries to which it is to be exported. Accordingly manufacturer is expected to follow either F.D.A. or G.M.P. or W.H.O. norms. The norms for manufacturing particular product decide design parameter required for particular clean room. Following are some common products which require clean rooms for their processing & packing.

A) Medicines: Clean rooms required for this product is sub classified in to following categories. 1) External drugs 2) Internal oral drugs 3) Betelactum drugs 4) powder & tablets 5) Capsules 6) Saline's & injections (Intravenous drugs) 7) Repacking units of bulk drugs 8) Raw material quarantines 9) Primary, secondary & tertiary packing rooms 10) Microbiology laboratories 11) Chemical analysis laboratory.

B) Food & beverages: Requirements for food & beverages clean room is dependent on type of food product being manufactured.

C) Electronic Industries: Many electronic industries such as, an assembly unit of Camera, cell phones, control equipments, precision medical equipments.

D) Painting & surface coating industries: For heat treatment & for providing thin coats of precious metals certain controlled atmosphere is required, which can be provided by specially designed clean rooms.

E) Horticulture, biotechnology & agro based products: Agro firms developing advanced agro products are using various methods involving genetic modifications & tissue culture technique. Hence this sector also has wide range of clean room applications.

VI. CONCLUSIONS

As a consulting engineer working in the field of clean room technology, we are observing many small scale units being closed down because of non-availability of affordable clean room technology. For switching over from existing manufacturing system to the manufacturing system as per mandatory norms development of low cost clean room is the need of hour. This inspired us for carrying out experimentation to design a system using commonly available ductable split units. These efforts were well accepted by the industry & are fruitful to them.

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