GatewayAnalytical
an Aptar pharma company

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CLIENT GOALS:

A biopharmaceutical manufacturing company needed to determine the container closure integrity of their drug product vials. Using positive and negative controls, laser head-space analysis would be conducted to validate a method to allow the client to submit finished product vials to assess the presence of a defect.

KEY OUTCOMES:

- Through data interpretation, a method was successfully validated to allow routine sample analysis submission.
- Through carbon dioxide headspace analysis, enough justifiable data was obtained in the experiment to support yielded results.
- Clear and concise communication was maintained throughout the duration of the experiment.
- Comprehensive reports, a validation plan, and test methods detailing the laboratory steps and methods for the obtained results of the analysis were provided.

CASE STUDY
CONTAINER CLOSURE INTEGRITY

EXECUTIVE SUMMARY

Container closure integrity testing (CCIT) is a part of the recommendations given by USP <1207> Packaging Integrity Evaluation – Sterile Products. The current revision of the chapter suggests that more deterministic methods are to be used over the destructive methods that have been used previously, such as blue dye methods or microbial ingress. Laser headspace analysis is a non-destructive analysis method that detects breaches in sample integrity. Carbon dioxide headspace analysis was utilized to identify the loss of integrity of the vials submitted by the client.

The client required a method to be validated that could analyze 36-month stability study samples stored at a deep cold storage temperature and pulled at various time points for analysis. Additionally, this client was looking for a lab capable of investigating potential breaches of CCI during the testing to assist in troubleshooting potential manufacturing or storage issues. Gateway requested all vial configuration raw materials and filled sample vials to assist in properly developing and validating the requested method. In return, Gateway created different sets of positive and negative controls that would be stored, conditioned, and tested over different periods to generate extensive data and create specific validation testing parameters.

Gateway Analytical's expertise involves two components for the proposed CCIT analyses — communication and data interpretation of the results obtained through carbon dioxide headspace testing. Sub-contract laboratories are leveraged to help create high-quality NIST traceable calibration standards and micron laser drilled controls utilized during analysis. Gateway maintains reliable communication with the sub-contract laboratories to keep the project on track and completed within the client's expectations.

Ultimately, Gateway Analytical successfully developed and validated a CCIT method that allows the client to submit samples for routine analysis and provides the client with detailed reports that summarize the preparation and analysis and includes data interpretation of the results yielded from the development and validation. Gateway has since been able to determine the integrity of the submitted samples from the customer based on the successful method validation.

THE CHALLENGES

The client had previously submitted samples to another laboratory for headspace analysis of their samples. This laboratory, however, is not Current Good Manufacturing Practices (cGMP) compliant. As a result, the client was referred to Gateway Analytical by this laboratory.

The client needed to recreate an environment similar to which their samples were being created and stored in order to evaluate any possible integrity loss of their samples. The client required proper communication throughout the experiment.

OUR APPROACH

Gateway Analytical performed method development and validation utilizing a carbon dioxide laser headspace detector. In this case, different sets of positive and negative control vials and frozen sample-filled vials were created and stored by Gateway in a deep cold storage environment. Additionally, reference standards and micron laser drilled controls provided by a sub-contract laboratory were utilized.

Two sets of positive controls were created from the submitted vials. One involved a gross defect and the other involved laser-drilled holes in the vials. The positive controls were expected to detect elevated carbon dioxide levels during sample analysis. Negative control vials were prepared to show the crimping process if the positive control vials were prepared and sealed correctly and were not expected to have any carbon dioxide detected. NIST traceable calibration standards show that the instrument functions properly for the vial configuration before any sample analysis through known values.

Next, the submitted sample vials, the two (2) positive control vials, and the negative control vials were all placed in deep cold storage, a carbon dioxide-enriched environment, for a total length of ten (10) days. Multiple measurements were taken on separate days to track the ingress of the carbon dioxide into the vial headspace. The presence/absence of carbon dioxide was determined via measurement of the amount of laser light absorbed while passing through the container. Gateway Analytical obtained all expected results for the positive and negative control vials, justifiable data that the client's submitted samples had not lost their integrity throughout the analysis.

Comprehensive reports, a full method validation plan, and a validated test method for routine analysis were submitted to the client, which detailed the experiment's preparation, analysis, and results.

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