



Validation guide and performance testing summary

BioClamp



Contents

1 Introduction

2 Sterilisation

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 legislation
- f. RoHS
- g. Storage conditions

5 Compendial and non compendial testing

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

6 Extractables

7 Performance data

8 Conclusions

1. Introduction

BioPure based in Horndean, Hampshire produces a range of components for use in biotechnology and pharmaceutical manufacturing.

BioClamp is manufactured in ISO 14644 class 7 cleanrooms within a facility operating an ISO 9001 quality management system.

BioClamp is compliant with a range of compendial testing as detailed in Section 5A. Developed for the biotechnology and pharmaceutical industry, BioClamp is suitable for sterilisation by autoclave and gamma irradiation.

2. Typical sterilisation conditions

BioClamp can be sterilised by autoclave up to 135C (275F) and gamma irradiated up to 50 kGY.

2a Working temperature and pressure rating

The working temperature range of the BioClamp is -4C to 40C (24.8F to 104F). BioClamp can be used up to a pressure rating of 7 bar.

3 Chemical compatibility

No data on the chemical compatibility has been generated on the finished BioClamp with regards to how it performs in the presence of different solvents. However, the raw materials have been evaluated with a range of different chemicals and were found to be compatible with a variety of common solvents. For specific applications, it is recommended that BioClamp is tested under the actual process conditions.

4 Materials, manufacturing and regulatory compliance statements

4a Materials of construction

BioClamp is made out of glass reinforced nylon.

4b Manufacturing environment

BioClamp is manufactured according to the principles of GMP in an ISO 14644 class 7 cleanroom within a facility operating an ISO 9001 quality management system.

4c Country of origin

BioClamp is manufactured in Horndean, Hampshire, United Kingdom.



4d Compliance declaration summary

Table 1 details the different substances that are not present in the raw material, manufacturing processes or final composition of BioClamp.

For full compliance statements please refer to the compliance summary sheet available on request from the website.

Table 1: List of compliance statements for BioClamp and substances not found in the processing of or raw materials for BioClamp

Named substance	Raw material	Manufacturing process	Final product
Gluten	–	–	–
Animal Derived Content (ADC)	–	–	–
Melamine	–	–	–
Phthalates	–	–	–
Bisphenol A	–	–	–
Latex	–	–	–
Allergens (as defined FDA CFR 21)	–	–	–

‘–’ denotes not present or not added

4e REACH legislation

All raw materials, compounds used in the manufacturing process and the final BioClamp comply with the REACH regulation. None of the chemicals used in the manufacture of BioClamp are on the candidate list of substances or 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 BioClamp.

4g. Storage conditions

Normal warehouse conditions of –10C to 40C (14F and 104F) should be acceptable. BioClamp should be stored in the original packaging where possible and in a cool dry environment away from direct sunlight without exposure to stress or harsh chemicals. Stock should be rotated on a first in, first out (FIFO) basis.

5. Compendial and Non compendial testing

5a Summary table

Table 2 contains a summary of all the compendial and ISO testing BioClamp has been evaluated for. All samples were gamma irradiated from 45–55kGY prior to testing. Full test methods and results are available on request of the full validation guide.

Table 2: List of compendial and non compendial testing performed

Test reference	Test description	Result
USP 88	Biological reactivity test, <i>In Vivo</i>	PASS
USP 87	Biological reactivity test, <i>In Vitro</i>	PASS
ISO 10993-6	Biological evaluation of medical devices, implanatation	PASS
ISO 10993-5	Biological evaluation of medical devices, tests for <i>In Vitro</i> cytotoxicity	PASS
ISO 10993-11	Biological evaluation of medical devices, systemic toxicity	PASS
ISO 10993-10	Biological evaluation of medical devices, irritation	PASS

BioClamp has passed a number of compendial and ISO testing, a summary of the results are disclosed within.

5b USP <88> Biological reactivity tests, *In Vivo*, post gamma irradiation samples

USP Class VI Plastics Test assesses the potential toxicity of given test articles systemically, intracutaneously and through implantation.

Samples of BioClamp were tested in accordance with USP39, NF34, <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 sodium chloride and polyethylene glycol 400 at 70C (158F) for 24 hours.

Results: BioClamp extracts and implants show no signs of toxicity, therefore they passed the requirements of USP <88 > biological reactivity tests.

5c 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 BioClamp were tested in accordance with USP 39 NF34, <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 the BioClamp, therefore it passed the requirements of USP <87 > biological reactivity tests and is non cytotoxic.



5d 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 BioClamp (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: BioClamp did not demonstrate any remarkable difference as compared to the control implant sites when in contact with tissue for 2 weeks. Therefore BioClamp passed the requirements of ISO 10993-6.

5e ISO 10993-5 Biological evaluation of medical devices—tests for *In Vitro* cytotoxicity

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

The cell cultures were incubated for 48 hours at $37 \pm 1^\circ\text{C}$ (98.6°F). Biological reactivity was evaluated by a photo spectrometer at 450nm wavelength.

Results: Based on the results, BioClamp is considered to be non cytotoxic

5f ISO 10993-11 Biological evaluation of medical devices, systemic toxicity

The purpose of the systemic injection study is designed to screen test articles (BioClamp) extracts for potential toxic effects as a result of a single dose systemic injection. BioClamp was extracted using 0.9% sodium chloride for injection, cottonseed oil, 1 in 20 parts ethanol in sodium chloride or polyethylene glycol 400 at 70°C (158°F) for 24 hours.

Results: BioClamp met the requirements of ISO 10993-11 guidelines for systemic toxicity.

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

The purpose of the incutaneous injection study is designed to evaluate local responses to BioClamp extracts for potential toxic effects. BioClamp was extracted using 0.9% sodium chloride for injection, cottonseed oil, 1 in 20 parts ethanol in sodium chloride or polyethylene glycol 400 at 70°C for 24 hours.

Results: BioClamp meets the requirements of ISO 10993 guidelines for intracutaneous injection.

6. Extractables

BioClamp was subjected to extraction using a 50% ethanol and water solution at 40°C (104°F). The solvent extracts were analysed using high performance 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 there are extractables present which are related to the materials of construction of the BioClamp. WMFTG can provide assistance in the evaluation of extractables data to risk assessment purposes.

7. Performance testing

Bioclamp has been tested at maximum and working pressures under ambient conditions and different sterilisation conditions.

8. Conclusions

BioClamp has been evaluated using a range of compendial and ISO testing summarised within this guide. For further information with full compliance statements and test reports, please fill in the request form on the wmftg.com website.

The compliance summary and the full validation guide for Bio-Clamp are available by filling in a request form on the wmftg.com website:

www.wmftg.com/biopure-validate-us





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