MediZap
Advanced Sterilization

Understanding How Contract Microbiology Laboratory Out-Of-Specification Results Are Handled and Resolved

What Does OOS Mean?

The Out-Of-Specification (OOS) process is an adjunct to microbiology testing at a contract research laboratory. For compounders, this can include research and development USP testing (e.g. potency, container closure), ISO 11137 irradiation sterilization validations, and compendial USP release testing (e.g. potency, sterility, endotoxin). The OOS process involves thoroughly investigating the results against defined parameters to ascertain whether the root cause is derived from the sample submission, the laboratory testing process (e.g. equipment, media), and/or personnel.

The first step in the OOS process is investigating the root cause(s). Every testing facility has its own system of handling OOS results. Contract research laboratories follow the FDA's guidance for the industry entitled "Investigating Out-Of-Specification (OOS) Test Results for Pharmaceutical Production." This involves reviewing the defined testing protocol to determine if any errors were made. The laboratory should also review its quality control procedures to ensure they are appropriate and working as intended. Once the cause of the OOS result has been identified, the laboratory should document the investigation and any corrective actions taken. This documentation should be included in the laboratory's records and should be made available to the client.

It is important to note that the OOS process is not just about identifying and correcting errors. It is also about identifying trends and improving to prevent future OOS results. Therefore, laboratories must track OOS results over time and use this data to improve their testing processes.
The laboratory should communicate any OOS results to the client promptly and transparently, including information on the cause of the OOS result and any corrective actions are taken. The client should also be informed of any changes made to the testing process or quality control procedures as a result of the OOS investigation.

In Phase One of the laboratory investigation, asses the initial data and determine if it was accurate. Did the microbiology research analyst who tested the sample make any human errors in the execution of the microbiology testing protocol? Were there any laboratory equipment malfunctions? Was the correct media used, and was it within its expiration date? This part of the investigation acts to eliminate errors by laboratory analyst, laboratory equipment, and growth media from the list of potential root causes of the OOS result. What are the possible outcomes?

- If the laboratory determines that a laboratory error may have occurred, your sample may be retested.
    - If your sample is retested, a different microbiology research analyst will perform the new test to rule out human error.
- If the laboratory investigation identifies a source of laboratory error in the initial test, the initial test results are invalidated, and the retest results are reported.
- If no clear laboratory error is identified, retesting will not be performed.
- If no testing error is found in the lab, and test results appear to be accurate, we move on to the second phase of the investigation.

Phase Two of an OOS investigation aims to identify the root cause of the OOS results so that proper corrective and preventive action can be taken. Within this phase, the compounded drug manufacturing production will be reviewed. Were the raw materials (APIs, Excipients) certificates of conformance reviewed and raw materials tested for potency as required by 503B designation? Were there any abnormalities in the environmental monitoring system at the time of compounding/manufacturing? Were the internal SOPs properly followed and documented by trained pharmacists and signed off by quality representatives? If sterilization is not done internally (terminal sterilization by irradiation is leveraged at an external contract sterilizer), then an OOS investigation must be requested separately.

As mentioned before, every contract research laboratory will have its own system for handling an OOS result. Additionally, an OOS investigation may be required for external terminal sterilization processes against a validated protocol and report. In the FDA guidance, Phase One is the microbiology laboratory investigation, and Phase Two is the full-scale investigation at the 503A compounding or 503B outsourcing facility in addition to contract terminal sterilization provider if applicable. For contract research laboratories, Phase One involves reviewing the test results and data to identify laboratory errors. If there are none, we can presume the results are valid, and the client can investigate on their site.

If laboratory errors are found, corrective actions are taken, and retesting of the samples is conducted. With so many factors, every investigation must be thorough, unbiased, scientifically sound, and well-documented. Having MediZap as the preferred choice for E-Beam | X-Ray terminal sterilization guarantees our commitment to do all the document 'heavy lifting' on your behalf, ensuring that any OOS or quality investigation conducted will be taken through our extensive process and resolved.