MediZap

Advanced Sterilization

Bioburden & Sterilization Validation Of Pharmaceuticals

Ensuring products are contaminant-free is necessary for patient safety and drug efficacy, as contamination causes adverse effects on patient health and outcomes. Additionally, contamination can alter the pharmacology of drugs, with negative effects on efficacy due to the decomposition of ingredients, as well as safety issues due to toxicity.

Eliminating Bioburden Through Sterilization

Attribute	Sterile Drugs	Non-Sterile Drugs
Manufacture	Terminally sterilized aseptically manufactured	Controlled environment
Environmental Monitoring (EM)	Stringent requirement class 100 clean rooms	Expectations for EM No classified clean rooms
Critical test to control microbes	Sterility (Absence of bacteria, yeast, Fungi)	Bioburden (case by case limits for aerobic bacteria and fungi) absence of objectionable organisms
Microbial quality	Tested for absence of aerobic and anaerobic bacteria, yeast and fungi	Enumeration of aerobic bacteria, yeast and fungi; Not tested for anaerobic bacteria, tested for objectionable organisms
Applications	Parenteral injections, applied to sensitive tissues	Topical

For many sterile drugs, microbes are eliminated through a terminal sterilization process, including either heat or radiation. Ensuring the absence of contaminants such as bacteria or fungus requires validation by sterility testing for sterile drugs, and manufacturing process controls are used to ensure consistency.

Terminally sterilized drugs that use bioburden-based cycles require control testing to ensure the microbial load was sterile beyond the range setup for the procedure. Proper controls should always be in place whenever the process is bioburden-based or based on an overkill approach.

The recommended level of microorganisms is 10CFU/100mL. If the mass of microorganisms surpasses this point, it is sensible to ask and to determine where the microorganisms are coming from. Given that many raw materials come from non-synthetic sources, there may be an unavoidable number of microorganisms in the product, and other testing would be needed to ensure sterility.

Building Microbiological Quality Into Drugs

Microbiological quality should always be at the forefront of pharmaceutical quality assurance. Ensuring that products undergo extensive environmental monitoring and proper bioburden testing at different stages of the manufacturing process, including as their final drug component and as they are being packaged, is fundamental. Environmental monitoring is an essential way to exhibit sterility control and provide a proper testing environment. The quality of sterile drugs is critical and can be assured through appropriate controls.

Available Types Of Sterility Testing

A variety of means are available to test for sterility. These include:

Test	Incubation time
Total aerobic microbial count	3-5 days
Total yeast and mold count	5-7 days
Sterility tests	14-21 days
Absence of specified microorganisms tests	18-72 hrs
Limulus amebocyte lysate endotoxin tests	1 hr
Microbial identification, phenotypic	3-5 days
Microbial identification, genotypic	1 day

- **Immersion/Direct Inoculation:** A type of test performed by directly inoculating the sample into different kinds of media that allow for the growth and development of aerobic and anaerobic bacteria. Fungi can also be detected. Only a small sample volume is required, and it can be replicated quite easily.
- **Membrane Filtration:** Bulk articles from the vials of the final product are passed through a membrane filter. These filters are then rinsed to remove inhibitors and incubated in the same fashion as the inoculation method. Large sample volumes can be tested this way.
- **Direct Transfer:** This process immerses various pharmaceutical agents in growth media to test for bacteriostatic and fungistatic activity. Detection is performed similarly to direct inoculation after a 14-day cycle. However, this process also requires that a bioburden identification assay be performed subsequently.