Environmental Monitoring Based On IOT

The Purpose of an Environmental Monitoring Program

The CGMP (current good manufacturing practise) notes states that the purpose is to:

1.Provides crucial information on the quality of the aseptic processing environment during manufacturing.

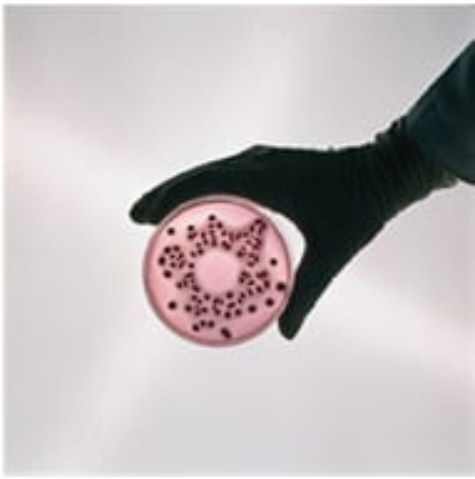
2.Prevents the release of potentially contaminated batch if appropriate standards are not fulfilled.

3.Prevents future contamination by detecting adverse trends.

Microbial Monitoring is a program designed to demonstrate the control of viable (living microorganisms) and non-viable particles in critical areas.

These areas include clean-rooms for drug fill/finish, operating rooms formulation tank rooms, laminar flow hoods, biological safety hoods, isolators, Intravenous (IV) compounding areas and sterile packaging.

•**Viable monitoring -**Testing for the detection and enumeration of bacteria, yeast and mold. It includes the monitoring of personnel, air and area surfaces for microbial contamination.



•**Non-viable monitoring** –A reference for particle counts measured by a laser counter.

Environmental monitoring describes the processes and activities that need to take place to characterise and monitor the quality of the environment.

Environmental monitoring is a surveillance system for microbiological control of clean rooms and other controlled environments.

It is a process which provides monitoring, testing and feedback to the microbiological quality levels in aseptic environments.

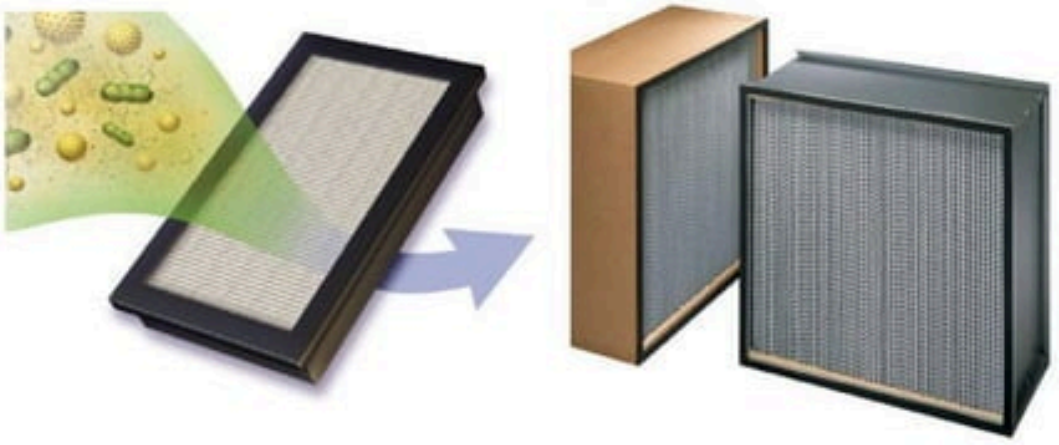
Sources of contamination : can come from air, personnel, equipment, cleaning agents, containers, water and compressed gases amongst other things.

Sound monitoring required understanding the various stringent regulatory specifications by various organizations such as the Food and Drug Administration (FDA), International Standards Organization (ISO), Parenteral Drug Associates (PDA), European Union (EU) and United States Pharmacopeia (USP).

What is a HEPA Filter????

HEPA filter: High Efficiency Particulate Air filter

Class of air filters which meet a minimum performance level of 99.97% on 0.3 microns efficiency. In the clean room market HEPA is normally rated at 99.99% and an additional face scan test is performed to assure no pin holes or leaks are found.



Monitoring Criteria

- Daily Monitoring: (Micro Area-LAF/UV Passbox /Room)
- Monthly Monitoring: (MFG Area/Equipments/Drain Points)
- Quarterly Monitoring: (Compressed Air)
- Half Yearly Monitoring: (Operators/Personnel Hygiene monitoring)
- Yearly Monitoring: (HVAC/AHU System Validations)
- Occasional Monitoring: (As and When required-During Technical issues with filters/ on maintenance/Filter change)

Specimens to be covered

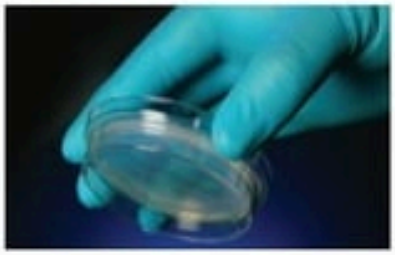
1. **Air** (For Both viable & Non-viable & compressed air)
2. **Surfaces** (Floors, Walls, Equipment, etc.)
3. **Personnel** (Operators/Working personnel's)
4. **Drains** (In the MFG Areas)

Air Quality

Air Sampling

- **Passive Air Sampling (Plate Exposure)**
  - Open pre-incubated media plates (90mm) keep exposed for 4 hrs
- **Active Air Sampling (Volumetric)**
  - For a known Qty (1000L) of Air/cubic meter

Surface monitoring in a Clean Room



Surface monitoring

By contact plates (RODAC)

By Swab sampling

55 mm Plates to be fixed on a flat surface

Swabs are rubbed over the test surface & tested for microbial contamination.

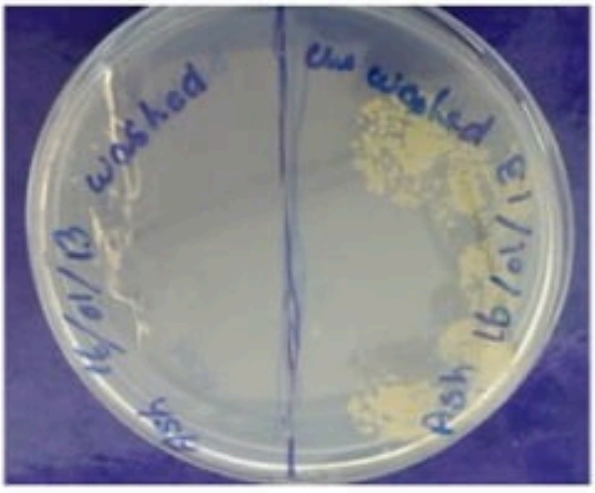
Swabs are used for the surfaces that are not flat

Personnel Monitoring

Once in 6 months

-By Contact plates (Finger Dab Testing)

-By Swabs Near mouth,
Arm pits,Tips of finger & palm (with gloves),
Upper Surface of footwear

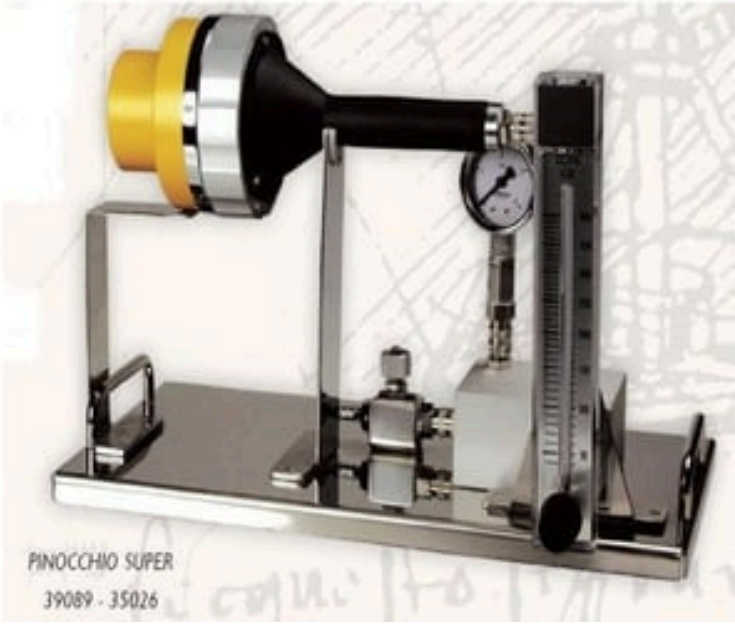


Drain monitoring

-By swabs
-Monthly to cover all the critical / non critical drains

Compressed Air monitoring

55mm RODAC plates
Drawing of 1000L of Air
Quarterly



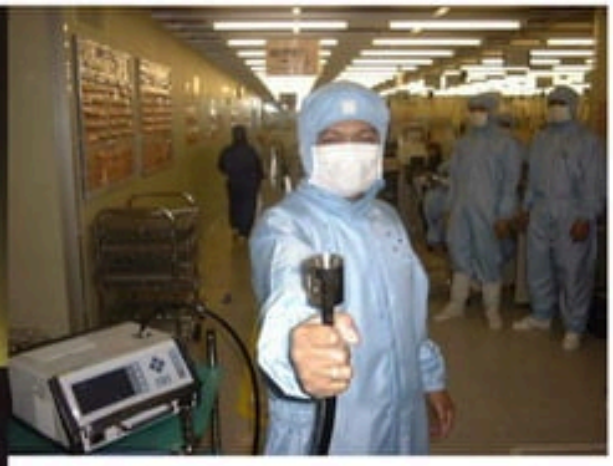
Particle Counting

Useful in detecting significant deviations in air cleanliness from qualified processing classifications.

Immediate understanding of air quality can be realized.

Useful as a tool for qualification and monitoring before /during and after operations.

Used To Identify Sensitive Locations For Continuous Monitoring.



HVAC Validation

HVAC; Heating, Ventilation and Air conditioning

-Yearly by external party

Parameters:

1.Temperature
2.Air velocity
3.Air Changes
4.Filter integrity
5.Non-viable air borne particles
6.Viable air borne particles

HVAC Validation

Parameters

1.Temperature/RH/PD

Check the Temperature of the rooms with calibrated thermometer (For Temp)/ Hygrometer (For RH) and record every two hours (5 readings per day) consecutively for three days.

Acceptance Criteria:

- **The temperature** should be within 23° ± 2°C
- **The relative humidity** should be within 45 ± 5% and the low RH should be within 20 ± 5%.
- **The pressure differential** in the area should be more than 10 Pascal across the room.

HVAC Validation

2. Air velocity

Check the air velocity at the four corners & center of HEPA filter-using anemometer. Calculate the average velocity of filter

Acceptance Criteria:

Average velocity should be 90 feet/minute ± 20%. (0.45m/sec)

3. Air Changes

Calculate the number of air changes per hour in the area using the formula:

$$\frac{\text{Average Air velocity (ft/min)} \times \text{Area of the filter (Sq.ft)} \times 60}{\text{Volume of the room (Cu.ft)}}$$

Acceptance Criteria: 20 air changes/hr

4. Filter integrity

For the efficiency of HEPA

Acceptance Criteria: The efficiency of all the terminal HEPA filters should not be less than 99.97%

HVAC Validation….!!

Anemometer

Filter integrity

HVAC Validation

5. Non-viable Airborne particle Count:

Derive the minimum number of sampling point locations (NL) from the following equation.

NL = √A

A = Area of clean room in square meters.

Check the particle counts in the locations using a calibrated particle counter.

EX: For Secondary gowning- NL is 02,
Where as in Blister Pkg room, NL is 05

Acceptance Criteria: For Class 100,000
Particles of ≥0.5µ should not be more than 3520000
Particles of ≥1.0µ should not be more than 832000
Particles of ≥5.0µ should not be more than 29300 per Cubic Meter of air.

Acceptance Criteria: For Class 100
Particles of ≥0.5µ should not be more than 3520
Particles of ≥1.0µ should not be more than 832
Particles of ≥5.0µ should not be more than 29 per Cubic Meter of air.

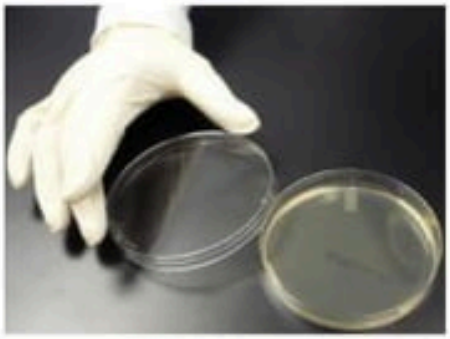
Clean room classification based on airborne particulates

Grade	At Rest		In Operation	
	Max. permitted particles / m^3		Max. permitted particles / m^3	
	≥ 0.5 µm	≥ 0.5 µm	≥ 0.5 µm	≥ 0.5 µm
A	3,520	20	3,520	20
B	3,520	29	352,000	2,900
C	352,000	2,900	3,520,000	29,000
D	3,520,000	29,000	Not defined	Not defined

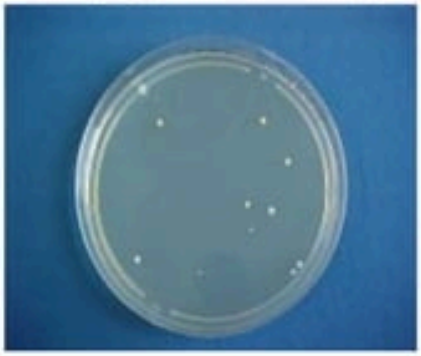
HVAC Validation

Airborne particle Counter

SAS(super air sampler)



Settle plate method



Exposed plate after incubation

HVAC Validation

6. Viable Airborne particles:

-After the HVAC Validation

-By Settle plate method & Volumetric Air sampling

LIMITS:

Test	Alert Limit	Action Limit
Settle Plate Exposure (CFU/90mmPlate/4 Hrs)		
Under Dispensing and Sampling Booth	NMT 1	NMT 1
Other locations	NMT 75	NMT 100
Active Air Sampling (CFU/Cubic Meter of air)		
Under Dispensing and Sampling Booth	NMT 3	NMT 5
Other locations	NMT 100	NMT 200
Surface Monitoring (CFU/55 mm Plate)		
Surface of Dispensing and Sampling Booth	NMT 10	NMT 25
Other locations	NMT 25	NMT 50

Actions

Alert Limit: (Non Pathogen)

If microbial count exceeds the alert limit in environmental monitoring inform the same to Quality Assurance, Production head and continue monitoring on next day.

If the contaminant levels are seen consistent or increase, advise to increase the frequency of cleaning.

Monitor the area frequently till the environment count comes below alert limit. During this period production activity will be continued.

Action Limit: (Non Pathogen)

If microbial count exceeds the action limit in environmental monitoring stop all production activity of particular area and carry out the investigation. Quarantine all the products which are manufactured during that period.

Recheck the bioload of all products, which were manufactured during the last two weeks by drawing extra samples in order to evaluate the effect on product.

Actions

Pathogen:

If pathogen is found in monitoring, inform the same to Quality Assurance, Production head and stop all production activity of particular area and carry out the investigation. Quarantine all the products which are manufactured during that period.

Recheck the bioload of all products, which were manufactured during the last two weeks by drawing extra samples in order to evaluate the effect on product.

Proactive action:

Clean/Sanitize the Manufacturing facilities as per Standard operating Procedure.

Airborne Particulate Cleanliness Class Comparison

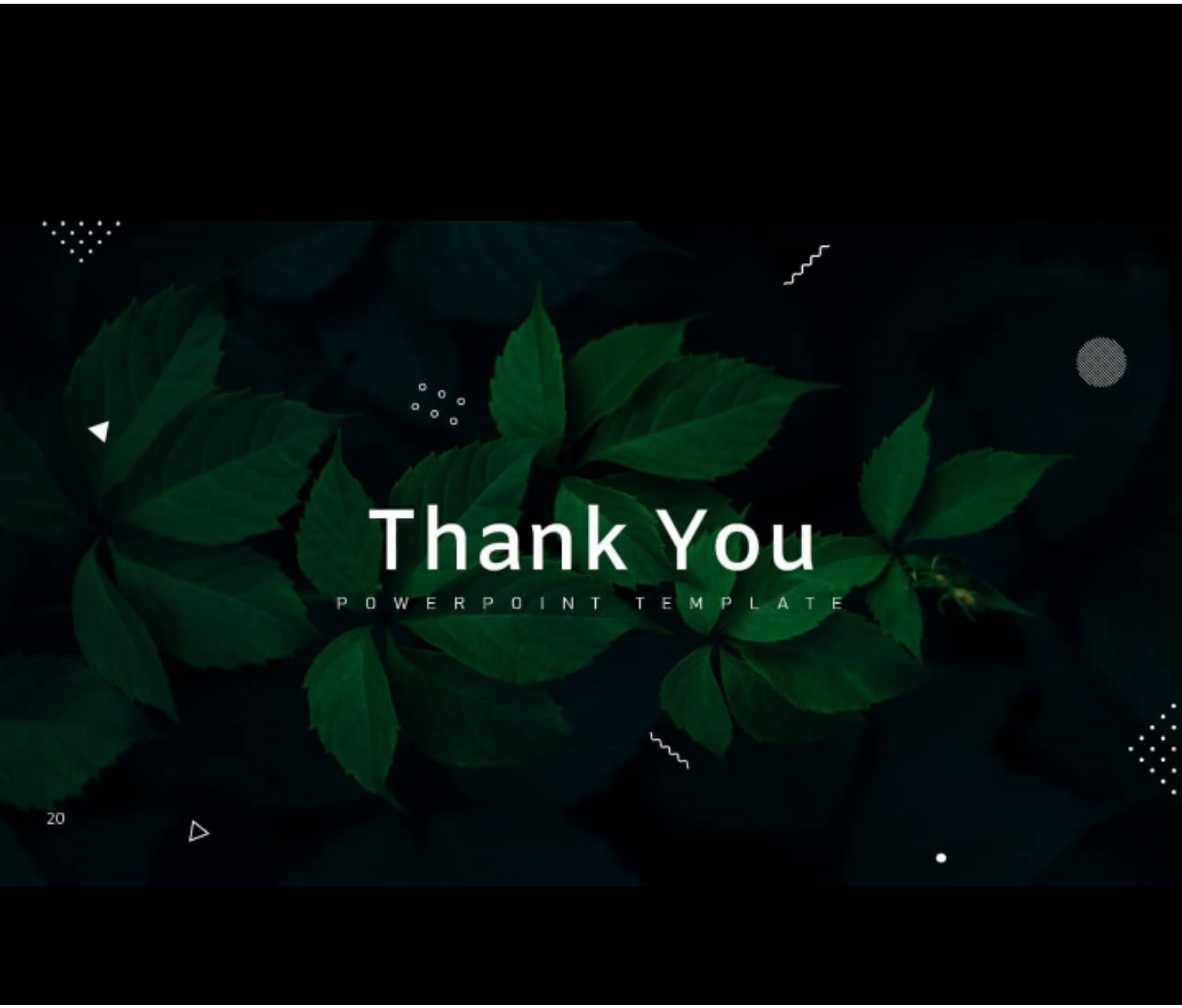
ISO 14644	FEDERAL STANDARD 209E		EU
ISO Class	E	M	Class
ISO 1			
ISO 2			
ISO 3	1	M1.5	
ISO 4	10	M2.5	
ISO 5	**100**	**M3.5**	**Grade A**
ISO 6	1,000	M4.5	**Grade B**
ISO 7	10,000	M5.5	
ISO 8	**100,000**	**M6.5**	**Grade C**

Airborne Particulate Cleanliness Classes:

CLASS	Number of Particles per Cubic Meter by Micrometer Size					
	0.1 micron	0.2 micron	0.3 micron	0.5 micron	1 micron	5 microns
ISO1	10	2				
ISO2	100	24	10	4		
ISO3	1,000	237	102	35	8	
ISO4	10,000	2,370	1,020	352	83	
ISO5	100,000	23,700	10,200	3,520	832	29
ISO6	1,000,000	237,000	102,000	35,200	8,320	293
ISO7				352,000	83,200	2,930
ISO8				3,520,000	832,000	29,300

ISO Documents for Clean room facility

ISO Document	Title
ISO 14644-1	Classification of Air Cleanliness
ISO 14644-2	Cleanroom Testing for Compliance
ISO 14644-3	Methods for Evaluating and Measuring Cleanrooms and Associated Controlled Environments
ISO 14644-4	Cleanroom Design and Construction
ISO 14644-5	Cleanroom Operations
ISO 14644-6	Terms, Definitions and Units
ISO 14644-7	Enhanced Clean Devices
ISO 14644-8	Molecular Contamination
ISO 14698-1	Biocontamination: Control General Principles
ISO 14698-2	Biocontamination: Evaluation and Interpretation of Data
ISO 14698-3	Biocontamination: Methodology for Measuring Efficiency of Cleaning Inert Surfaces


Thank You
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