



Validation guide summary

Platinum-cured silicone transfer tubing



Contents

1 Introduction

2 Conditions of use

3 Chemical compatibility

4 Materials, manufacturing and regulatory compliance statements

- a. Compliance declaration summary
- b. REACH legislation
- c. RoHS
- d. Storage conditions

5 Compendial and non compendial testing

- a. Summary table
- b. USP <87>
- c. USP <88>
- d. ISO 10993-5
- e. ISO 10993-6
- f. ISO 10993-10
- g. ISO 10993-11
- h. European Pharmacopeia 3.1.9

6 Total Organic Carbon (TOC)

7 Conclusions

1. Introduction

Our factory in Seaford, Delaware USA produces a range of BioPure products including high purity silicone hose, gaskets and tubing for use in biopharmaceutical and pharmaceutical manufacturing. The facility contains 3,000 square feet of cleanroom manufacturing.

BioPure silicone transfer tubing is manufactured in ISO 14644-1 Class 7 cleanrooms according to GMP principles within a facility operating an ISO 9001 quality management system.

Silicone transfer tubing has a number of key features and benefits. These include:

- **USP Class VI, EP 3.1.9 compliance testing**
- **Animal Derived Component Free**
- **Sterilisable by autoclave or gamma**
- **Full lot traceability via labeling and packaging**

BioPure silicone transfer tubing is compliant with a range of compendial testing as detailed in Section 5A. Developed for the biopharmaceutical industry, silicone tubing is suitable for sterilisation by autoclave and gamma irradiation.

The Seaford factory was formed in 2003 and has been providing a range of single-use components to the biopharmaceutical industry for 14 years. It was acquired by Watson-Marlow Fluid Technology Group (WMFTG) in 2015.

WMFTG is a wholly owned subsidiary of Spirax-Sarco Engineering plc.

Spirax-Sarco's headquarters are in Cheltenham, England and is listed on the London Stock Exchange.

2. Conditions of use

BioPure silicone transfer tubing can be sterilised by autoclave and gamma irradiation up to 50 kGY

2a Working temperature and pressure rating

The working temperature range of BioPure silicone transfer tubing is -65°C to 254°C (-85°F to 490°F).

3 Chemical compatibility

Currently, there is no data available on the chemical compatibility of the finished BioPure silicone transfer tubing with regards to how it performs in the presence of different solvents. As such, it is recommended that the BioPure silicone transfer tubing is tested under the actual process conditions.

4 Materials, manufacturing and regulatory compliance statements

4a Compliance declaration summary

Table 1 details the different substances that are not present in the raw material, manufacturing process or final composition of BioPure silicone transfer tubing.

4b REACH legislation

All raw materials, compounds used in the manufacturing process and the final BioPure silicone transfer tubing complies with the REACH regulations.

None of the chemicals used in the manufacture of BioPure silicone transfer tubing are on the candidate list or the list of substances of very high concern (SVHC).

Table 1: List of compliance statements for BioPure silicone transfer tubing and substances not found in the processing of/ or raw materials for BioPure silicone transfer tubing

Named substance	Raw material	Manufacturing process	Final product
Animal Derived Content (ADC)	–	–	–
Phthalates	–	–	–
Bisphenol A (BPA)	–	–	–
Latex	–	–	–
Allergens per Annex II of Regulation (EU) No 1169/2011	–	–	–

‘–’ denotes not present or not added

4c RoHS

In compliance with the Restriction of Hazardous Substances (RoHS) directives, no listed substances are used in the manufacture of BioPure silicone transfer tubing.

4d Storage conditions

To maintain the performance of the components throughout their lifecycle, they should be stored in a cool, dry environment away from direct sunlight without exposure to chemicals and not subjected to stress. Normal warehouse conditions of 5C–40C (40F–86F) are acceptable. Wherever possible, original packaging should be maintained. Stock should be rotated on a first in, first out (FIFO) basis.

The performance of any component beyond its use by date, or which has not been stored according to the recommendations outlined above, cannot be assured.

Extracts, positive control (rubber) and negative control articles were prepared at 37C (98.6F) for 48 hours. Biological reactivity was rated on a scale ranging from Grade 0 (no reactivity) to Grade 4 (severe reactivity).

Results: No reactivity was exhibited by the cell cultures when exposed to BioPure silicone transfer tubing. Therefore they passed the requirements of USP 87 biological reactivity tests and have no cytotoxic potential.

5c USP <88> Biological Reactivity tests, In Vivo, Post Gamma Irradiation samples

USP Class VI Plastics Test assesses the potential toxicity of a given test article systemically, intracutaneously and through implantation. Samples of silicone transfer tubing were gamma irradiated at 45–55 kGy and tested in accordance with USP 39, NF 34 <88>, Biological reactivity tests, In Vivo. This included the immersion of the test articles in the following solutions: USP 0.9% sodium chloride, cottonseed oil, 1 in 20 ethanol in NaCl and polyethylene glycol 400 at 121C (250F) for 1 hour.

Results: BioPure silicone transfer tubing extracts and implants showed no toxicity. Therefore, they passed the requirements of USP <88> biological reactivity tests.

5a Summary table

Table 2 (page 5) contains a summary of all the compendial testing and ISO qualifications that silicone transfer tubing fluid path components have been evaluated for. Full test methods and results are available on request. All test work was performed on silicone transfer tubing samples and this was used to represent silicone transfer tubing product family as the components are manufactured using the same material at the same manufacturing site. The silicone transfer tubing was gamma irradiated from 45–55 kGy prior to testing.

5b USP <87> Biological Reactivity tests, In Vitro, Post Gamma Irradiation samples

USP 87 determines the biological reactivity of a cell culture in response to a given test article. Samples of silicone transfer tubing were gamma irradiated at 45–55 kGy and tested in accordance with USP 39, NF 34, <87>, Biological reactivity tests, In Vitro.

5d ISO 10993–5 Biological evaluation of medical devices – part 5: tests for In Vitro cytotoxicity

The biological reactivity of a cell culture, in response to extracts from silicone transfer tubing was determined. The maintenance medium on the cell cultures was replaced by extracts of silicone transfer tubing or control article.



Table 2: List of compendial and non compendial testing performed

Test reference	Test description	Result
USP <87>	Biological reactivity test, In Vitro	PASS
USP <88>	Biological reactivity test, In Vivo	PASS
ISO 10993–5	Biological evaluation of medical devices, tests for In Vitro cytotoxicity	PASS
ISO 10993–6	Biological evaluation of medical devices, implantation	PASS
ISO 10993–10	Biological evaluation of medical devices, irritation	PASS
ISO 10093–11	Biological evaluation of medical devices, systemic toxicity	PASS
E.P. 3.1.9	European Pharmacopeia 3.1.9 silicone elastomer for closures and tubing	PASS

BioPure silicone transfer tubing has passed a number of compendial and ISO testing, a summary of the results are disclosed within.

The cell cultures were incubated for 48 hours at 37±1C (98.6F±33.8F). Biological reactivity was evaluated by a photo spectrometer at 450 nm wavelength.

Results: BioPure silicone transfer tubing showed no signs of cytotoxic potential. Therefore they passed the requirements of ISO 10993–5.

5e ISO 10993–6 Biological evaluation of medical devices, implantation

The purpose of this test is to evaluate the solid material in direct contact with living tissue.

Silicone transfer tubing and the negative control plastics were tested. The test sites were examined for encapsulation, necrosis, haemorrhage and discolouration macroscopically.

Results: BioPure fluid path components did not demonstrate any remarkable difference as compared to the control implant sites when in contact with tissue for two weeks.

5f 10993–10 Biological evaluation of medical devices, irritation

The intracutaneous test is designed to evaluate local responses to the extracts of silicone transfer tubing

Table 3: List of physiochemical tests that form EP 3.1.9 – Silicone elastomer for closures and tubing

Test	Test Results	Evaluation Criteria	Result
Appearance of solution	Clear as water 0.3 NTU	Clear as water < 3 NTU	PASS
Acidity or alkalinity	0.0 mL of 0.01 M NaOH (blue colour) 0.0 mL of 0.01 M HCl (yellow changes to orange)	≤ 2.5 mL of 0.01 M NaOH change to blue ≤ 0 mL of 0.01 M HCl change to yellow to orange	PASS
Relative density	1.16 g/mL	Between 1.05 – 1.25 g/mL	PASS
Reducing substances	0.5 mL	Diff. between sample and blank ≤ 1.0 mL	PASS
Substances soluble in hexanes	12.4 mg	≤ 15 mg (or 3%)	PASS
Volatile matter	0.17 %	< 2 % (Pt cured)	PASS
Mineral Oils	Less fluorescence than 1 ppm standard	Less fluorescence than 1 ppm standard	PASS
Phenylated compounds	< 0.4 AU from 250 to 340 nm	Absorbance < 0.4 A.u. (between 250 and 340 nm)	PASS
Platinum	0.0 ppm	Less coloured than Pt reference (30 ppm)	PASS

following intracutaneous injection. Silicone transfer tubing is extracted using 0.9% sodium chloride for injection, cottonseed oil, 1 in 20 ethanol in NaCl or polyethylene glycol 400 at 121C for 1 hour.

Results: BioPure silicone transfer tubing meet the requirements of ISO10993–10 guidelines for the intracutaneous injection test.

5g ISO 10993–11 Biological evaluation of medical devices, systemic toxicity

The purpose of the systemic injection study is designed to screen test articles (silicone transfer tubing) extracts for potential toxic effects as a result of a single dose systemic injection. Silicone transfer tubing is extracted using 0.9% sodium chloride for injection, cottonseed oil, 1 in 20 ethanol in NaCl or polyethylene glycol 400 at 121C for 1 hour.

Results: BioPure fluid path components meet the requirements of ISO 10993–11 guidelines for the systemic injection test toxicity.

5h European Pharmacopeia 3.1.9

Extracts of silicone transfer tubing were prepared in accordance with the requirements of European pharmacopoeia, 2009, Chapter 3.1.9 Silicone elastomer for closures and tubing. The results of test are summarised in Table 3.

Results: Based on the results of the tests, BioPure silicone transfer tubing meet the requirements of EP 3.1.9 section Physiochemical tests.

6. Total Organic Carbon (TOC)

TOC is an analytical technique used to measure the level of organic molecules or contaminants present or extracted into purified water. For this TOC test the extraction procedure performed on a BioPure platinum cured silicone tubing sample is in accordance with USP <381>.

7. Conclusions

BioPure silicone transfer tubing have been shown to pass a number of compendial and ISO testing summarised in this guide. For further information with full compliance statements and compendial test reports, please contact your WMFTG representative.

The compliance summary and the full validation guide for BioPure fluid path components are available by filling in a request form on the wmftg.com website:

watson-marlow.com/biopure-validation/





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