Summary validation guide

BioClamp

WATSON MARLOW Fluid Technology Solutions

Executive Summary

This is the summary validation guide for BioClamps. 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/

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1. Introduction

BioPure, Havant, UK produces BioClamps used in biotechnology and pharmaceutical manufacturing.

BioClamps have the following features:

- Lot numbers moulded in for full traceability

2. Conditions of use

BioClamps are suitable for use according to the conditions in Table 1.

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

Manufacturing	Sterilisation	Working	Storage
USP Class VI glass reinforced nylon	Gamma irradiation ≤ 50 kGy	-4°C–40°C (24.8°F–104°F)	5°C–40°C (41°F–104°F)
ISO 14644–1 class 7 cleanrooms	Autoclave to 135°C (275°F) for 30 minutes	≤ 10 bar*	Dry environment, away from direct sunlight
ISO 9001 quality management system			No exposure to chemicals or stress

*For some product codes the working pressure is ≤ 6 bar, please see the technical data sheet.

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 BioClamps with regards to how they perform in the presence of different solvents. As such, it is advisable for BioClamps 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 <87>	Biological reactivity tests, *in vitro*	PASS
USP <88>	Biological reactivity tests, *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, Tests for local effects after implantation	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 <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.*

4c. 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 immerged in: USP 0.9% NaCl, cottonseed oil, 1 in 20 ethanol in NaCl and polyethylene glycol 400 at 70°C (158°F) for 24 hours. Injection sites were monitored for 72 hours.

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

4d. 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°C (98.6°F). Biological reactivity was evaluated by a photospectrometer at 450 nm.

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

4e. 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.*

4f. 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 at 70°C for 24 hours. Injection sites were monitored for 72 hours.

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

4g. 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 at 70°C for 24 hours.

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

4h. Extractables

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

- Liquid Chromatography- Diode Array Detector-Mass Spectrometry (LC-DAD/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.*

4i. 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.

Testing for X-ray irradiation equivalency was conducted as follows:

- Extractables (Reduced BPOG)
- Cytotoxicity (USP <87> / ISO 10993-5)
- Hydrostatic pressure testing
- Dimensional measurement

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

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
- Pressure
- Extractables
- Leachables
- Sterility assurance
- Nitrosamines
- Chemical compatibility

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

6. Conclusions

BioClamps 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 biopurequality@wmfts.com.

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