wmarchitect
single-use solutions

**Validation summary guide**

# Fill/finish single-use assemblies

WATSON MARLOW Fluid Technology Solutions

This is the summary validation guide for WMArchitect™ fill/finish assemblies. 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/

## Contents

# 1. Introduction

WMArchitect™ single-use solutions deliver sterility assured configurations for a wide range of bioprocessing applications including Fill/Finish. In support of Watson-Marlow Flexicon Filling Systems, WMArchitect manages a range of standard components and assemblies for use in Flexicon's filling and dispensing equipment. All fluid-contacting components have been validated to fulfil requirements for aseptic filling of pharmaceutical products. This validation guide covers the components, materials, and the manufacturing processes, including sterilisation of the whole assembly.

Standard WMArchitect fill/finish single-use assemblies are made to optimised specifications (specific to Flexicon systems) at our BioPure manufacturing facility in Havant, UK.

Custom configurations are available upon request. Depending on the extent of customisation, this validation guide may or may not apply. Please check with your local Watson-Marlow representative when necessary.

Standard WMArchitect fill/finish single-use assemblies will be from now known as filling assemblies.

# 2. Conditions of use

Filling assemblies are suitable for use using 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 25–45 kGy | 10°C–35°C (50°F–95°F) | Ambient Temperature |
| ISO 9001 quality management system | ISO 11137-2 sterilisation including dose mapping validation | | Dry environment, away from direct sunlight |
| ISO 14001 environmental management | Radiation-sensitive strip*: Changes colour upon exposure | | No exposure to chemicals or stress |
| | Lot release irradiation certificate provided | | |

* production control measure.

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

Based on the material of construction, filling assemblies are compatible with a variety of fluids including weak and strong acids and bases. For specific applications, it is advisable for fill/finish assemblies to be tested under actual process conditions (see section 5 validation testing services).

# 4. Validation testing

Each assembly has a unique lot number that enables each component to be fully traced to its constituent materials. Reference is also made to the quality processes employed at every stage in the manufacture of the assemblies.

Each component is represented within model assemblies and tested routinely for:

- Endotoxin (USP <85>)
- Particulate (USP <788>)
- Sterility assurance (ISO 11137)

Please note that compliance stated in Table 2 may come from the suppliers of the various components and not be based on in-house testing.

## 4a. Summary table

*Table 2. Testing summary of evaluated standards.*

| Product | Biocompatibility | | | | | | | | | | Physiochemical/ Material Safety | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | USP <85> Endotoxin | USP <87> Biological Reactivity, *in vitro* | USP <88> Biological activity, *in vivo* | USP <788> Particulate | FDA 21 CFR part 177 Food additives | ISO 10993-4 Interactions with blood | ISO 10993-5 - Cytotoxicity | ISO 10993-6 - Implantation | ISO 10993-10 - Sensitisation | ISO 10993-11 – Systemic Toxicity | ADCF or EMA/410/01 | USP <661> Materials of Construction |
| **Product bag** | ✓ | ✓ | ✓ | ✓ | | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| **Accusil™ tubing** | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | |
| **PEI 1000 filling nozzle** | ✓ | ✓ | ✓ | ✓ | | | ✓ | | | | ✓ | |
| **Stainless steel/ PEEK filling nozzle** | ✓ | | | ✓ | | | | | | | ✓ | |
| **Y-connector** | ✓ | | | ✓ | | | | | | | ✓ | |
| **Straight connector** | ✓ | | | ✓ | | | | | | | ✓ | |
| **Straight reducer connector** | ✓ | | | ✓ | | | | | | | ✓ | |
| **Quick release inlet connector** | ✓ | ✓ | ✓ | ✓ | ✓ | | ✓ | | ✓ | ✓ | ✓ | ✓ |
| **Filters – Sartopore 2** | ✓ | | ✓ | ✓ | | | | | | | ✓ | |

## 4b. Components in the fluid path

### Single-use product bags

The product bags are made of low-density polyethylene (LDPE) films which are separated by an ethylene-vinyl alcohol copolymer (EVOH) gas barrier film.

*Table 3. Testing summary of single-use product bags.*

| Test | Description | Result |
|---|---|---|
| USP Class VI | Material biocompatibility | PASS |
| USP <85> | Bacterial endotoxins test | PASS |
| USP <87> | Biological reactivity tests, *in vitro* | PASS |
| USP <88> | Biological reactivity tests, *in vivo* | PASS |
| USP <661> | Plastic packaging systems and their materials of construction | PASS |
| USP <788> | Particulate matter in injections | PASS |
| ISO 10993-4 | Biological evaluation of medical device, Selection of tests for interactions with blood | 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<br>Klingman maximisation | Biological evaluation of medical devices, Tests for skin sensitisation | PASS<br>PASS |
| ISO 10993-11 | Biological evaluation of medical devices, Tests for systemic toxicity | PASS |
| European Pharmacopeia 3.1.5 | Polyethylene with additives for containers | PASS |
| Extractables | Analysis of material extracts for organic extractables and extractables metals | REPORT |

### Tubing

Flexicon Accusil™ tubing is entirely manufactured from virgin raw material: no rework material is used. Full traceability is assured through the lot number of the tubing, enabling identification of the raw material throughout manufacture, and in the quality control and production records.

*Table 4. Testing summary of Accusil tubing.*

| 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 <381> | Elastomeric closures for injections | PASS |
| USP <788> | Particulate matter in injections | PASS |
| ISO 10993-4 | Biological evaluation of medical device, Tests for interactions with blood | 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 |

| Test | Description | Result |
|---|---|---|
| ISO 10993-10<br>Klingman maximisation | Biological evaluation of medical devices, Tests for skin sensitisation | PASS<br>PASS |
| ISO 10993-11 | Biological evaluation of medical devices, Tests for systemic toxicity | PASS |
| European Pharmacopeia 3.1.9 | Silicone elastomer for closures and tubing | PASS |
| Extractables | Analysis of material extracts for organic extractables and extractables metals | REPORT |

### Filling nozzles

Two types of filling nozzle are available for filling assemblies: SUSTA PEI and PEEK/ stainless steel.

- PEI 1000 filling nozzle

*Table 5. Testing summary of PEI filling nozzles.*

| 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 |
| Food and Drug Administration (FDA) guidance | Nitrosamines | REPORT |
| BioPhorum Operational Group (BPOG) | Analysis of extractables | REPORT |

- Stainless steel/PEEK filling nozzle

Only the stainless steel (AISI 316 L) has contact with the fluid pathway.
This material has been evaluated for endotoxin USP <85>, particulate USP <788> and sterility assurance ISO 11137 during internal periodic testing.

### Fittings

Y-connectors, straight connectors and reducing connectors are made from KYNAR 740 (PVDF).

*Table 6. Testing summary of inlet connectors.*

| Test | Description | Result |
|---|---|---|
| Extractables | Analysis of material extracts for organic extractables and extractables metals | REPORT |

This material has also been evaluated for endotoxin USP <85>, particulate USP <788> and sterility assurance ISO 11137 during internal periodic testing.

### Inlet connectors

These connectors (male and female) are constructed from moulded Class VI polycarbonate.

*Table 7. Testing summary of inlet connectors.*

| Test | Description | Result |
|---|---|---|
| USP Class VI | Material biocompatibility | PASS |
| USP <85> | Bacterial endotoxins test | PASS |
| USP <87> | Biological reactivity tests, *in vitro* | PASS |
| USP <88> | Biological reactivity tests, *in vivo* | PASS |
| USP <661> | Plastic packaging systems and their materials of construction | PASS |
| USP <788> | Particulate matter in injections | PASS |
| USP <1231> | Water for pharmaceutical purposes | PASS |
| ISO 10993-5 | Biological evaluation of medical devices, Tests for *in vitro* cytotoxicity | PASS |
| ISO 10993-10 | Biological evaluation of medical devices, Tests for 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 |

### Filters

The filters are constructed from polypropylene, housing polyethersulfone membranes (supported by polyester). The manufacturers guarantee compliance to EMEA 410/01 rev.2.

*Table 8. Testing summary of filters.*

| Test | Description | Result |
|---|---|---|
| USP Class VI | Material biocompatibility | PASS |
| Sterile water for injection | Bacterial endotoxins test | PASS |
| Large volume parenterals for single dose infusion | Particulate matter in injections | PASS |

## 4c. Components with no direct fluid contact

### Medical clamps

- USP Class VI polypropylene material

### Cable ties

Nylon cables ties are used in the assembly to secure the tubing to connectors, to product bags, filling nozzles and filters.

### Packaging

Filling assemblies are double pouched, and heat sealed within transparent polyamide/ polyethylene (PA/PE) pouches.

A label specifying the part number, lot number (traceable through to individual batch numbers for all components used in each finished product assembly), date of manufacture and use by date is placed on the outside of the inner pouch. For irradiated and sterile assemblies, a Gamma Irradiation Indicator is present on the label.

ISO 11607 (packaging for terminally sterilised medical devices) (ASTMs F1929, F2054, F1980, and F1886) has been taken as the guide for tests evaluating packaging integrity. These tests follow the principle of establishing that the packaging provides an adequate sterile barrier system for the assembly over its intended lifetime. The packaging meets all the requisite criteria for providing a sterile barrier during transportation in excess of the declared shelf life of two years.

### Control systems

Suppliers are audited on a three-year cycle and qualified for their ability to supply components according to specification, encompassing not only the physical part but also the cleanliness of packaging. Incoming parts are checked by our quality assurance department.

## 5. Validation Testing

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

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

## 6. Conclusions

WMArchitect fill/finish single-use assemblies 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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