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Purity testing protocols for silicone tubing

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Purity Testing Protocols for Silicone Tubing

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INTRODUCTION

Silicone tubing is widely used for fluid transfer in critical biopharmaceutical processes that require high-purity product-contact single-use components. For drug product safety, the risk for particulate, endotoxin and microorganism contaminations must be evaluated. The industry standards applied for purity testing were originally intended for drug product packaging and for medical devices; consequently, their implementation is not well-defined for single-use components and systems. In this poster presentation, we describe the developmental work completed for sample preparation and implementation of the protocols for the ISO and USP tests.

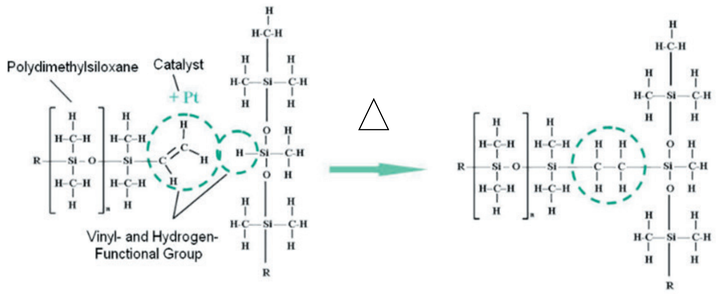
TESTED PRODUCTS

Tubing Type	Durometer Shore A
DOW CORNING™ Pharma-50 Tubing	50
DOW CORNING™ Pharma-65 Tubing	65
DOW CORNING™ Pharma-80 Tubing	80
DOW CORNING™ Pharma-Advanced Pump Tubing	50

Tubing sizes ranged from: 0.125" to 0.750" (ID).

MATERIAL AND MANUFACTURING IMPACT

Platinum-Catalyzed Addition Cure: A Clean Chemistry



- No processing aids
- No organic plasticizers
- No stabilizers
- No by-products
- Low extractables profile

SILASTIC™ biomedical-grade silicone elastomer is used to extrude the DOW CORNING™ Pharma Tubing family of products.

Vertical integration: Our vertically integrated supply chain allows control from starting materials production to the tubing extrusion, and it provides traceability as well as quality control.

ISO 11737-1 BIOBURDEN TEST

Sterilization of medical devices – Microbiological methods
Part 1: Determination of a population of microorganisms on products

- The most comprehensive test method was selected and plate count technique was used for total aerobic bacteria, yeast, molds and spores
- 12 lots were tested in triplicate
- Testing involved large fluid contact surface area of tubing samples
  - 15-meter coils with ID up to 0.625"

Procedure

- Validation of the removal method:
  - Validations were performed on both larger-bore (ID 5/8") and smaller-bore (ID 3/16") tubing
  - Tubing samples were sterilized by gamma irradiation (≥25 kGy)
  - The fluid path of the tubing was inoculated with a known concentration of *Staphylococcus aureus*; recovery efficiency of the microorganisms was determined and compared with the reference inoculum suspension to establish the correction factor
- Enumeration technique:
  - The inner lumen of the tubing was flushed under aseptic conditions (LAF Class 5) to remove the microorganisms and the eluent was filtered through a membrane; the filter was then transferred onto agar for incubation
  - Counts for total aerobic bacteria, yeast, molds and spores were determined by multiplying the number of counted colonies on the plate with the correction factor

Results

- No bioburden of any kind was detected for all products tested

USP ⟨85⟩ BACTERIAL ENDOTOXINS TEST

- 40 samples tested for each lot
- Testing performed under internal method developed for medical device tubing
- Gel clot method was selected for the detection of endotoxin
  - Based on clotting of a limulus amebocyte lysate (LAL) reagent
- The inner lumen of the tubing was extracted with pyrogen-free water
- The tubing extract was exposed to LAL reagent with ≥0.125 EU/mL sensitivity
- Acceptance criteria: Pass if no gel formation, meaning the LAL reagent does not react/clot with extract that has <0.125 EU/mL

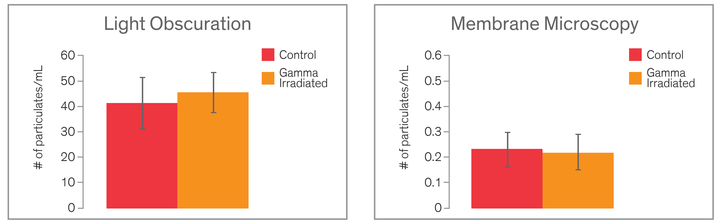
Results

- All the silicone tubing batches tested pass the acceptance criteria of <0.125 EU/mL
  - More stringent than USP ⟨85⟩ Water For Injection: 0.25 EU/mL

USP ⟨788⟩ PARTICULATE MATTER IN INJECTIONS

- Subvisible particulates testing per USP ⟨788⟩ is originally intended for packaged drugs
- Method 1: Light Obscuration Particulate Count Test – enumerates liquid and solid particles and gas bubbles; detected liquid particulates may be related to extractables
- Method 2: Microscopic Particulate Count Test – only enumerates solid particulates; solid particulates are the most concerning

Method 1 vs. Method 2



<1% of total particulates counted by LO are solids
Minimal particulates ≥25µm
(<0.15 particulates/ml by both methods)

Method 2 testing

- 19 lots of tubing were tested in triplicate
- Particulates were extracted from inner lumen of the tubing with PFW
- Extract volume was collected after multiple inversions of the tubing samples and filtered on membrane for counting

USP 788 criteria for Method 2:
<12/mL for particulates ≥10µm
<2/mL for particulates ≥25µm

Results

- Minimal amount of solid particulates found in tested samples:
  <0.6 particulate/mL (≥10 µm size)
  <0.2 particulate/mL (≥25 µm size)

CONCLUSION

- Industry standards currently applied for purity testing of single-use components were originally developed for medical devices and drug product packaging; therefore, more applicable methods have been developed
- A large number of samples and multiple tubing sizes were tested to support our sample preparation and protocol development process
- The study was designed to address the worst-case scenario conditions for method development
- The bioburden endotoxin and particulate testing results support the high level of purity of the tested DOW CORNING™ Pharma Tubing silicone products