

Front & Center

Particulates, Endotoxins, and Bioburden Characterization of Silicone Tubing for Biopharmaceutical Applications

Silicone tubing is widely used in biopharmaceutical manufacturing processes, especially in downstream processes after final sterile filtration and in fill finish operations where high purity is key. As a result, the quality, compendial and regulatory requirements for particulate, endotoxin, and bioburden content have become increasingly stringent for single-use components used for biopharma manufacturing.

“Biopharmaceutical players have increased requirements from suppliers for testing the purity of the single-use components to prove low contamination risk,” stated Dr. Pennadam Sivanand, MBA, Medical TS&D Manager, at Dow Medical Solutions, during a presentation delivered at CPhI Worldwide 2017 in Frankfurt, Germany. “And so, they expect us to provide testing data in support of their application’s final requirements.”

Sivanand explained how Dow Pharma Solutions has built strong experience in extractables testing on its Pharma tubing products. To ensure that its biopharmaceutical components meet and exceed customer and regulatory requirements, Dow expanded its validation testing documentation package



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to not only include extractables, but also cover all the required testing for particulates, endotoxins, and bioburden, per the industry standards.

“We are committed to help the biopharma industry in minimizing contamination risk from the supply chain,” said Sivanand, “So, we developed the most appropriate and stringent tubing-specific testing protocols to provide a supreme data package. We have tested the entire range of our Dow Corning Pharma Tubing product family.”

These tubing products were tested for endotoxins by Dow QC biolab in the United States and for particulates and bioburden by certified external laboratories in the United States and Europe, respectively. Studies were executed in multiple batches and in various sizes of tubing. “This provides a broad confidence in the data package we developed for our customers,” said Sivanand.

Particle Testing

The industry standard for testing sub-visible particulates is the *USP* <788> Particulate Matter in Injections. Dow selected the Method 2; Microscopic Particle Count Test, which counts solid particulates alone that pose high risk to patients if present in the final drug product and does not enumerate gas bubbles and liquid particulates such as silicone oil extractables droplets.

Dow protocol involved the extraction of particulates from internal tubing surfaces using particulate-free water that was filtered through a membrane that was then microscopically examined and the particles, if any, were enumerated. The Membrane Microscopy counts results show that solid particulate counts obtained on the

entire Dow Corning™ Pharma Tubing products were well below the *USP* <788> acceptance criteria (less than 12 particulates per mL for particulates $\geq 10 \mu\text{m}$ and less than 2 particulates per mL for particulates $\geq 25 \mu\text{m}$).

“If you look to the results obtained on our range of pharma tubing that has gone through this testing, the average particulates count $\geq 10 \mu\text{m}$ is <0.3 particulate/mL, and <0.15 particulate/mL for particulates $\geq 25 \mu\text{m}$. It is very evident that our tubing products pass with flying colors in terms of the subvisible particulates per *USP* criteria,” said Sivanand. “That gives our customers much confidence in the reliability of our tubing.”

More information on the *USP* <788> testing of Pharma tubing range is available. Please contact the Technical Service & Development, Dow Medical Solutions. Details of personal for EU & NA region respectively can be found at the end of this report.

Endotoxin Studies

Bacterial endotoxin content was tested using the limulus amoebocyte lysate (LAL) gel clot method described in *USP* <85> Bacterial Endotoxins Test. Endotoxin was extracted from the tubing with pyrogen-free water and the extract was exposed to the quantity of LAL reagent sensitive to 0.125 EU/mL endotoxin. If the extract does not cause clotting, the test article contains less than 0.125 EU/mL of endotoxins and the test article passes the test.

All the Pharma tubing products passed the Dow acceptance criteria of

less than 0.125 EU/mL. These results show that endotoxin content exceeds the very stringent limit of *USP* (as a comparison, the *USP* requirement for endotoxin in Water for Injection is less than 0.25 EU/mL and *USP* <161> Medical Devices—Bacterial Endotoxin and Pyrogen Tests have a limit of less than 20 EU per medical device or 2.15 EU/mL for medical devices that come in contact with the cerebrospinal fluid).

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“According to the *USP* method that we followed, we anticipate to have less than 0.25, but our products resulted with value well below the maximum limit. Hence again, this gives confidence to our customers and consumers that our tubing has got very high purity and high standards in the biopharmaceutical field,” stated Sivanand.

Bioburden Testing

The Pharma tubing products were tested for aerobic bacteria, yeast, molds and

spores using ISO 11737-1 “Sterilization of Medical Devices—Microbiological Methods—Part 1: Determination of a Population of Microorganisms on Products.” The removal method for these organisms was validated with a very high recovery efficiency. After filtration of the extract and incubation of the filter, the retained micro-organisms were counted. The results show that none of the micro-organisms were detected from the Pharma Tubing samples.

Conclusion

The test results clearly demonstrate that the entire range of Pharma tubing products has a minimal potential for particulates, endotoxins and bioburden contamination, and thus a high level of purity that is particularly sought for bioprocess components usage in aseptic manufacture of drug products. Based on over 60 years’ experience in Healthcare Tubing Materials Science, Dow offers testing protocol development and data packages that support its leadership in high-purity solutions and that accelerate the validation process of Dow Pharma tubing products for biopharmaceutical manufacturing.

More detailed information on the clean tubing is available from Technical Service & Development, Dow Medical Solutions:

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