Bioprene®
VALIDATION GUIDE

Thermoplastic elastomer tubing
Biopharm validated
long life and excellent chemical compatibility

www.wmtubing.com
In printed form this document is uncontrolled and updates will not be automatically included. For the current issue of the validation guide, please contact your local Watson-Marlow Pumps representative or visit: www.wmpg.com/bioprene-uk
### Change history

<table>
<thead>
<tr>
<th>Issue</th>
<th>Change</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>First issue</td>
<td>April 2005</td>
</tr>
<tr>
<td>2</td>
<td>ISO certificates updated, title corrected to include 800 series tubing</td>
<td>June 2007</td>
</tr>
<tr>
<td>3</td>
<td>Raw material change; complete update of testing, etc.</td>
<td>June 2013</td>
</tr>
</tbody>
</table>
Introduction

**Bioprene**

Bioprene® is a high performance USP Class VI validated thermoplastic elastomer tube manufactured from a USP Class VI raw material in an ISO 14644-1 Class 7 cleanroom according to cGMP principles, and operating within an ISO9001:2008 quality system. Manufacturing is located at Watson-Marlow Ltd in Falmouth, England.

Bioprene tubing has the following key features:

- meets USP Class VI requirements
- on-going biocompatibility testing
- FDA DMF (Food and Drug Administration Drug Master File)
- meets FDA regulations CFR 177.2600 for contact with aqueous food
- made from NSF51 food compliant raw material
- long peristaltic life
- broad chemical compatibility
- opaque to visible and UV light
- low extractables; no phthalates added, no latex used
- can be sterilised by autoclaving and gamma irradiation and EtO
Bioprene tubing is a high specification thermoplastic elastomer, which is especially suitable for the biopharmaceutical industry through its USP Class VI validation. For peristaltic pump applications Bioprene tubing is designed and manufactured to give optimal performance in Watson-Marlow pumps. In addition to the original USP Class VI qualifying tests on raw material and tubing, further validation assurance is provided by executing indicative biocompatibility tests on each batch of both raw material and a sample of tubing extruded from it, demonstrating that both should continue to satisfy USP Class VI. The three raw material hardness grades used in four different Bioprene grades have been tested so that they should satisfy USP Class VI requirements. A Drug Master File (DMF) has been created for the tubing and submitted to the FDA. It contains details of the tubing manufacture and biocompatibility qualification. Authorised parties (e.g. biopharmaceutical manufacturers) can then request the FDA to declare the suitability of Bioprene tubing for a particular application.

The tubing is manufactured in a state-of-the-art facility from virgin pellet; no regrind is used. Only synthetic components are used in the manufacture; no natural rubber such as latex is used. The raw material is manufactured under strict controls of ingredients, operating procedure and packaging. Each lot of raw material has undergone mechanical testing at the supplier to ensure compliance with the material specification. Full traceability is assured through the lot number of the tubing; enabling identification of the raw material, primary manufacturing equipment, quality control records and production records.

Bioprene products include all part codes with the structure 933.XXXX.XXX and 088.T250.XXX. 088.T400.XXX codes are not included.

Biocompatibility testing

**Raw material**

The 64 Grade and 87 Grade hardness raw materials have been fully tested to meet USP Class VI requirements:

- USP <88> Biological reactivity tests, in vivo

The following additional tests were also performed and are later used as indicative tests for every batch of raw material and a tubing sample extruded from it.

- USP <87> Cytotoxicity test, in vitro
- USP <661> Physicochemical tests (heavy metals, etc.)

A 73 Grade material is also used. Both 64 Grade and 73 Grade raw materials have the same ingredients but in different ratios to achieve the designated hardness. From a biocompatibility perspective, the 64 Grade raw material has greater amounts of certain constituents which theoretically pose a greater risk compared with the 73 Grade. In practice, as summarised above, the 64 Grade meets the requirements of all the biocompatibility tests. For this reason full USP Class VI testing has not been carried out on 73 Grade material.

The 87 Grade raw material has a different constitution from both the 64 and 73 Grades and therefore, as noted above, the full suite of biocompatibility tests were performed (USP<88>, USP<87> and USP<661>).
Other biocompatibility qualifications
From the supplier we have assurances that the raw material meets the requirements of RoHS and REACH.
Phthalates and bisphenol A are not normal ingredients in the raw material and based on information provided by the supplier, the Bioprene raw material is free from these materials.

Extruded tubing
Full USP Class VI testing, alongside other evaluations, has been carried out on the 64 Grade tubing. 87 Grade tubing has also been tested to USP Class VI requirements. In terms of qualifying 73 Grade tubing to USP VI, the same argument as for raw material is applied.

The following table lists the evaluations carried out on the 64 Grade tubing. In the Appendix there are links to the original test certificates.

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class VI – In vivo toxicity – USP 35 NF30 &lt;88&gt;</td>
<td>Pass</td>
</tr>
<tr>
<td>L929 Elution Test – ISO 10993-5/ USP 35 NF30 &lt;87&gt;</td>
<td>Pass</td>
</tr>
<tr>
<td>Bacterial Endotoxins Test – USP 35 NF30 &lt;85&gt;</td>
<td>Pass</td>
</tr>
<tr>
<td>Haemolysis – Human Blood - ISO 10993 - 4</td>
<td>Pass</td>
</tr>
<tr>
<td>Physicochemical Tests - USP 35 NF30 &lt;661&gt;</td>
<td>Pass</td>
</tr>
<tr>
<td>PCBs EPA 8082</td>
<td>Pass</td>
</tr>
<tr>
<td>Kligman dermal sensitization - ISO 10993-10</td>
<td>Pass</td>
</tr>
<tr>
<td>Total extractables (aqueous) FDA 21CFR177:2600(e)</td>
<td>Pass</td>
</tr>
<tr>
<td>Physicochemical Tests incl. TOC - USP 35 NF30 &lt;381&gt;</td>
<td>Pass</td>
</tr>
</tbody>
</table>

On-going biocompatibility assurance
The concept of USP Class VI testing, as recognized in the biopharmaceutical industry, is that the qualifying tests are carried out once only. It is then accepted that if both the materials used and manufacturing conditions remain unchanged, the USP classification is maintained. Economic and ethical (animal testing) reasons drive this. Repeat testing is then at the discretion of the manufacturer.
In today’s biopharmaceutical industry, safety concerns and legislation are driving the requirement for assurance on the biocompatibility of components. Watson-Marlow provides extra assurance to its Bioprene users by conducting batch testing of both raw materials and final tubing.
This testing is not the full USP Class VI evaluation but similar tests, which demonstrate that the raw material or tubing should satisfy the full suite of tests, were they to be executed. Thus, each batch of raw material for all three hardness grades 64, 73 and 87 Shore A is tested for USP <87> (cytotoxicity) and USP <661> (physicochemical evaluation). Furthermore, samples of the three types of tubing extruded from their respective batches undergo the same tests – USP <87> and <661>. A fourth grade of tubing is made from a blend of the 73 and 87 raw materials and is therefore covered by the extreme ratios argument cited in the Raw material and tube structure section.
**Animal origin statement**

Bioprene tubing is made from primarily synthetic materials, but some process aids are used in raw material manufacture and these may contain some animal-derived components such as tallow derivatives. We recognize the importance to our customers of understanding the risk to biological safety from the use of such materials. Two considerations are important in assessing the risk from TSE/BSE (transmissible/bovine spongiform encephalopathies) in tallow derivatives. These are the origin of the animals and the processing of the tallow derivatives. We have received the following statements from our raw material supplier which specifically address these considerations.

“When leaving the factory, this product contains substances of animal origin. Based on information received from our supplier(s), the following can be stated regarding the substances of animal origin:

Tallow derivatives are of North American origin. The USDA recognizes that such products are so highly processed so as to be of extremely low risk. See 66 Fed. Reg. 42,595 (August 14, 2001). Specifically, tallow… are processed at high temperatures, high pressures, and in many cases in an alkaline chemical environment.

Similarly, the Commission of the European Communities (EC) has published guidance on safe processing methods for tallow derivatives for use in cosmetics and medicinal products. We have received assurances from our suppliers that they meet or exceed these conditions during production of derivatives from beef tallow. Thus, the processing conditions for the tallow derivatives used comply with Section 6.4 of the European “Note for guidance on minimising the risk of transmitting animal spongiform encephalopathy agents via human and veterinary medicinal products” (EMA/410/01 Rev.3 – May 2011). Furthermore, the starting materials for the tallow derivatives comply with EC/1774/2002 Article 6 (“Category 3 material”) as published in the Official Journal on October 3, 2002.”

There is no additional risk from processing of the raw material at Watson-Marlow as no extra materials are used in the extrusion of Bioprene tubing.
Physical and mechanical properties

**Raw material and tube structure**

Bioprene is a highly cross-linked synthetic rubber dispersed in a continuous matrix of thermoplastic material (polypropylene). The mean particle size of the rubber is 1 micron or less and this results in very favourable physical properties. The combination of materials gives excellent restitution and pump performance, outstanding fatigue resistance and hence excellent pump life. The harder grades of Bioprene enable higher pressure pumping (up to 7 bar in a suitable pump).

The general chemical resistance of Bioprene tubing is very good, particularly for acids, alkalis and oxidizing substances. For full chemical resistance details please see www.watson-marlow.co.uk/wmb-gb/p-chem-a.htm

Bioprene tubing is opaque beige in colour. Slight variations in colour occur between different batches of raw material but this has no impact on either tubing peristaltic performance or biocompatibility.

**Tolerance**

The tolerances on the wall and bore for all standard sizes are shown below (other sizes are available on request). In practice, much tighter tolerances are maintained during production (see note under ‘Control systems’).

<table>
<thead>
<tr>
<th>Bore Diameter (mm)</th>
<th>Wall Thickness (mm)</th>
<th>Tolerance (± mm)</th>
<th>Wall Diameter (mm)</th>
<th>Tolerance (± mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤1.6</td>
<td>0.2</td>
<td>0.8</td>
<td>+0.2, -0</td>
<td></td>
</tr>
<tr>
<td>0.5 – ≤ 4.0</td>
<td>0.05</td>
<td>1.05</td>
<td>0.08</td>
<td></td>
</tr>
<tr>
<td>&gt; 0.5 - ≤ 1.6</td>
<td>0.05</td>
<td>&gt; 1.05 - ≤ 1.6</td>
<td>+0.2, -0</td>
<td></td>
</tr>
<tr>
<td>&gt; 1.6 - ≤ 2.4</td>
<td>0.05</td>
<td>&gt; 1.05 - ≤ 1.6</td>
<td>0.1</td>
<td></td>
</tr>
<tr>
<td>&gt; 2.4 - ≤ 8.0</td>
<td>0.15</td>
<td>&gt; 1.05 - ≤ 1.6</td>
<td>0.1</td>
<td></td>
</tr>
<tr>
<td>0.5 – &lt;2.4</td>
<td>0.17</td>
<td>≥2.4 - ≤ 2.4</td>
<td>0.12</td>
<td></td>
</tr>
<tr>
<td>2.4</td>
<td>0.17</td>
<td>2.4</td>
<td>+0.2, -0</td>
<td></td>
</tr>
<tr>
<td>0.5 – ≤ 9.6</td>
<td>0.17</td>
<td>≥2.4 - ≤ 2.4</td>
<td>0.12</td>
<td></td>
</tr>
<tr>
<td>3.2 – ≤ 12.7</td>
<td>0.20</td>
<td>≥2.4 - ≤ 3.2</td>
<td>0.15</td>
<td></td>
</tr>
<tr>
<td>&gt; 12.7 - ≤ 25.4</td>
<td>0.40</td>
<td>≥2.4 - ≤ 3.2</td>
<td>0.30</td>
<td></td>
</tr>
<tr>
<td>8.0 – ≤ 12.0</td>
<td>0.30</td>
<td>≥3.2 - ≤ 4.0</td>
<td>0.30</td>
<td></td>
</tr>
<tr>
<td>&gt;12.0 – ≤ 17.0</td>
<td>0.40</td>
<td>≥3.2 - ≤ 4.0</td>
<td>0.30</td>
<td></td>
</tr>
<tr>
<td>&gt; 9.6 – ≤ 12.7</td>
<td>0.30</td>
<td>≥4.0 - ≤ 4.8</td>
<td>0.40</td>
<td></td>
</tr>
<tr>
<td>&gt;12.7 – ≤ 25.4</td>
<td>0.40</td>
<td>≥4.0 - ≤ 4.8</td>
<td>0.40</td>
<td></td>
</tr>
<tr>
<td>&gt; 25.4</td>
<td>0.50</td>
<td>≥4.0 - ≤ 4.8</td>
<td>0.40</td>
<td></td>
</tr>
<tr>
<td>&gt; 25.4 – ≤ 38.1</td>
<td>0.50</td>
<td>≥4.8 - ≤ 6.4</td>
<td>0.50</td>
<td></td>
</tr>
<tr>
<td>&gt; 38.1 – ≤ 44.5</td>
<td>0.70</td>
<td>≥4.8 - ≤ 6.4</td>
<td>0.75</td>
<td></td>
</tr>
<tr>
<td>25.0</td>
<td>0.4</td>
<td>9.0</td>
<td>0.25</td>
<td></td>
</tr>
</tbody>
</table>
Mechanical properties

64(1) Grade Bioprene

<table>
<thead>
<tr>
<th>Property tested</th>
<th>Minimum</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hardness/durometer Shore A (5s)</td>
<td>62</td>
<td>68</td>
</tr>
<tr>
<td>Specific gravity at 23C</td>
<td>0.95</td>
<td>0.99</td>
</tr>
<tr>
<td>Ultimate tensile strength</td>
<td>798psi / 5.5MPa</td>
<td>99999 / 687MPa</td>
</tr>
<tr>
<td>Elongation at break</td>
<td>340%</td>
<td>600%</td>
</tr>
<tr>
<td>Stress at 100% elongation</td>
<td>276psi / 1.9MPa</td>
<td>435psi / 3.0MPa</td>
</tr>
</tbody>
</table>

(1) Standard 933.xxx.xxx Bioprene tubing is made from 64 Grade raw material

73(2) Grade Bioprene

<table>
<thead>
<tr>
<th>Property tested</th>
<th>Minimum</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hardness/durometer Shore A (5s)</td>
<td>71</td>
<td>68</td>
</tr>
<tr>
<td>Specific gravity at 23C</td>
<td>0.95</td>
<td>0.99</td>
</tr>
<tr>
<td>Ultimate tensile strength</td>
<td>1044psi / 7.2MPa</td>
<td>99999 / 687MPa</td>
</tr>
<tr>
<td>Elongation at break</td>
<td>380%</td>
<td>99999%</td>
</tr>
<tr>
<td>Stress at 100% elongation</td>
<td>406psi / 2.8MPa</td>
<td>638psi / 4.4MPa</td>
</tr>
</tbody>
</table>

(2) 4 bar 620 elements, all ‘P’ rated tubing (e.g. 933.0064.P24) and all 2 bar 800 series tubing (e.g. 088.T250.00P) are made with 73 Grade raw material

87(3) Grade Bioprene

<table>
<thead>
<tr>
<th>Property tested</th>
<th>Minimum</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hardness/durometer Shore A (5s)</td>
<td>85</td>
<td>91</td>
</tr>
<tr>
<td>Specific gravity at 23C</td>
<td>0.93</td>
<td>0.97</td>
</tr>
<tr>
<td>Ultimate tensile strength</td>
<td>2002psi / 13.8MPa</td>
<td>99999 / 687MPa</td>
</tr>
<tr>
<td>Elongation at break</td>
<td>500%</td>
<td>99999%</td>
</tr>
<tr>
<td>Stress at 100% elongation</td>
<td>885psi / 6.1MPa</td>
<td>1131psi / 7.8MPa</td>
</tr>
</tbody>
</table>

(3) Only one element (933.H032.PFT) uses solely 87 Grade raw material. Elsewhere it is blended with the materials above to achieve the required hardness

Burst pressure

<table>
<thead>
<tr>
<th>Tubing grade</th>
<th>Maximum pressure</th>
<th>Burst</th>
<th>Pressure rating</th>
<th>Safety factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>64</td>
<td>9.8</td>
<td>5</td>
<td>2</td>
<td>2.5</td>
</tr>
<tr>
<td>73</td>
<td>13</td>
<td>6</td>
<td>4</td>
<td>1.5</td>
</tr>
<tr>
<td>87</td>
<td>41</td>
<td>39</td>
<td>7</td>
<td>5.6</td>
</tr>
</tbody>
</table>

All pressures are measured in bar atmospheres. The burst pressures were assessed using a hydrostatic test method BS EN ISO 1402 1997. Three tests were carried out on each grade of tubing and the results are the mean values. Note that burst pressure is generally less than the maximum pressure due to plastic deformation of the tube and ‘ballooning’.
**Permeability**

These tests apply to standard Bioprene made from 64 Grade material.

<table>
<thead>
<tr>
<th>Gas</th>
<th>Permeability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Air</td>
<td>2.8 x 10^-8</td>
</tr>
<tr>
<td>Nitrogen</td>
<td>2.2 x 10^-8</td>
</tr>
<tr>
<td>O₂</td>
<td>5.8 x 10^-8</td>
</tr>
<tr>
<td>CO₂</td>
<td>3.5 x 10^-8</td>
</tr>
</tbody>
</table>

Permeability = \( \frac{\text{cm}^3 \text{gas(RT). cm thick}}{\text{sec}.\text{ cm}^2.\text{ atm}.\Delta r} \)

For example, CO₂ permeability = 3.5\(\times\)10^-8 cm³ carbon dioxide gas (RT) will move across a 1 cm thick Bioprene sheet every second for every cm² surface area and for every 1 atmosphere difference in pressure.

**Safety aspects**

At normal operating temperatures, including autoclave temperatures, Bioprene is non-toxic. If Bioprene is heated to processing temperatures (>circa 150°C/302°F) fumes are released which can cause respiratory tract irritation. If fumes are inhaled, remove the affected individual to fresh air.

The self-ignition temperature of Bioprene is >370°C (700°F); water spray, foam, dry chemical or CO₂ extinguishing agent can be used. Carbon monoxide, formaldehyde and other toxic decomposition products are liberated when Bioprene is ignited.

No special handling precautions are required for Bioprene; there are no potential health effects (other than when the tubing is heated to extremes as outlined above).
Traceability and storage

Packaging (bag, box) is labelled with the part number, product description, lot number and use-by date and a barcode of this information. The certificate of conformance contains the same information without the barcode.

As part of the Watson-Marlow Limited ISO9001:2008 system, lot records and process data are stored for all tubing produced in the plant. Full lot traceability to raw material supply is therefore assured. All records are kept for the shelf life of the tubing. For security, paper production records are scanned and the pdf files held on a backed-up drive. All records are kept for at least the shelf life of the tubing. The lot number of the tubing enables the raw material lot numbers, key equipment production equipment and production personnel to be identified for any batch of extruded tubing.

The plastic packaging used in direct contact with the tubing is also lot traceable and lot records are kept for the shelf life of the tubing.

A sample of every production batch of Bioprene tubing is retained for reference.

Packaging
Bioprene tubing is double-bagged in two heat-sealed polyethylene bags in the cleanroom. The standard coil length is 15m/50’; other coil lengths or cut lengths are available on request. Tubing reels are also available for 1.6, 2.4 and 3.2mm wall tubing.

The 15m/50’ Bioprene coils are packed in a corrugated card outer box outside of the cleanroom. Bioprene tubing reels are double-bagged with a cardboard outer.

825 (088.T250.XXX) series tubing is packed in cut lengths in a plastic sleeve in the cleanroom.

Shelf life
The use-by date of the tubing is included on the bag and the box labels. To maintain the performance of the tubing throughout its life, tubing should be stored in a dry environment away from direct sunlight.

Normal ambient temperatures are recommended but storage within the following range, -10C to 40C (14 to 104F), is allowable without loss in performance. Tubing should be equilibrated to ambient conditions before use.

High humidity should be avoided as Bioprene tubing can absorb small quantities of moisture, although this will not affect the physical performance of the tubing.

Stock should be rotated on a FIFO (first in, first out) basis. The performance of any tubing beyond its use-by date, or which has not been stored according to the recommendations outlined above, cannot be assured.

Wherever possible, original packaging should be maintained.
Sterilisation, welding and operating temperature

Bioprene tubing may be sterilised using:
- Gamma radiation (maximum recommended 35kGy, but tubing has been tested to 40kGy)
- Autoclave (1 bar / 14.5psi, 121C/250F for elements; continuous tubing can be autoclaved at 134C/273F).
- EtO (ethylene oxide).

Welding

Bioprene tubing can be thermally bonded by a variety of techniques, including hot plate, multipoint, hot air, spin, linear vibration and electromagnetic induction. The surface temperature of the tubing needs to be heated to above the melting point of 155 to 160C (311 to 320F), with sufficient surface contact to achieve adequate bonding.

Bioprene can be very successfully bonded to itself or polypropylene, with bond strengths of 50 to 70% of the original material. The optimum bond conditions will depend on the process used and the wall thickness of the tubing. Generally, thinner wall thickness tubes will require either shorter melt times and/or lower melt temperatures. Under- or overheating should be avoided, as this will reduce the bond strength.

It is also possible to bond Bioprene to other materials, but the bond strength may be lower. Please contact Watson-Marlow concerning your specific welding requirements.

Working temperature range

Bioprene tubing can be used in a pump from +5C to +80C. In static applications the working temperature range can be extended. The brittle temperature is <-60C.
Control systems

Bioprene tubing is extruded in an ISO 14644-1 class 7 (class J/10,000) clean room according to cGMP principles, operating within an ISO9001:2008 quality system. The cleanrooms are air-conditioned ensuring that temperature and humidity are controlled and maintaining a stable extrusion environment. The air conditioning is run 24 hours per day, 365 days per year to eliminate any variation in atmospheric conditions.

Key processes including raw material handling, drying and extruding through to finished product packaging are documented in detail in Standard Operating Procedures (SOPs) and Work Instructions (WIs) to ensure batch-to-batch consistency. In addition, all key production variables are monitored using process control to ensure consistently high quality tubing.

Raw materials are stored in hermetically sealed bags until immediately prior to use. Prior to the manufacture of Bioprene tubing, the raw material is dried for a pre-determined period to ensure the correct conditions for extrusion.

The Watson-Marlow manufacturing process line uses closed loop feedback control from an on-line laser micrometre to ensure tight dimensional tolerances are maintained at all times - tighter than those outlined in the table above (section marked Tolerance).

In addition, periodic off-line inspections of tube appearance and dimensions are carried out. Batch production records, detailing raw material lot numbers, primary production equipment and key process variables are retained. A sample of every production batch of Bioprene tubing is retained.
Company and quality systems

Watson-Marlow Limited was founded in 1956, producing the first successful peristaltic pump. In 1969 the company moved to Falmouth, England, into a facility that now comprises over 7,500 square meters (80,000 square feet) of production and office space.

Watson-Marlow Limited is a wholly owned subsidiary of Spirax-Sarco Engineering plc. Spirax-Sarco is headquartered in Cheltenham, England, and is listed on the London Stock Exchange.

Watson-Marlow employs ISO 9001 quality systems in every part of its business. Watson-Marlow also has ISO 14001:2004 certification for environmental management.

Mission statement; Watson-Marlow

- Is the world leader in solving fluid handling problems with peristaltic pumping technology
- Is approved to BS EN ISO 9001, BS EN ISO 14001 and BS OHSAS 18001
- Strives to provide its customers with nothing less than the best products, service and knowledge
- Is committed to continual improvement in every area of its business
- Conducts its business ethically, and stands by its word, its recommendations and its products
- Provides a safe working environment, open communications, and opportunities for advancement for all employee

David Cole
Managing Director, Watson-Marlow
Issue 8 April 2010
CERTIFICATE OF APPROVAL

This is to certify that the Quality Management System of:

Watson-Marlow Ltd
Bickland Water Road, Falmouth, Cornwall
United Kingdom

has been approved by Lloyd's Register Quality Assurance to the following Quality Management System Standards:

ISO 9001:2008

The Quality Management System is applicable to:


This certificate forms part of the approval identified by certificate number LRQ 0773000

Approval Certificate No: LRQ 0773000/B

Original Approval: 13 July 1994
Current Certificate: 1 August 2012

Issued by: Lloyd's Register Quality Assurance Limited
Watson-Marlow environmental policy

With over one million peristaltic pumps designed, manufactured and sold around the world, Watson-Marlow has identified the importance of its environmental aspects and impacts. The company aims to continually improve its environmental performance in the design, development, manufacture and in-house repair of peristaltic pumps and accessories, the supply of associated products and development and manufacture of tubing.

To achieve improvement we operate an Environmental Management System that as a minimum meets the requirements of ISO14001 and have set the following general aims:

• Identify the significant environmental impacts of our company’s activities
• Aim to continually improve the environmental performance of our company by setting environmental objectives, targets and processes
• Promote optimum and efficient use of resources and energy
• Work towards the reduction or elimination of any potential or actual pollution
• Raise the awareness and understanding of all staff about the company’s environmental policy and maintain awareness of environmental issues and related matters
• Provide interested parties with relevant and appropriate information and establish open and on-going dialogue
• Ensure these aims are achieved by the use of appropriate processes that will be monitored, audited, reviewed and improved if necessary
• It is the responsibility of directors and managers to be aware of environmental risks and regulations and to identify and implement best practice
• The Operations Director has specific responsibility to monitor and implement our environmental system

Specifically,

Legislation: We meet or, where practical, exceed all UK legislative, regulatory and other requirements appropriate to our business.

Product design: We select materials to eliminate hazardous substances (RoHS), ensure resource saving and make continual improvement in energy efficiency, keeping ‘end of life’ in mind.

Manufacturing: Ensuring efficient processes we reduce material use, minimise waste and emissions and ensure energy efficiency within our processes.

Use: Our designs ensure controllability to reduce energy consumption and our increased tube life and controlled waste minimises risk of contamination throughout the world.

Applications: Environmental applications, water treatment, control of hazardous substances, contributing to a cleaner environment.

End of Life: Where practical Watson-Marlow pumps are produced from recyclable materials and simple disassembly ensures end of life issues are minimised.

David Cole
Managing Director, Watson-Marlow Limited.
Issue 8 June 2010
ISO 14001: Watson-Marlow Ltd

CERTIFICATE OF APPROVAL

This is to certify that the Environmental Management System of:

Watson-Marlow Ltd
Bickland Water Road, Falmouth, Cornwall
United Kingdom

has been approved by Lloyd’s Register Quality Assurance to the following Environmental Management System Standard:

ISO 14001: 2004

The Environmental Management System is applicable to:


This certificate forms part of the approval identified by certificate number LRQ 0773000

Approval Certificate No: LRQ 0773000/A

Original Approval: 26 July 2001
Current Certificate: 1 August 2012

Issued by: Lloyd’s Register Quality Assurance Limited

This document is subject to the provision on the reverse

7 Fenchurch Street, London EC3M 4BD United Kingdom

This approval is carried out in accordance with the LRQA management and certification processes and monitored by LRQA.

The use of the UKAS Accreditation Mark indicates Accreditation in respect of those activities covered by the Accreditation Certificate Number 001.
Certificate of Conformance

A certificate of conformance is delivered with each product lot. A sample is reproduced here.

This certifies that Watson-Marlow Bioprene tubing is manufactured in Falmouth, UK, in an ISO14644-1 Class 7 (Class J/10,000) cleanroom according to cGMP principles, operating within an ISO 9001 quality system.

Bioprene meets the requirements of USP Class VI (70C), USP<87>, ISO 10993-4, and ISO 10993-10 tests. It also meets FDA 21CFR177.2600(e) (aqueous food). Further details on these and additional tests may be found in the validation pack. A Drug Master File (DMF) has been submitted to the FDA.

The raw material used in the production of Watson-Marlow Bioprene tubing meets the requirements of USP Class VI (121C) and conforms to NSF51.

The raw material supplier asserts adherence to the EMA 410/01 rev.3 regulations with regard to the use and processing of animal-derived materials in the manufacture of the raw material. Watson-Marlow does not add any additional material in the manufacture of Bioprene.

On-going biocompatibility assurance is provided by batch testing of both raw material and tubing extruded from it.

Material Analysis

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
<th>Specification Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hardness/durometer Shore A</td>
<td>65.000</td>
<td>62.000 - 68.000</td>
</tr>
<tr>
<td>Specific gravity</td>
<td>0.980</td>
<td>0.950 - 0.990</td>
</tr>
<tr>
<td>Ultimate tensile strength (psi)</td>
<td>957.200</td>
<td>798.000 - 99999.000</td>
</tr>
<tr>
<td>Elongation at break (%)</td>
<td>460.000</td>
<td>340.000 - 99999.000</td>
</tr>
<tr>
<td>Stress at 100% elongation (psi)</td>
<td>362.000</td>
<td>276.000 - 435.000</td>
</tr>
</tbody>
</table>

The tubing part number, lot number and use-by date are included on the tubing bag and box labels.

Tubing should be be stored under dry conditions away from direct sunlight. Ambient temperatures are preferable but storage between -10C and 40C (14F to 104F) is allowable without loss in performance. Wherever possible, original packaging should be retained.

The performance of any tubing beyond its use-by date or where it has not been stored according to the above recommendations, cannot be guaranteed.

Quality Assurance

This is to certify that the above designated material complies with the stated specifications when supplied in the original packaging.

Frank Bason,
Quality, Health & Safety and Environmental Controller.

For further information contact your local Watson-Marlow representative.

For contact details visit our website:
www.wmtubing.com
Appendix

Links to Toxikon certificates
64 Grade Bioprene tubing:

USP Class VI <88> Systemic toxicity
USP <87> Cytotoxicity
10993-4 Indirect haemolysis
10993-10 Kligman maximization test
21 CFR 177:2600 Total extractables: Rubber Articles Intended for Food Contact (aqueous)
USP <661> Physicochemical tests
USP <85> Bacterial endotoxin test
EPA 8082 PCBs test
USP <381> Physicochemical tests on elastomeric closures for injections

73 Grade Bioprene tubing:
USP <87> Cytotoxicity

87 Grade Bioprene tubing:

USP Class VI <88> In vivo toxicity
USP <87> Cytotoxicity
10993-10 Kligman maximization test