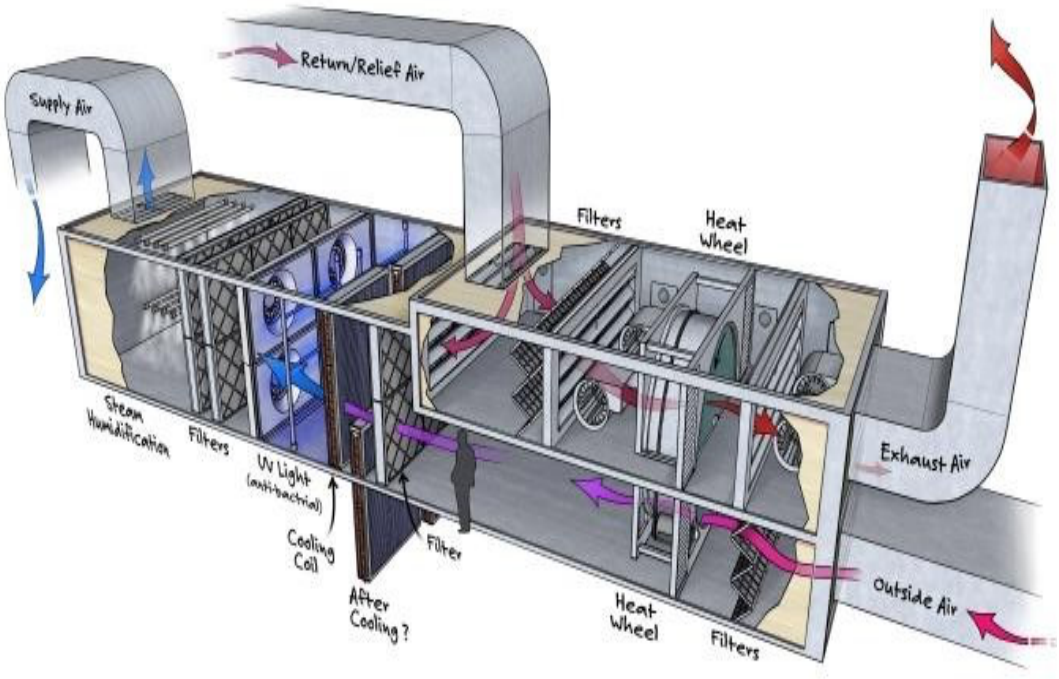
HVAC SYSTEM & TEST FOR HVAC QUALIFICATION

1. What is HVAC ?

It controls Temperature, Humidity and Air quality inside a building. HVAC technology aims to provide thermal comfort and acceptable indoor air quality. HVAC system design is a sub discipline of mechanical engineering, based on the principles of thermodynamics, fluid mechanics, and heat transfer. The HVAC system is an extremely vital concern, which aids to enhance and maintain the quality of drug products. It mainly helps in achieving an optimal temperature, ventilation, and air conditioning in the production areas. The HVAC system design directly impacts prevention and control of cross contamination; and maintains hygienic condition at the work place. Certain pharmaceutical products such as parenteral, bulk drug etc.

In order to achieve a proper cleanliness in the storage and quarantine area, High efficiency particulate air (HEPA) filters are used. They also maintain the aseptic condition in the working area. The efficiency and integrity of the filters that are used in this system must be checked at regular intervals by performing leak test. HEPA filters are the main part of the air handling unit (AHU). The AHU collects the outside fresh air and combines it with the air returning from the cubicles and then supplied the treated air back to the laboratory area. A part of the air exiting from the laboratory rooms is directly exhausted into the atmosphere by an exhaust fan, while the remaining air is directed to the AHU where it is filtered by passing through prefilters which is attached to the medium filters, to remove any entrapped particles and then the same air is conditioned for humidity and temperature control, and this filtered air is passed to the laboratory and other areas by a supply fan at desired pressure. HEPA filers are terminal filter which is attached at the entrance to the clean rooms.



2. BASIC CYCLE OF REFRIGERATION:

Principles of Refrigeration:

- Liquids absorb heat when changed from liquid to gas.
- Gases give off heat when changed from gas to liquid.

Working of Refrigeration Cycle:

i. The refrigerant comes into the compressor as a low pressure gas, it is compressed and then moves out of the compressor as a high pressure gas.

ii. The gas then flows to the condenser. Here the gas condenses to a liquid and gives off its heat to the outside air.

iii. The liquid then moves to the expansion valve under high pressure. This valve restricts the flow of the fluid, and lowers its pressure as it leaves the expansion valve.

iv. The low pressure liquid then moves to the evaporator, where heat from the inside air is absorbed and changes it from a liquid to a gas.

v. As a hot low-pressure gas, the refrigerant moves to the compressor where the entire cycle is repeated.

Components of Refrigeration Cycle		
No.	**Component**	**Function**
1	*Compressor*	Increases the pressure and temperature of the gas by mechanical work done.
2	*Condenser*	Change of phase from Gas to Liquid. Heat is rejected to atmosphere from the R-gas.
3	*Expansion Device*	Decreases the pressure and temperature of the gas by expansion.
4	*Evaporator*	Change of phase from Liquid to Gas. Heat is absorbed by R-gas from the indoor.

2.1. Compressor:

The function of a compressor is to compress the fluid or gas and increase its pressure and temperature by some mechanical action done. Compressors are broadly classified as two types:

i. Positive Displacement Compressors
   a. Reciprocating – Single-Acting, Double-Acting, Diaphragm
   b. Rotary – Lobe, Liquid Ring, Screw, Scroll, Vane

ii. Dynamic Compressors
   a. Centrifugal
   b. Axial

2.2. Condenser:

Condensation is a process of change of phase from gas form to liquid form, the same process happen inside a condenser. A condenser converts the refrigerant gas at high pressure & temperature into a liquid refrigerant at nearly high pressure & temperature by releasing the latent heat from the gas. Condensers are broadly classified as

i. Air Cooled
ii. Water Cooled
iii. Air and Water Cooled (or) Evaporative Condenser

2.3. Expansion Device:

The function of expansion device is to decrease the pressure & temperature of the liquid refrigerant by the process of expansion. Types of Expansion Devices:

i. Capillary Tubes
ii. Thermostatic Expansion Valves
iii. Electronic Expansion Valves

2.4. Evaporator:

Evaporation is a process of change of phase from liquid to gas form, the same process happens inside an evaporator. The evaporator converts the liquid refrigerant at low pressure & temperature into its gaseous form by absorbing the latent heat from the room air. Types of Evaporators:

i. Shell and Tube Evaporator
   a. Shell and Tube with the Refrigerant Boiling in Shell
   b. Shell and Tube with the Refrigerant Boiling in Tubes
ii. Plate Type Evaporator

Refrigerants: Refrigerants are the heat transfer media used in the refrigeration cycle, which absorb heat from the room air during the process of evaporation at a region of low-pressure & temperature and releases the heat during the process of condensation at a region of high pressure & temperature.
Ex: Air, Water, Refrigerants like R-12, R-22, R-134a, R-410a etc.

3. CLASSIFICATION OF AIR CONDITIONING SYSTEMS:

Based on the fluid media used in the thermal distribution system, air conditioning systems can be classified as:

i All Air Systems
ii All Water Systems

iii Air-Water Systems
iv Unitary Refrigerant Based Systems

3.1. All Air Systems:

In this system, air is used as the media that transports energy from the conditioned space to the A/C plant. In these systems air is processed in the A/C plant and this processed air is then conveyed to the conditioned space through insulated ducts using blowers and fans.

It is further classified into 2 sub-systems:

a. Single Duct System – It can provide either cooling or heating using the same duct, but not both heating /cooling simultaneously.
b. Dual Duct System

3.2. All Water Systems:

In this systems, the fluid used in thermal distribution system is water i.e. water transports energy between the conditioned space and the A/C plant. When cooling is required in the conditioned space then cold water is circulated between the plant & the conditioned space, while hot water is circulated through the distribution system when heating is required.

It is further classified into 2 sub-systems:

a. 2 Pipe System – It is used either cooling or heating only application, but cannot be used for simultaneous cooling and heating.
b. 4 Pipe System – It consists of two supply pipelines – one for cold water and one for hot water, and two return water pipelines.

3.3. Air-Water Systems:

In this system, both air and water are used for providing required conditions in the conditioned space. The air and water are cooled or heated in a central plant. The air supplied to the conditioned space from the central plant is called as primary air, while the water supplied from the plant is called as secondary water. The complete system consists of a central plant for cooling or heating of water & air, ducting system with fans for conveying air, water pipelines and pumps for conveying water and a room terminal. The room terminal may be in the form of a FCU, an induction unit or a radiation panel.

3.4. Unitary Refrigerant Systems:

It consist of several separate air conditioning units with individual refrigeration systems. These systems are factory assembled and tested as per standard specifications and are available in the form of package units of varying capacity and type. Each package consists of a refrigeration and / or heating units with fans, filters, controls etc.

4. HVAC SYSTEM COMPONENTS:

The basic components in a common central HVAC system are:

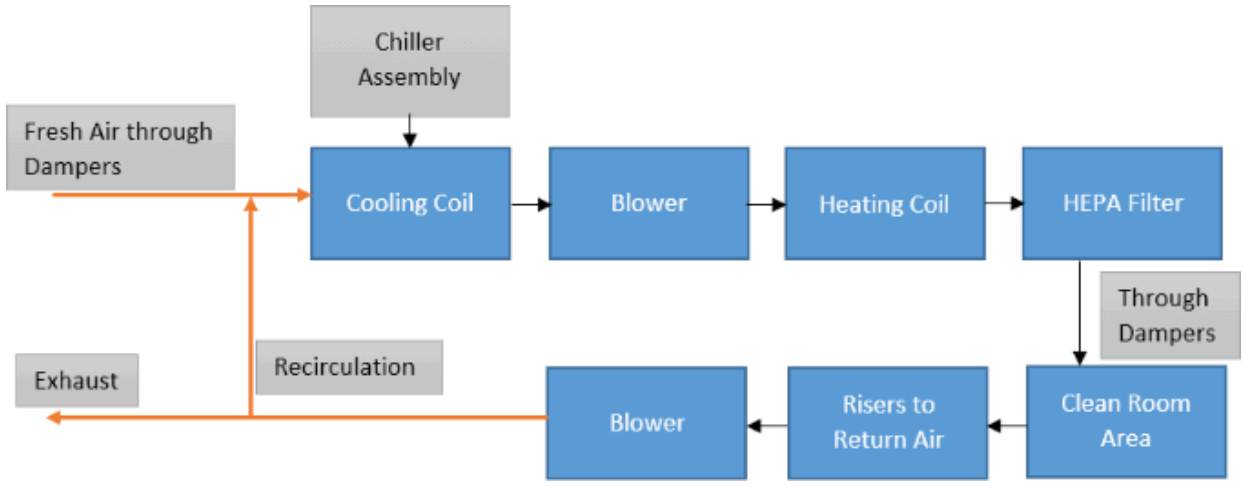
- Fan(s) to circulate the supply air (SA) and return air (RA).
- Supply air ductwork in which the air flows from the supply fan to the conditioned space.
- Air devices such as supply air outlets and return air inlets.
- Return air path or ductwork in which the air flows back from the conditioned space to the mixed air chamber (Plenum).
- Outside air (OA) device such as an opening, louver or duct to allow for the entrance of outside air into the mixed air chamber.
- Mixed air chamber to receive the return air and mix it with outside air.
- Filter section(s) to remove dirt and dust particles from the mixed air.
- Heat exchanger(s) such as hot water coil(s), steam coil(s), refrigerant evaporator(s), or chilled water coil(s) to add heat to or remove heat from the circulated air.

- Auxiliary heating devices such as natural gas furnace(s) or electric heating element(s).
- Compressor(s) to compress the refrigerant vapor and pump the refrigerant around the system.
- Condenser(s) to remove heat from the refrigerant vapor and condense it to a liquid.
- Fan(s) to circulate outside air across air-cooled condenser(s).
- Pump(s) to circulate water through water-cooled condenser(s); condenser water pump (CWP); and condenser water supply (CWS) and return (CWR).
- Pump(s) to circulate hot water from the boiler(s) through the hot water coil(s) and back or to circulate chilled water from the chiller(s) through the chilled water coil(s) and back to the chiller(s).
- For central systems, water or steam boiler(s) as a central heating source.
- For central systems, water chiller(s) as a central cooling source.
- For central systems, cooling tower(s) with water-cooled condenser(s).
- Controls to start, stop, or regulate the flow of air, water, steam, refrigerant and electricity.

Components of Air Distribution System:

i. Supply Fan
ii. Coil
iii. Filter
iv. Transition fitting
v. Supply Air Grill
vi. Return Air Grill
vii. Supply Air Duct
viii. Return Air Duct
ix. Fresh Air Duct
x. Supply Air Diffuser
xi. Return Air Diffuser

HVAC Scheme



5. TYPE OF TEST FOR HVAC QUALIFICATION:

a) Air Velocity / Air Changes
b) Integrity Test Of HEPA Filters
c) Air borne non-viable particle monitoring
d) Recovery test
e) Smoke test (air flow direction)
f) Pressure differential, temperature and relative humidity test
g) Air borne viable particle monitoring by settle plate (Passive Air Sampling)
h) Air borne viable particle monitoring by air sample (Active Air Sampling)
i) Measurement of sound level

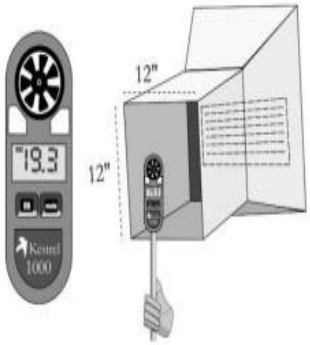
5.1. Air Velocity / Air Changes:

5.1.1. Objective:

To verify that the HVAC system is capable of delivering required airflow velocities, airflow volumes and providing required number of air changes.

5.1.2. Instruments:

Digital Anemometer, Air Capture Hood.



5.1.3. Procedure:

i. Switch "ON" the air-handling unit.
ii. Put 'ON' the anemometer and allow some time for warming up of the instrument.
iii. Keep the anemometer range as 20-2500 FPM or 0.1-12.7 m/sec.
iv. Remove filter grill and keep the probe at approximately 150 mm below the face of filter and velocity recordings shall be noted.
v. Each filter requires minimum 5 test spots. Measure the air velocity at 4 corners and one centre of the filter.
vi. Measurement should be taken for a minimum of 15 seconds.
vii. Calculate the air velocity and number of air changes.
viii. The results shall be recorded in report.

5.1.4. Calculation:

$$\textbf{Average air velocity } (V_A) = \frac{V1 + V2 + V3 + V4 + V5}{m}$$

m : Number of Samples location Taken

V_A : Average air velocity in FPM (Foot per minute)

$$\textbf{Air Flow volume } (\textbf{in CFM}) \textbf{ of a grill } = V_A \times \textbf{Area of Filter } (\textbf{in } ft^2)$$

CFM: Cubic feet per minute

$$\text{So, } \textbf{Total Air Flow volume } (\textbf{in CFM}) = \frac{\sum \textbf{CFM for each Grill}}{\textbf{Number of filter}}$$

$$ACPH = \frac{\textbf{Total Air Flow Volume } \times \textbf{Time } (\textbf{60 minutes})}{\textbf{Volume of room } (\textbf{in } ft^3)}$$

ACPH: Air Changes per Hour

V1	**V2**
V5	
V3	**V4**

Air sampling point at filter

5.1.5. Acceptance Criteria:

Not less than 20 ACPH

5.2. Integrity Test of HEPA Filters:

5.2.1. Objective:

To verify the integrity of HEPA filters

5.1.2. Instruments:

PAO Aerosol generator, Aerosol Photometer

5.2.3. Procedure:

i. Filter integrity test shall be performed after the verification of operational velocities and adjustment at the same.
ii. Supply the compressed air/nitrogen to the Aerosol Generator NLT 2 Kg/cm².
iii. Introduce the aerosol PAO as a challenge agent into the upstream side of the HEPA
iv. Switch ON the photometer and select the knob to upstream side.
v. Ensure that the Aerosol concentration in air stream is 20-80 ug/ lit. Then set the upstream concentration to 100% and close the upstream aerosol port.
vi. Once the 100% setting are established at the upstream sides turn the instrument knob to downstream. Keep the scanning probe one inch below the HEPA filter face, and start scanning the HEPA filter face area and fitment of HEPA filter with frame, the speed of scanning of probe shall be NMT 5 cm/sec.
vii. If any leak is observed then assure that the leakage is coming through the fitment part or HEPA filter itself.

viii. If fitment leakage is there, tightening the HEPA filter fitment with pressure plate and it can arrest the leakage. If not arrested then apply silicon sealant to mounting joint. If leakage observed through filter face, the same can be arrested by applying silicon sealant, but the leakage filter face should not be exceeds 5% of the total filter face. If the leakage area is more than 5% of the total area than replace the filter with ne filter as per new SOP.

ix. After completion of activity fix the grill properly to HEPA boxes.

x. The results shall be recorded in respective report.

5.2.4. Acceptance Criteria:

Leakage should be NMT 0.01%.

5.2.5. Evaluation of result:

i. Results, complying with the acceptance criteria, shall establish the leak of the HEPA filter is acceptable. If any leakage is observed from the mounting, it has to be rectified through, adjustment and application of silicone sealant.

ii. Any leakage greater than 0.01% of the upstream challenge aerosol concentration is considered unacceptable and wants replacement.

iii. If the sealed area is more than 5% of the filter face area /or any individual sealed area is more than 1 in a filter shall be replaced with new one as per the define procedure and qualify the same after replacement of filter.

5.3. Air borne non-viable particle monitoring:

5.3.1. Objective:

To establish that at different locations within the core process areas, a count of less than specified number of particles per cubic meter of air of 0.5μm or larger is maintained.

5.3.2. Instruments:

Laser particle counter

5.3.3. Procedure:

AHU shall be in continuous operation for at least 15 minutes prior to performing this test. Keep the particle counter ON. Set the particle size channel at 0.5 micron and 5.0 micron. The volume sample at each location shall be at least 2, 10 liters, with a minimum sampling time of 1 min for grade D and Grade C area respectively at each predefined location. Select the location number and room ID in particle counter and set it for pre-defined sampling time then keep the isokinetic probe at working height in the area at predefined location and start the particle counter for taking the particle count, particle count should be done in static condition. Particle count shall be taken at all pre-defined locations number of location shall be calculated by following formula *(as per ISO 14644-1).*

- Location of particle counts will be based on where the maximum numbers of Non-Viable Particle Counts are getting highest on specified area such as near riser, equipment positioned man movement and near entry & exit door.
- Calculate the number of sampling point location as per table given below:

Area of cleanroom (m^2) less than or equal to	Min No. of sampling locations to be tested (N_L)	Area of cleanroom (m^2) less than or equal to	Min No. of sampling locations to be tested (N_L)
2	1	76	15
4	2	104	16
6	3	107	17
8	4	116	18
10	5	148	19
24	6	156	20

28	7	192	21
32	8	232	22
36	9	267	23
52	10	352	24
56	11	436	25
64	12	636	26
68	12	1000	27
72	14	>1000	$N_L = 27 \times (A/1000)$

NOTE 1: If the considered area falls between two values in the table, the greater of the two should be selected.
NOTE 2: In the case of unidirectional airflow, the area may be considered as the cross section of the moving air perpendicular to the direction of the airflow. In all other cases the area may be considered as the horizontal plan area of the cleanroom or clean zone.

$$N_L = 27 \times (\frac{A}{1000})$$

N_L : is the minimum number of sampling locations to be evaluated, rounded up to the next whole number
A : is the area of the cleanroom in m^2

5.3.4. Establishment of single sample volume and sampling time per location:

At each sampling location, sample a volume of air sufficient to detect a minimum of 20 particles if the particle concentration for the largest selected particle size were at the class limit for the designated ISO Class.

$$V_S = 1000 \times (\frac{20}{C_{n,m}})$$

V_S : is the minimum single sample volume per location
$C_{n,m}$: is the class limit (number of particles per cubic metre) for the largest considered particle size specified for the relevant class
20 : is the number of particles that could be counted if the particle concentration were at the class limit

5.3.4 Acceptance Criteria:

Grade	At Rest		At Operation	
	Maximum number of permitted particles per cubic meter equal to or above			
	≥ 0.5 μm	≥ 5.0 μm	≥ 0.5 μm	≥ 5.0 μm
A	3500	0	3500	0
B	3500	0	350000	2000
C	350000	2000	3500000	20000
D	3500000	20000	Not Define	Not Define

As per Revised Schedule M of Drug and Cosmetic Act

5.4. Recovery test:

5.4.1. Objective:

To determine whether the core process area is capable of returning to its reference specified class within a finite time.

5.4.2. Instruments:

Laser particle counter, Aerosol generator

5.4.3. Procedure:

i. Take the initial reading of the area (at working height) for enumeration of particles of > 0.5 μ and 5.0 μ particles.
ii. Generates the particles in the area with the help of aerosol generator, start the particle count monitoring until the particles shall reach more than the specified class.
iii. Stop generating particles through aerosol generator once the area reaches to more than approx. 100 times of specified class/initial count.
iv. Take the sample at an interval of 1 minutes and it shall be continued till the desired level of cleanliness (approx. initial particle count reading or class limit) is achieve.

5.4.4. Acceptance Criteria:

The Recovery time (or decontamination time) shall be not more than 15 minutes.

5.5. Smoke test (air flow direction):

5.5.1. Objective:

To visualize airflow pattern of process area operation and to prove that there is no cross contamination from one area to the other.

5.5.2. Instruments:

Camera to record the airflow pattern of smoke generator

5.5.3. Procedure:

i. Take solution of Poly Glycol and water or purified water in fogger machine for generating the smoke.
ii. After generating, Smoke flow from supply filter to return riser and high to low pressure w.r.t adjacent room.
iii. Use video camera for recording the flow of smoke.

5.5.4.. Acceptance Criteria:

The flow of air from the filter shall sweep the area and shall be towards return air point. Photography / videography shall be performed for testing airflow pattern. Airflow pattern shall be from positive to negative differential pressure area.

5.6. Pressure differential, temperature and relative humidity test:

5.6.1. Objective:

To demonstrate the capability of the HVAC System to consistently maintain Differential Pressures (DP), Temperatures and Relative Humidity in different rooms.

5.6.2. Instruments:

Magnehelic Gauge, Thermometers and Hygrometers

5.6.3. Procedure:

i. Ensure that the Thermo hygrometer, Differential Digital Pressure Gauges or digital gauges are calibrated.
ii. Record the Temperature, RH and Differential Pressure shall be monitored at every 04 hours of interval.

5.6.4. Acceptance Criteria:

The system shall be capable of maintaining a Temperature, RH and Differential Pressure as per specified limits (like Temperature: NMT 27°C, RH: NMT 60% and DP: -5 to -30 Pascal).

5.7. Air borne viable particle monitoring by settle plate (Passive Air Sampling):

5.7.1. Objective:

To determine the viable particle levels in environment of controlled area by settle plate.

5.7.2. Instruments:

Media plates

5.7.3. Procedure:

i. Test shall be performed at operation condition by the microbiologist.
ii. Prepare the SCDA and SCA plate and enter in to the respective area as per Entry and Exit procedure.
iii. Expose the plates at various locations as per the settle plate location layout.
iv. The plate exposure shall be carried out for the controlled area for three consecutive days after taking the particle count.
v. After completion of plate exposure, SCDA Plate incubate at 30-35°C for 48 hours and SCA plate incubate at 20-25°C for 5 days.
vi. After incubation observe the results and record in the data sheet.

5.7.4. Acceptance Criteria:

Plates	***Alert Limit***	***Action Limit***
Total Bacterial Count	NMT 60 CFU/Plate	NMT 60 CFU/Plate
Total Fungal Count	< 1 CFU/Plate	< 1 CFU/Plate

5.8. Air borne viable particle monitoring by air sample (Active Air Sampling):

5.8.1. Objective:

To determine the viable particle levels in environment of controlled area by Air Sampler

5.8.2. Instruments:

Air Sampler

5.8.3. Procedure:

i. Test shall be performed at operation condition by the microbiologist.
ii. Prepare the SCDA plate and enter in to the respective area as per Entry and Exit procedure.
iii. Place the SCDA plate on air sampler and operate the air sampler as per SOP.
iv. Take sampling volume 1000 liter of air as per sampling plan.
v. After completion of sampling incubate the SCDA plate at 20-25^{o}C for 72 hours and further transfer at 30-35^{o}C for 48 hours.
vi. After incubation observe the results and record in the test data sheet.

5.8.4. Acceptance Criteria:

Area (Grade)	*Limit (CFU/M^3)*	*Alert Limit*	*Action Limit*
A	<1	<1	<1
B	10	6	8
C	100	60	80
D	200	120	160

5.9 Measurement of sound level:

5.9.1. Objective:

To verify the sound level in different rooms

5.9.2. Instruments:

Calibrated Sound Level meter

5.9.3. Procedure:

Operate the sound level meter as per the SOP. Measure the sound level when there is activity in the areas and record the in test data sheet.

5.9.4. Acceptance Criteria:

Not more than 80 db.

6. Conclusion:

Qualification of HVAC system has been carried out as per approved qualification plan. All the equipments and instruments used for the testing of the performance qualification are calibrated qualified. On assessment of data it was found that uniformity is observed. It can be concluded that obtained values found meeting the acceptance criteria specified in the plan. Based on the results of qualification data for HVAC system, it is concluded that system consistently producing air are meeting its predetermined specifications and quality attributes. Hence the HVAC system is considered to be qualified and can be routinely used.