# Cleaning and Disinfection – Environmental Monitoring

Your Objectives:

At the end of the lesson, you should be able to recognise the environmental monitoring equipment.

While microorganisms in the manufacturing environment are common, it is important to keep them under control, especially during critical steps. In order to ensure that the environment where manufacturing occurs is clean, and that microorganisms in that environment remain within acceptable limits, Biogen performs regularly scheduled environmental and utility monitoring.

The 21 CFR states that drug manufacturing premises must be of a suitable size and design in such a way as to facilitate cleaning, maintenance and proper operations. Additionally, there should be control systems in place to prevent contamination during the course of aseptic operations, which includes a system for monitoring environmental conditions.

**Routine monitoring**

Routine monitoring provides data that are used to detect the possibility of a trend towards deterioration of the environment or utility over time. Conclusions based on the collected data assist in defining new procedures, refining existing procedures, determining equipment maintenance intervals and initiating further monitoring processes.

- **Static monitoring** is performed either after initial construction or modification or after sanitisation of a room. It is intended to establish the baseline conditions of the facility and focuses on the air system performance in the absence of routine activity within the room.
- **Dynamic monitoring** is performed during periods of routine use, when personnel and materials are present and when equipment is in operation. The results of dynamic monitoring are the basis for the establishment of **alert** and **action** levels.

During routine monitoring, the environment or the utility being monitored may occasionally fail to conform to expected results. Depending on the severity and duration of the excursion (deviation from an expected course), two different responses are defined:

- **Alert** level values are slightly outside the **tolerable** range of cleanliness. No intervention is required, but because this level may indicate potential problems, further observation is needed.

- **Action** level values, which include a series of alert level values, pertain to levels that are **outside of the adequate** range of cleanliness. Action level values quite simply require immediate investigation &/ intervention.

**Monitoring zones**

Clean areas at Biogen are classified according to (1) the extent of product exposure to environment, (2) the extent of personnel gowning, and (3) the degree of asepsis required.

Biogen also uses a multiple zone approach, whereby more than one zone in an area is monitored. The monitoring frequency, as well as particulate and microbial limits, differ in each zone. Separate protocols and procedures are specified for each operational area in the SOPs for monitoring specifics for a given area.

**Types of monitoring:**

**Utility monitoring**

Utilities typically include a production/generation element and a distribution system. Utilities at Biogen include, but are not limited to, the following:

- Purified water system
- WFI system
- Clean steam system
- Glycol system
- Heating, ventilation and air-conditioning system (HVAC)

These systems are monitored on a rotating schedule delineated for each system.

**Water monitoring**

According to the USP (U.S. Pharmacopeia), organic molecules and other contaminants can be introduced into the water system either from source water or from purification & distribution system materials.

Routine monitoring of WFI and purified water at Biogen includes collection of samples on which TOC testing is performed.

Total organic carbon (TOC) is a testing procedure that measures the total organic material present in a sample. TOC provides a useful way of measuring the purity of water. TOC sampling

is a sensitive process. So, for example, for TOC sampling, one does not sanitise either gloves or sampling containers with 70% alcohol, since alcohol is an organic compound; any alcohol residue, therefore, would impart a positive TOC reading.

Specially cleaned TOC vials are used to collect 40-millilitre samples. These vials must be carefully handled so that the sample is not compromised. One must follow proper TOC sampling and documentation procedures described in the SOPs.

**Viable air sampling**

Biogen uses several different devices for air sampling. Technicians typically use a hand-held battery-powered **air sampler**. That device is cleaned with a 70% alcohol solution prior to sampling.

The operator places **contact plates** into the retaining slots in the air sampler, aspirates the specified volume of air, typically 320 litres. Trypticase Soy Agar (TSA) plates are used for routine sampling. Sabouraud Dextrose Agar (SDA) plates are used for yeast and mold sampling.

The plates are removed and sent to QC (Quality Control), where they are placed into an incubator. After incubation, QC counts the number of colonies that appear on the agar surface. Results are compared with alert levels to determine if any level of contamination has been exceeded.

Please follow air sampling and documentation procedures described in the SOPs.

**Particulate air sampling**

Particulates consist of mobile, extraneous substances, other than gas, that cannot be analysed chemically because of their heterogeneous composition.

Air particulate samplers collect particulates on a filter, which can then be analysed for its constituents. Results are compared with alert levels so as to determine if any level has been exceeded.

One will have to follow air sampling and documentation procedures described in the SOPs.

**Settling plates**

Settling plates contain trypticase soy agar (TSA). They are typically used to monitor surfaces in horizontal laminar airflow workstations, bio-safety cabinets, or other clean room surfaces while operations are being performed.

The room temperature plates are placed face down on the area surface. Maximum exposure time is 1 hour per plate. At the conclusion of the operation or the end time, the plate is covered and sent to QC, where it is incubated. After the incubation period, QC determines whether the number of bacterial colonies is within appropriate limits.

One must always follow proper sampling and documentation procedures described in the SOPs.

**Viable surface-monitoring**

Replicate Organism Detection and Counting (RODAC) plates are used to monitor both personnel and surfaces.

TSA plates are used for routine surface and personnel monitoring.

Sabouraud Dextrose Agar (SDA) plates are used for yeast and mold sampling.

The agar in the room temperature plates is pressed against the test site surface and removed. The plate is covered and sent to QC where it is incubated. After the incubation period, QC determines if the number of bacterial, mold, or yeast colonies is within appropriate limits.

One need follow the proper sampling and documentation procedures described in the SOPs.

**Personnel monitoring**

Personnel monitoring is done at the asepsis of critical operations, which is performed in horizontal laminar airflow workstations or bio-safety cabinets.

The operator's gloved fingertips are placed on the room-temperature TSA plate. The plate is covered and sent to QC where it is incubated. After the incubation period, QC determines if the number of bacterial colonies is within appropriate limits.

One is required to follow proper sampling and documentation procedures described in the SOPs.

video: https://youtu.be/F9K8DAupOFg

**Toxic gas monitoring**

At Biogen, toxic gas monitoring typically occurs in:

- Cold rooms, where asphyxiant gases are used and where there is a potential for oxygen deficiency,
- Enclosed areas where cryogenic liquids are stored,
- Areas where chillers are located and where there is a potential for a refrigerant leak.

Personnel that work in areas where continuous gas monitors are installed must be trained, by their supervisor, to recognise the fault, to caution, warn, and alarm conditions associated with the gas-monitoring equipment.