

# How to avoid test of sterility positives in radiation dose audits and what to do when it happens to you



Navigating Sterility Failures in Radiation Sterilization Dose Audits: Ideas on Navigating the Inevitable

Imagine the painstaking efforts that go into developing a life-saving device, only to have it compromised by a radiation dose audit test of sterility positive. Unfortunately, such incidents do happen when conducting dose audits for the validation and maintenance of radiation sterilization processes. Maintenance of the dose typically includes quarterly dose audits where devices are subjected to a test of sterility in accordance with the international radiation sterilization standards (e.g. ISO 11137 series and ANSI/AAMI/ISO TIR13004). Whether it's a contamination issue during manufacturing or a test laboratory breach in aseptic techniques, the consequences can be time consuming and costly to determine the root cause. This article delves into practical measures to potentially reduce the event of a dose audit failure, while also providing actionable steps to take should you find yourself facing this situation.

## Test of Sterility for Maintaining Radiation Sterilization Dose

Dose audit sterility testing is a quality control measure to validate the effectiveness of a sterilization method. This test involves subjecting samples of medical devices to suitable culture media and an incubation period to detect the presence of viable microorganisms. By carefully monitoring the results, companies can ensure that the radiation sterilization dose is precisely calibrated to eliminate harmful microbes without compromising the integrity and functionality of the medical device. The absence of microbial growth is a confirmation that the medical device is sterile and meets the required regulatory standards.

## Getting To The Root Cause of Dose Audit Failures

Dose audit failures can stem from various causes, and identifying and understanding the root cause of such an event is crucial to prevent repeated occurrences. Common causes of sterility test positives include human error, equipment malfunction, environmental contamination, and procedural lapses. We provide some examples for each below:

### Human Error

Improper aseptic technique, inadequate training, or negligence, can introduce contaminants during the manufacturing process.

### Equipment Malfunction

A breach in the integrity of sterilization systems (i.e., autoclaves) or faulty HEPA filters can compromise sterility.

### **Environmental Contamination**

Air or surface contamination in cleanrooms can introduce microorganisms into the product.

### **Procedural Lapses**

Inadequate cleaning or improper handling of materials can also contribute to dose audit failures.

In addition to the common causes described above, there are some less common factors that can contribute to dose audit failures. These include:

### **Inadequate Facility Design**

Poorly designed facilities that do not effectively control airflow, minimize cross-contamination, or provide adequate segregation of processing areas are at high risk of failing sterility.

### **Inadequate Container Closure Integrity**

Defects or compromised integrity of container closures, such as seals, stoppers, or caps, can allow microbial ingress into the product.

### **Raw Material Contamination**

Contaminated raw materials or packaging components can introduce microorganisms into the manufacturing process.

### **Insufficient Process Validation**

Inadequate validation of critical processes, such as sterilization methods or aseptic techniques, can lead to dose audit failures if the processes are not properly optimized and validated.

### **Supply Chain Issues**

Problems within the supply chain, such as improper storage, or transportation under inappropriate conditions can compromise sterility after product release.

Typically getting to the root cause of a dose audit failure requires identifying the contaminating microorganism(s). Some microbes are commensal to human skin and these failures can be traced down to personnel error. Other microbes are more challenging to assign an isolated root cause. Resistant-to-dose

microbes can compromise product sterility by withstanding harsh sterilization processes employed during manufacturing, such as heat, radiation, or chemical sterilization. Despite applying appropriate sterilization techniques, a small fraction of these resilient microbes may survive and remain viable in the final product.

Ultimately, a thorough root cause analysis is needed to determine the cause of dose audit failures.

## **Sterility Test Positives Are a Significant Challenge**

Sterilizing medical devices may seem like a straightforward task, but the reality is far more intricate and challenging, as the unique characteristics of these devices often present significant hurdles in achieving effective sterilization. Sterilizing a medical device is especially challenging for these key reasons:

### **Device Complexity**

Some devices have intricate components or hard to reach areas that make complete sterilization difficult to accomplish.

### **Material Compatibility**

Medical devices are composed of a wide range of materials, including metals, plastics, rubber, and electronics. Some materials may be sensitive to certain sterilization methods, leading to potential device damage or degradation. Finding a sterilization method that effectively kills microorganisms without compromising the device's integrity can be a complex task.

To overcome these challenges, manufacturers must carefully select appropriate sterilization methods based on device design.

## **Responding to a Sterility Test Positive**

If you are facing a dose audit failure, you need prompt action by quality personnel to address the issue and determine the impact..

First and foremost, you must **document and record the**

**details of the incident.** This includes a record of the date, time, and location of the discovery, the specific batch/lot information, the product description, and the sterility test results. Immediately, the test laboratory should identify the microorganism to aid in the investigation and potential sources of the microorganisms isolated.

Consult with internal experts, including quality assurance, regulatory affairs, and medical professionals to **assess the impact** of the dose audit failure on patient safety. Factors to consider here are the intended use of the device and the severity of the potential consequences should a non-sterile product reach the consumer.

It is critical to **initiate an investigation to determine the root cause** beginning at the time of the failure discovery. This may involve reviewing batch records, assessing package integrity, reviewing sterilization procedures, and analyzing quality control data such as microbial trends.

Communication about the incident is key as these investigations typically require interdepartmental involvement. It is important to **notify relevant parties** such as manufacturing supervisors and regulatory affairs that a dose audit failure has occurred.

Once a root cause is identified, it is pertinent that you **implement corrective and preventive actions** to ensure the dose audit failure won't be a repeated incident.

Remember to review and update procedures regularly to ensure the long-term effectiveness and reliability of your sterility assurance program.

## Strategies to Guard Against Dose Audit Failures

It is generally accepted that dose audit failures are a normal part of radiation sterilization, however, it is essential to implement several key practices. Begin by conducting regular audits of your manufacturing plant and your sterility testing lab to assess compliance with sterility requirements.

### Audit the Manufacturing Facility Cleanrooms

High risk devices typically require ISO Class 7 level cleanrooms for manufacturing. The cleanroom should be in conformance with the ISO cleanroom standards and include both viable and non-viable particulate monitoring of the cleanroom environment.

Here are some questions to ask when auditing your manufacturing facility:

- Does historical data for air and surface microbial levels reveal any trends or potential links to product contamination?
- Are non-sterile gloves worn and does the manufacturing process require extensive handling with non-sterile gloves? Non-sterile gloves can be a source of contamination during handling of the medical device.
- Has there been an increase in personnel in the cleanroom potentially increasing contamination? Review the associated cleanroom validation to assess requirements for the maximum number of personnel allowed in the room.
- What actions are required for out-of-specification environmental monitoring results?
- Are the cleaning and disinfection practices being used appropriate for the cleanroom level? Here it is important to assess the cleaning agents used and their frequency of application.

### Audit the Microbiology Lab

The environment in the sterility testing lab is also critical to ensuring the prevention of false positive results. The lab should have a cleanroom or Class 100 bench ("clean bench") to minimize airborne contaminants during sterility testing. It is typical for the clean bench to reside in an ISO Class 7 or ISO Class 8 cleanroom with strict gowning and entrance requirements that reduce the potential for contamination.

The following are questions to consider when auditing the Microbiology testing lab:

- What is the false positive rate for the laboratory?
- What measures are in place to prevent cross-contamination between samples, cultures, and laboratory equipment?
- How are the analysts trained and qualified to

handle microbiological testing?

- What validation procedures are in place for test methods used in microbiological analysis?
- What are the lab's procedures for media preparation, sterilization, and quality control?

### Revisit the Validation Plan

If a dose audit sterility test positive occurs, it may be linked to a rise in bioburden counts from the pre-sterilized state of the medical device. Manufacturers should revisit the original validation program and compare bioburden counts obtained during the dose audit with those from the initial validation. Should a significant increase in bioburden be identified, it may be necessary to initiate a new dose setting validation to ensure that the sterilization dose is adjusted to effectively eliminate the higher microbial load.

### Consider Validating an Alternative Sterilization Method

In cases where dose audit sterility positives persist despite optimizing the existing sterilization process, we recommend manufacturers to explore alternative sterilization methods. The most common industry methods include radiation, ethylene oxide gas and steam sterilization. By exploring alternative methods, manufacturers can diversify their sterilization strategies, further reducing the risk of dose audit failures and enhancing overall quality control.

### Summary

Addressing dose audit failures requires swift and decisive action to uphold patient safety and maintain product quality. By promptly documenting the incident and conducting a thorough investigation, you can identify the root cause and implement necessary corrective and preventive actions. Collaboration among multiple departments is crucial for an effective response to a dose audit failure. By adhering to these practices, your company can maintain a strong commitment to patient safety, quality management and regulatory compliance in the face of a dose audit

failure.

### About QA Consulting, Inc.

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By choosing QA Consulting, you gain access to a team of highly skilled professionals with deep expertise in testing methodologies, quality system development, and industry best practices, and gain a competitive edge in today's fast-paced and demanding market.

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