WATSON MARLOW Tubing

Summary validation guide

Silicone braided hose

WATSON MARLOW Fluid Technology Solutions

This is the summary validation guide for Platinum-cured silicone braided hose. Full test methods and results are available in the full validation guide, by filling in a request form on the website: https://www.wmfts.com/en/validation/request/

Contents

1. Introduction

Platinum-cured silicone braided hose is manufactured at Watson-Marlow Manufacturing Inc., Devens, MA, USA.

Braided hose has the following features:

- High pressure flexible hose with continuously extruded platinum-cured silicone core ensures product integrity
- Withstands sterilisation
- Lot numbering enables full product traceability

2. Conditions of use

Braided hose is suitable for use using the conditions in Table 1.

Table 1. Conditions for manufacturing, sterilisation, working and storage.

Manufacturing	Sterilisation	Working	Storage
Platinum-cured Silicone	Gamma irradiation up to 50 kGy	-65°C to 254°C (-85°F to 489.2°F)	5°C to 40°C (41°F to 104°F)
ISO 14644–1 class 7 cleanroom (at rest)	Autoclavable		Dry environment, away from direct sunlight
ISO 9001 quality management system			No exposure to chemicals or stress

Original packaging must be maintained, and stock rotated on a first in, first out (FIFO) basis. The performance of the tubing cannot be assured beyond use by date or when not stored according to recommendations above.

3. Chemical compatibility

A general guide on chemical compatibility of transfer tubing can be found on the Watson-Marlow Fluid Technology Solutions website: www.wmfts.com/en/support/chemical-compatibility-guide/. It is advisable for transfer tubing to be tested under actual process conditions (see section 5 Validation Testing services).

4. Validation Testing

4a. Summary table

Table 2. Testing summary of evaluated standards.

Test	Description	Result
USP <85>	Bacterial Endotoxin test	PASS
USP <87>	Biological Reactivity tests, *in vitro*	PASS
USP <88>	Biological Reactivity tests, *in vivo*	PASS
USP <788>	Particulate matter in injections	PASS
ISO 10993-4	Biological evaluation of medical device, interactions with blood	PASS
ISO 10993-5	Biological evaluation of medical devices, *in vitro* cytotoxicity	PASS
ISO 10993-6	Biological evaluation of medical devices, local effects after implantation	PASS

Test	Description	Result
ISO 10993-10	Biological evaluation of medical devices, skin sensitisation Klingman maximisation	PASS
ISO 10993-11	Biological evaluation of medical devices, systemic toxicity	PASS
European Pharmacopeia 3.1.9	Silicone elastomer for closures and tubing	PASS
Extractables	Analysis of Material Extracts for Organic Extractables and Extractables Metals	REPORT
X-ray equivalency	Equivalency for X-ray and Gamma irradiated product	REPORT

4b. USP <85> Bacterial endotoxins

Limulus Ameobocyte Lysate (LAL) detects and quantifies endotoxin levels in samples. Test samples, negative control and endotoxin standards were extracted in LAL reagent water at room temperature for 60 minutes. LAL was added to samples and incubated at 37°C (98.6°F).

Results: *<0.005 EU/mL*
Result is <0.25 EU/mL (water for injection limit), passing <USP 85> requirements.

4c. USP <87> Biological Reactivity tests, *in vitro*

USP <87> determines the biological reactivity of cell cultures in response to samples. Test, positive and negative control samples were prepared at 37°C (98.6°F) for 24 hours. Biological reactivity was rated on a scale from Grade 0 (no reactivity) to Grade 4 (severe reactivity).

Results: *Grade 0 - No reactivity or cytotoxicity, passing USP <87> requirements.*

4d. USP <88> Biological Reactivity tests, *in vivo*

USP Class VI Plastics Test assesses the toxicity of test articles systemically, intracutaneously and through implantation. Samples were immersed in: USP 0.9% NaCl, cottonseed oil, 1 in 20 ethanol in NaCl and polyethylene glycol 400 at 70°C (249.8°F) for 24 hours. Injection sites were monitored for 72 hours.

Results: *No toxicity, passing USP <88> requirements.*

4e. USP <788> Particulate matter in injections

This test determines the number of particulates measuring ≥10 µm and ≥25 µm present in the fluid pathway. Samples were filled with low particulate water, shaken and the particles were measured.

Results: *155 particles/container ≥10 µm and ≤1 particle/container ≥25 µm, passing USP <788> requirements.*

4f. ISO 10993-4 Biological evaluation of medical device, interactions with blood

The haemolysis test assesses the potential to cause rupture of erythrocytes (red blood cells) from indirect contact of samples. Phosphate buffered saline was added to samples and incubated in rabbit blood for 3 hours at 37°C (98.6°F). The absorbance of each sample was measured.

Results: *No haemolytic activity, passing ISO 10993–4 requirements.*

4g. ISO 10993–5 Biological evaluation of medical devices, *in vitro* cytotoxicity

The biological reactivity of a cell culture, in response to samples was determined. The cell culture medium was replaced by samples and control articles. The cultures were incubated for 24 hours at 37°C (98.6°F).

Results: *No cytotoxicity, passing ISO 10993–5 requirements.*

4h. ISO 10993–6 Biological evaluation of medical devices, local effects after implantation

This test evaluates samples for inflammation, encapsulation, necrosis, haemorrhage and discolouration in direct contact with living tissue. Strips of test samples and negative controls were tested.

Results: *No reactivity, passing ISO 10993–6 requirements.*

4i. ISO 10993–10 Biological evaluation of medical devices, skin sensitisation

The systemic injection study evaluates samples for toxic effects from a single dose systemic injection. Samples were extracted using 0.9% NaCl, cottonseed oil, 1 in 20 ethanol in NaCl or polyethylene glycol 400 at 70°C for 24 hours.

Results: *No toxicity, passing ISO 10993–11 requirements.*

Kligman Maximisation

This test detects the allergenic potential of a test article. Samples were extracted using 0.9% NaCl, cottonseed oil,1 in 20 ethanol in NaCl or polyethylene glycol 400 at 70°C for 24 hours and injected intracutaneously.

Results: *No allergic potential, passing ISO 10993–10 Klingman maximisation requirements.*

4j. ISO 10993–11 Biological evaluation of medical devices, Tests for systemic toxicity

The systemic injection study evaluates samples for toxic effects from a single dose systemic injection. Samples were extracted using 0.9% NaCl, cottonseed oil, 1 in 20 ethanol in NaCl or polyethylene glycol 400 at 70°C for 24 hours.

Results: *No toxicity, passing ISO 10993–11 requirements.*

4k. European Pharmacopeia 3.1.9

Extracts were prepared in accordance with the requirements of European pharmacopoeia, Chapter 3.1.9 Silicone elastomer for closures and tubing.

Results: *All results pass E.P. 3.1.9 requirements.*

4l. Extractables

Samples were subjected to extraction in multiple solvents at controlled temperatures. The solvent extracts were analysed using:

- Liquid Chromatography- Mass Spectrometry (LC/MS) to detect the presence of non-volatile and UV active compounds
- Direct injection Gas Chromatography-Mass Spectrometry (DI-GC/MS) to detect semi-volatile compounds
- Headspace Gas Chromatography-Mass Spectrometry (HS-GC/MS) to detect volatile compounds
- Inductively Coupled Plasma-Mass Spectrometry (ICP/MS) to identify elemental impurities

Results: *Extractables were indicative of materials of construction. Validation Testing services can provide further information in the evaluation of extractable data for risk assessment purposes. Please see section 5.*

4m. X-ray equivalency

There is a foreseeable shortage of gamma irradiation capacity. BioPhorum and Bio Process Systems Alliance (BPSA) committees have steered supply chain representatives to adopt X-ray irradiation to mitigate this risk. The mechanism of X-ray irradiation is very similar to gamma.

WMFTS has chosen to qualify X-ray for irradiation. Testing was conducted as follows:

- Extractables (Reduced BPOG)
- Cytotoxicity (USP <87> / ISO 10993-5)
- Burst Testing
- Hardness
- Dimensional Measurements

Results: *Validated to be irradiated with Gamma or X-ray irradiation.*

5. Validation Testing Requests

Our Validation Testing team will design your validation studies using the most up to date industry recognised standards alongside fully qualified testing partners. We will provide a bespoke results assessment to ensure you meet your specific quality assurance requirements.

Testing protocols cover a wide range of industry recognized validation tests for one-off or lot-release testing. These include but not limited to:

- Bioburden
- Particulates
- Endotoxin
- Leak
- Pressure
- Extractables
- Leachables
- Sterility assurance
- Nitrosamines
- Chemical compatibility

Contact Validation.WMArchitect@wmfts.com or your WMFTS representative for more information.

6. Conclusions

Platinum-cured silicone braided hose has passed testing standards as summarised in this guide. For more information on quality and compliance information not stated in this guide, please contact your WMFTS representative or qualityrequests.devens@wmfts.com.

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