WATSON MARLOW Pumps

Summary validation guide

Quantum ReNu SU Technology® cartridge

WATSON MARLOW Fluid Technology Solutions

Executive Summary
This is the summary validation guide for the Quantum ReNu SU cartridge.

Contents

1. Introduction

This guide relates to Quantum ReNu SU cartridge and from this point will be referred to as Quantum ReNu.

Quantum ReNu cartridges comprise of polyurethane tubing installed on a high-density polyethylene (HDPE) manifold in accordance to USP <87>, formally USP Class VI, with nylon collets.

Quantum ReNu cartridges are manufactured across two sites in Watson-Marlow Fluid Technology Solutions, Watson-Marlow Ltd, Bickland Water Rd, Falmouth, UK, TR11 4RU and Biopure Technology, Fitzwygram Way, Dunsbury Park, Havant, UK, PO9 4EE.

Quantum ReNu has the following features:

- Excellent flow stability for accurate process control
- Repeatability of performance pressure and flow performance
- Full traceability is guaranteed even when the packaging is removed

2. Conditions of use

Quantum ReNu is suitable for use according to the conditions in Table 1.

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

Manufacturing	Sterilisation	Working	Storage
ISO 14644–1 class 7 cleanrooms	Gamma irradiation up to 45 kGy	5°C to 37°C (41°F to 98°F)	- 10°C to 40°C (14°F to 86°F)
ISO 9001 quality management system			Dry environment, away from direct sunlight.
			No exposure to chemicals or stress

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

3. Chemical compatibility

There is no data available on the chemical compatibility of the finished Quantum ReNu with regards to how they perform in the presence of different solvents. As such, it is advisable for Quantum ReNu 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 endotoxins 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 10993-5	Biological evaluation of medical devices, Tests for *in vitro* cytotoxicity	PASS
ISO 10993-6	Biological evaluation of medical devices, Tests for local effects after implantation	PASS
ISO 10993-10 Kligman Maximisation Test	Biological evaluation of medical devices, Tests for irritation and skin sensitisation	PASS
ISO 10993-11	Biological evaluation of medical devices, Tests for systemic toxicity	PASS
Extractables	Analysis of material extracts for organic extractables and extractables metals	REPORT

4b. USP <85> Bacterial endotoxins

Limulus Ameobocyte Lysate (LAL) gel clot test detects and quantifies endotoxin levels in samples. Test samples, negative control and endotoxin standards were extracted in LAL reagent water at 37°C (98.6°F) 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 for water for injection. 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 extracts were prepared at 37±1°C (98.6±33.8°F) for 24±2 hours. Biological reactivity was rated on a scale from Grade 0 (no reactivity) to Grade 4 (severe reactivity).

Results: *No cytotoxic potential, 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. Sample extracts were prepared using USP 0.9% NaCl, cottonseed oil, 1 in 20 ethanol in NaCl and polyethylene glycol 400 (PEG) at 70±2°C (158°F) for 24±2 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. The test article was filled with low particulate water and shaken 5 times, the remaining low particulate water was poured through the test article and collected. The extraction fluid was left to stand for 10 minutes and then the particles were measured.

Results: *7 particles/mL ≥10 µm and 1 particle/mL ≥25 µm, passing USP <788> requirements.*

4f. 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 48 hours at 37±1°C (98.6±33.8°F).

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

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

This test evaluates samples in direct contact with living tissue. Test article extracts were injected intracutaneously and observed for signs of haemorrhage, necrosis, discoloration, encapsulation and infection or inflammation.

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

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

The intracutaneous test evaluates local responses to samples following intracutaneous injection. Samples were extracted using 0.9% NaCl, cottonseed oil,1 in 20 ethanol in NaCl or polyethylene glycol 400 (PEG) at 70±2°C for 24±2 hours. Injection sites were monitored for 72 hours.

Results: *No reactivity, passing ISO 10993–10 requirements.*

4i. Kligman Maximisation

This test detects the allergenic potential of a test article. Samples were extracted using 0.9% NaCl and cottonseed oil at 70±2°C for 24±2 hours and injected intracutaneously.

Results: *No reaction, passing ISO 10993–10 Klingman maximisation test requirements.*

4j. ISO 10993–11 Biological evaluation of medical devices, 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 (PEG) at 70±2°C for 24±2 hours.

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

4k. Extractables

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

- Organic extractables using GC/MS and LC-DAD-MS (230nm, ESI +/-)
- GC-MS Headspace analysis
- ICP-MS analysis for extractable metals

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.*

5. Validation testing services

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 recognised validation tests for one-off or lot-release testing. These include but are not limited to:

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

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

6. Conclusions

Quantum ReNu SU cartridges have 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.wml@wmfts.com.

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