



## FULL VALIDATION GUIDE

### PureWeld XL tubing

# Executive Summary

This is the full validation guide for PureWeld XL tubing. This guide contains hyperlinks in section 8, page 6 to the reports which provide the reader with detailed test procedures and actual test results.

## Contents

- 1 Introduction**
- 2 Conditions of use**
- 3 Chemical compatibility**
- 4 Materials, manufacturing and regulatory compliance statements**
  - a. Materials of construction
  - b. Manufacturing environment
  - c. Country of origin
  - d. Compliance declaration summary
  - e. REACH status
  - f. RoHS legislation
  - g. Storage conditions
- 5 Compendial and non compendial testing**
  - a. Summary table
  - b. USP <87>
  - c. USP <88>
  - d. ISO 10993-4
  - e. ISO 10993-5
  - f. ISO 10993-6
  - g. ISO 10993-10
  - h. ISO 10993-11
  - i. Kligman maximisation
  - j. USP <788>
- 6 Extractables**
- 7 Conclusions**



## 1. Introduction

Watson-Marlow's PureWeld XL (942.) TPE tubing is USP 88 Class VI and ISO 10993 compliant, and produced from a USP 88 Class VI raw material. It is manufactured in an ISO 14644-1 class 7 cleanroom. The cleanroom is temperature and humidity controlled, thereby providing a stable extrusion environment.

PureWeld XL TPE tubing exhibits a number of key features:

- Low particulate generation in peristaltic pumping
- Provides exceptional life and accurate flow rates
- Sealable and weldable for sterile connectivity
- Excellent chemical resistance
- Very low extractables, non-toxic and Animal Derived Component Free (ADCF)
- Comprehensive stock of a wide range of sizes

Watson-Marlow Fluid Technology Solutions (WMFTS) is the world leader in niche peristaltic and sinusoidal pumps and associated fluid path technologies. Founded on nearly 60 years of supplying engineering and process expertise and with over one million pumps installed worldwide, our pumps are tried, tested and proven to deliver. WMFTS is a wholly owned subsidiary of Spirax-Sarco Engineering plc (LSE: SPX), a global organisation employing approximately 4,800 people worldwide. Watson-Marlow Fluid Technology Solutions comprises nine established brands, each with their own area of expertise, but together offering our customers an unrivalled breadth of solutions for their pumping applications.



## 2. Conditions of use

Watson-Marlow's PureWeld XL (942.) TPE tubing may be sterilised using:

- Gamma irradiation up to a maximum of 50 kGY
- Autoclave 1 bar at 121 C/250F
- Ethylene Oxide ( EtO)

### 2a Working temperature

Watson-Marlow's PureWeld XL (942.) TPE tubing can be used from -20C ( XF) to + 80C ( XF).

## 3. Chemical compatibility

A general guide on chemical compatibility of Pureweld XL tubing can be found on the Watson-Marlow Fluid Technology Solutions website: [wmfts.com/en-us/support/chemical-compatibility-guide/](http://wmfts.com/en-us/support/chemical-compatibility-guide/)

## 4. Materials, manufacturing and regulatory compliance statements

### 4a Materials of construction

PureWeld XL tubing is a thermoplastic elastomer (TPE) manufactured from a USP 88 Class VI raw material.

### 4b Manufacturing environment

PureWeld is manufactured in an ISO 14644-1 class 7 cleanroom within a facility operating under an ISO9001 quality management system.

### 4c Country of origin

PureWeld XL is manufactured at Bickland Water Road, Falmouth, Cornwall, United Kingdom, TR11 4RU.

### 4d Compliance declaration summary

*Table 1* details the different substances that are **not** present in the raw material, manufacturing process or final composition of PureWeld XL tubing.

*Table 1: List of compliance statements for Pureweld XL tubing and substances not present in the manufacture of Pureweld XL*

Named substance/compliance statement	Raw material	Manufacturing process	Final product
Animal Derived Content	–	–	–
Melamine	–	–	–
Phthalates	–	–	–
Bisphenol A (BPA)	–	–	–
Latex	–	–	–
Presence of heavy materials	–	–	–
Allergens	–	–	–

'–' denotes not present or not added

For a complete range of compliance statements relating to PureWeld XL please refer to the compliance guide

### 4e REACH legislation

All raw materials, compounds used in the manufacturing process and the final PureWeld XL tubing comply with the REACH regulations.

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

### 4f RoHS

In compliance with the restriction of hazardous substances (RoHS) directives, no listed substances are used in the manufacture of PureWeld XL tubing.

### 4g 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.

## 5. Compendial and non compendial testing

### 5a Summary table

Table 2 contains a summary of all the compendial testing and ISO qualifications that PureWeld XL tubing

have been evaluated for. Full test methods and results are available on request. The PureWeld XL tubing was gamma irradiated at 45–55 kGy prior to testing.

Table 2: List of compendial and non compendial testing performed

Test reference	Test Description	Result
USP <87>	Biological Reactivity tests, In Vitro, Post Gamma Irradiation samples	PASS
USP <88>	Biological Reactivity tests, In Vivo, Post Gamma Irradiation samples	PASS
ISO 10993-4	Hemolysis	PASS
ISO 10993-5	Biological evaluation of medical devices – part 5: 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 10993-10	Kligman Maximisation test	PASS
ISO 10993-11	Biological evaluation of medical devices, systemic toxicity	PASS

### 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 PureWeld XL tubing were gamma irradiated at 45–55 kGy and tested in accordance with USP <87>, Biological reactivity tests, In Vitro. Extracts, positive control (rubber) and negative control articles were prepared at 37C (98.6F) for 24 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 PureWeld XL tubing. Therefore they passed the requirements of USP 87 biological reactivity tests and have no cytotoxic potential.*

45–55 kGy and tested in accordance with USP <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 70C (158F) for 24 hours.

*Results: PureWeld XL tubing extracts and implants showed no toxicity. Therefore they passed the requirements of USP <88> biological reactivity tests.*

### 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 PureWeld XL tubing were gamma irradiated at

### 5d ISO 10993-4 (Hemolysis)

The hemolysis test assesses the potential for indirect contact of a given sample with blood to cause the rupture of erythrocytes (red blood cells).

Samples of PureWeld XL tubing were tested in accordance with ISO 10993-4, 2002, Biological Evaluation of Medical Devices – Part 4: Selection of Tests for Interactions with Blood.

*Results: PureWeld XL tubing showed no signs of haemolytic activity. Therefore they passed the requirements of ISO 10993-4.*



## 5e 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 PureWeld XL tubing was determined. The maintenance medium on the cell cultures was replaced by extracts of PureWeld XL tubing or control article.

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: PureWeld XL tubing showed no signs of cytotoxic potential. Therefore they passed the requirements of ISO 10993–5.*

## 5f 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.

Strips of PureWeld XL tubing (1mm x 1mm x 10mm) and the negative control plastics were tested. The test sites were examined for inflammation, encapsulation, necrosis, haemorrhage and discolouration macroscopically.

*Results: PureWeld XL tubing did not demonstrate any remarkable difference as compared to the control implant sites when in contact with tissue for 2 weeks. Therefore, it meet the requirements of the 10993-6*

## 5g ISO 10993–10 Biological evaluation of medical devices, irritation

The intracutaneous test is designed to evaluate local responses to the extracts of PureWeld XL tubing following intracutaneous injection. PureWeld XL tubing is extracted using 0.9% sodium chloride for injection, cottonseed oil, 1 in 20 ethanol in NaCl or polyethylene glycol 400 at 70C for 24 hours.

*Results: PureWeld XL tubing meet the requirements of ISO10993–10 guidelines for the intracutaneous injection test.*

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

The purpose of the systemic injection study is designed to screen test articles (PureWeld XL tubing) extracts for potential toxic effects as a result of a single dose systemic injection. PureWeld XL tubing

is extracted using 0.9% sodium chloride for injection, cottonseed oil, 1 in 20 ethanol in NaCl or polyethylene glycol 400 at 70C for 24 hours.

*Results: PureWeld XL tubing meet the requirements of ISO 10993–11 guidelines for the systemic injection test toxicity.*

## 5i ISO 10993–10 Kligman Maximisation test

The purpose of this test is to detect the allergenic potential of a test article.

Samples of PureWeld XL tubing were extracted in USP 0.9% sodium chloride for injection and cottonseed oil at 70C (158F) for 24 hrs and then injected interdermally. After two weeks, an additional topical application was introduced to the site of interdermal injections.

*Results: The sites that were exposed to the test articles and negative control showed no signs of erythema or edema. Therefore, PureWeld XL tubing are deemed not to contain any allergic potential.*

## 5j USP <788> Particulate testing/ microscopic particulate count analysis test

USP Limulus ameobocyte lysate (LAL) bacterial endotoxin assay Endotoxins are lipopolysaccharide complexes in gram negative bacterial cell walls. The limulus ameobocyte lysate (LAL) Kinetic Chromogenic assay is used to determine the quantitative level of endotoxin present within our products. PureWeld XL tubing was tested in accordance to the requirements of USP 85. PureWeld XL (29.0 cm<sup>2</sup> surface area) was extracted in 50mL of LAL reagent water at room temperature for 60 minutes. LAL-lysate was added to each sample well on an automated microtiter plate and then transferred to a plate reader where the absorbance of each well was read at 405 nm and 37 °C at set timepoints. A standard curve was generated using software based on reaction time versus endotoxin concentration which was then compared to the endotoxin concentration and reaction time of the sample extract.

*Results: PureWeld XL extracts had an EU/ml value of <0.009 EU/cm<sup>2</sup> which is comparable to the levels of endotoxin observed in water for injection.*



## 6. Extractables testing

PureWeld XL tubing connectors were subjected to extraction in multiple solvents at controlled temperatures. The solvent extracts were then analysed using high pressure liquid chromatography—diode array detector-mass spectrometry (HPLC-DAD/MS), Direct injection Gas Chromatography—Mass spectrometry (DI-GC/MS), Headspace Gas Chromatography—Mass spectrometry (HS-GC/MS) and Inductively Coupled plasma—Mass Spectrometry (ICP/MS). HPLC-DAD/MS is used to detect the presence of non-volatile and UV active extractables. DI-GC/MS identifies if there are any semi volatile compounds present in the extracts whilst volatile extractables can be detected using HS-GC/MS. Potential elemental impurities can be identified by ICP-MS.

The extracts were evaluated for the elemental impurities listed in the ICH Q3D and USP <232> guidelines.

*Results: These studies have shown that there were extractables indicative of the materials of construction. WMFTS can provide further information and assistance in the evaluation of extractable data for risk assessment purposes.*

## 7. Conclusions

PureWeld XL 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 WMFTS representative.

## 8. Hyperlinks to test reports

Section	Hyperlink to test data
5b/5e	<a href="#">USP &lt;87&gt; Biological Reactivity tests, In Vitro, Post Gamma Irradiation samples; ISO 10993-5 Biological evaluation of medical devices-part 5: tests for In Vitro cytotoxicity</a>
5c/5f/5g/5h	<a href="#">USP &lt;88&gt; Biological Reactivity tests, In Vivo, Post Gamma Irradiation samples; ISO 10993-6 Biological evaluation of medical devices, implantation; ISO 10993-10 Biological evaluation of medical devices, irritation; ISO 10993-11 Biological evaluation of medical devices, systemic toxicity</a>
5d	<a href="#">ISO 10993-4 Haemolysis</a>
5i	<a href="#">ISO 10993-10 Kligman maximisation</a>
5j	<a href="#">USP &lt;788&gt; Particulate testing/ microscopic particulate count analysis test</a> <a href="#">USP 85</a>
6	<a href="#">Extractables report</a>

BIOTECHNOLOGY AND PHARMACEUTICAL SOLUTIONS



**Watson-Marlow Fluid Technology Solutions**

Watson-Marlow Fluid Technology Solutions supports its customers locally through an extensive global network of direct sales operations and distributors

[wmfts.com/global](http://wmfts.com/global)

