Mycap® Bottle Closure

Validation Guide

SARTORIUS

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1. Introduction

Sartorius's Mycap® bottle closures and fluid management systems with Mycap® bottle closures are used in a variety of process areas for and in support of the discovery, development and clinical or commercial productionof drug products such as vaccines, recombinant proteins and monoclonal antibodies.

Fluid management systems with Mycap® bottle closures are qualified, manufactured and released under a quality control system which is compliant to the key principles of cGMP.

This Validation Guide describes qualification of materials, performance specifications, manufacturing conditions and quality control systems of fluid management systems with Mycap® bottle closures.

1.1 Scope Statement

Mycap® is a one-piece closure system for containers with threaded closures. Mycap® bottle closures feature integral tubing and a robust platinum-cured silicone seal. Mycap® bottle closures are available as free-standing units or as part of a fluid management system which may include containers, connectors, tubing, filters and other accessories.

Wherever possible, 'Sartorius' refers to our supplier's product validation documentation. Supplier documentation is available on request or by contacting the supplier directly.

1.2 Security of Supply

Assurance and security of supply is a significant market requirement for Mycap® bottle closures. The robustness of our supply chain relies on effective supplier management, multiple manufacturing sites with consistent industrial and quality processes, process automation, application of lean manufacturing practices, expertise for designing fluid management systems, close collaborative relationships with customers, and senior management's strong commitment to continuous and dynamic improvement.

1.3 Manufacturing Resources

Multiple manufacturing sites and reserve inventory all along the supply chain steps provides a robust business continuity plan. The details for manufacturing sites are mentioned in 'Supply Chain Specification' document; it is available upon request.

1.4 Quality Management System

Sartorius' quality system is compliant to ISO 9001 standard for all manufacturing sites. Mycap® CCX is qualified according to the current applicable regulatory and performance industry standards, as described in this guide.

Sartorius ISO certificates are available on the Sartorius website at:
www.sartorius.com/en/legal-documents/quality-management

These quality system processes direct and inform our entire quality system and all the procedures, work instructions, forms, etc. contained therein.

- Management responsibility and review
- Document control
- Records control and retention
- Corrective and preventive action
- Internal auditing
- Personnel training and competency
- Customer notification and recall

1.5 Gamma Irradiation

Mycap® products are packaged and shipped in cardboard boxes to the sterilization center for gamma irradiation. The sterilizers are qualified according to Sartorius' internal procedures.

Mycap® products are irradiated at a minimum dose of 25.0 kGy. The efficiency of the minimum dose of 25.0 kGy has been validated according to the ISO 11137 standards in order to obtain sterility assurance level (SAL) 10^{-6}.

The certificate of release issued with each lot of products indicates the gamma irradiation run identification number. Each shipment includes a certificate of processing which reports the irradiation dose and lists the lot number(s) of the Sartorius product(s) included in that irradiation run. The two documents may be cross-referenced.

1.6 Validation Test Summary

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- Biocompatibility Testing
  - USP <87>:
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  - USP <88>:
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- Mycap® closure barrier properties
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- Physicochemical
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  - 21 CFR 177.2600:
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  - Melamine
  - Bisphenol A

Monitoring Tests

- Particulate control
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    Particulate matter in injections
  - ISO 14644-1:
    Clean-rooms and associated controlled environments – classification of air cleanliness by particle concentration

- Bioburden and sterility
  - ISO 11137:
    Sterilization of healthcare products dose audit: quarterly
  - ISO 14698:
    Clean-rooms and associated controlled environments – biocontamination control

- Endotoxins
  - USP <85>:
    Bacterial endotoxins test

Lot Release Test

- 100% visual inspection
  - Visible particulate
  - Component defects

- Pressure decay testing of Mycap® closure and immediate connections*

- Packaging and labeling

- Verification of gamma irradiation

*Pressure Decay Testing is performed on lot sample basis when the system includes a bottle.

2. Production and Quality

2.1 Personnel

Sartorius recognizes that human resources and personnel competency are of utmost importance and have therefore established a comprehensive human resources management program. Stringent selection, motivation, initial and continuous training and qualification of personnel at all levels of the company ensure that every employee is at his or her best at all times for each step of the manufacturing and control processes. Comprehensive training records are kept for all employees.

2.2 Facilities

The buildings, equipment and work environment at Sartorius have been designed to maximize employee comfort and security while complying with the key principles of cGMP for the manufacture of fluid management systems with Mycap® bottle closures destined to the pharmaceutical industry. All infrastructure (equipment, utilities, etc.) that affects the product quality is inventoried and undergoes an appropriate qualification, calibration and maintenance.

2.3 Supply Chain

2.3.1 Supplier Evaluation and Qualification

Suppliers are carefully selected according to internal standards and applicable regulations. Typical requirements for suppliers include the following (not exhaustive list):

- Quality control system
- Quality assurance system
- Facility and clean-room controls
- Product | component lot traceability system
- Change notification procedures

Suppliers are evaluated and approved according to internal standards.

2.3.2 Component and Raw Material Qualification

Each raw material and | or component is qualified. This qualification includes a list of required statements from the supplier that is dependent on the final use of the component and | or raw material. Typical requirements for components that are in contact with the product flow include the following (not exhaustive list):

- USP Class VI and | or ISO 10993 conformity
- TSE | BSE statement
- EP conformity (if applicable)
- Change notification statement
- Reach compliance
- Bisphenol A free

Beyond these requirements, Sartorius may perform qualification of the proposed component and | or raw material internally.

For raw materials, the internal qualification will include physical performance of the component made with this raw material. For components, the qualification will be centered on the testing of the assembly of the new component with other components that will be attached.

2.3.3 Incoming Quality Controls

All raw materials, components and sub-contracted products are inspected on arrival at Sartorius against approved control specifications. Typical testing requirements applied at incoming quality inspection include (not exhaustive):

- Supplier documentation controls (certificates)
- Packaging identification and integrity
- Visual inspection
- Dimensional check

Only approved materials will be allowed to be used in production of fluid management systems with Mycap® bottle closures.

Approved materials are recorded in Sartorius ’s inventory and quality management system; labeled with an internal lot number and designated internal part number; and released for use.

3. Production

3.1 Equipment Qualification

All equipment used in production goes through qualification that includes installation qualification, operational qualification and performance qualification. This qualification effort is carried out by a multidisciplinary team and follows the rules described in the corresponding procedure in our quality system.

Equipment undergoes its applicable calibration schedule as described in our quality system.

3.2 Production Environment

Product manufacturing occurs in an ISO 7 (Class 100,000 clean-room) per ISO 14644-1 and in accordance with the key principles of cGMPs.

Contact us for further details or precise questions about our quality and operating systems or to schedule an on-site audit.

3.2.1 Viable Organism Control and Monitoring

Viable organisms are measured quarterly to monitor the effectiveness of the clean-room management and cleaning procedures and to be compliant to EU GMPs and ISO 14698.

3.2.2 Non-Viable Control and Monitoring

Line clearance, weekly cleaning of equipment and work surfaces, and monthly cleaning of the clean-room reduce and control non-viable particles.

Non-viable readings are periodically monitored to ensure 0.5 $\mu m/m^3$ and 5.0 $\mu m/m^3$ particles are within the ISO Class 7 acceptance criteria, per ISO 14644-1.

3.3 Material Receipt

Components arrive in two forms: double-bagged and clean or bulk-packed and cleaned. Double-bagged and clean materials (tubing, for example) are received into our Class 7 clean-room per incoming inspection and testing procedures.

Bulk-packed items are cleaned and transferred into the clean-room per incoming inspection and testing procedures.

3.4 Traceability and Batch Control

Sartorius has a process and maintains an effective traceability system which can be used in the event of product, component or manufacturing issue to alert affected customers.

Generally, all finished assemblies are composed of components and sub-assemblies. Sub-assemblies are built from components or sub-assemblies. Components are parts that are purchased or manufactured by Sartorius. Each component and sub-assembly has a unique part number. All components and sub-assemblies are assigned a unique lot number on receipt or manufacture | assembly. The lot number is recorded in batch records and maintained in our traceability system.

Batch records provide the operators all the necessary instructions, components and sub-assembly list to execute the designated procedure. Operators fill in batch records including recording lot number of components and sub-assemblies. This data is also entered into the traceability system.

The traceability system and batch record system links all manufacturing steps, components and sub-assemblies to the final assembly, allowing for complete backward and forward traceability of every assembled product.

3.5 In-Process and Product Release Controls

Quality controls are performed at various stages during the manufacturing process. Some of these controls are listed below. Other specific controls dependent on the specific application of the products may be performed but are not listed.

- Product conformity against technical drawing
- Visual inspection
  (particles or contamination, correctness assembly, etc.)
- Pressure decay test (Batch Release)
  Performed when system includes a bottle
- Product packaging controls
- Product labeling controls

After production, every batch of finished products is released by quality assurance before it can be shipped. The release will be documented in the batch record and in the traceability system.

The system for product release is constructed in such a way that only batches that have been released by quality can have the corresponding shipping and billing documents.

A certificate of release is issued for each batch of finished product that is shipped from Sartorius.

3.5.1 Pressure Decay Test

Batches of Mycap® bottle closure systems that include the container are pressure decay-tested before release.

Pressure decay at 2 psi is measured. Pass | fail criteria is a leak rate of less than 0.02 psi.

Only products where the representative for the batch passes pressure decay test are cleared for shipment.

3.5.1.1 Selection of Leak Rate

Deliberate defects were made on devices. Leak rates detected at 2 psi pressure on defective devices were noted and compared with leak rates of devices not made deliberately defective. The threshold of 0.02 psi decay was set.

Related validation testing, including bioburden testing and performance in the field, supports that 0.03 psi decay is a suitable threshold for device integrity.

4. Mycap® Bottle Closure Properties

4.1 Mycap® Structure

Mycap® is a one-piece closure with integral tubing or other components for rigid containers with threaded closures. Tubing or other components are inserted into pre-formed holes. Platinum-addition liquid silicone is dispensed into the cap, bonding to and encasing the inserted tubing or component. The assembly is heat-cured to form the Mycap® closure system.

Only the dispensed liquid silicone should be considered a fluid-contact surface, aside from tubing or components inserted into the cap or components used on the fluid management system with Mycap® bottle closure. This is true regardless of the tube materials, cap size or closure type.

4.2 Cap and Closure Sizes

Nearly any container with a threaded closure can be fitted with a Mycap® bottle closure. Cap and closure sizes available are listed below (not exhaustive list):

- 20–415 (with adaptor)
- 24–415
- 38–430
- 53B
- 83B
- GL25
- GL32
- GL45
- 33 mm
- 38 mm
- 43 mm
- 48 mm
- 70 mm

4.3 Properties

The following table describes general properties of the Mycap® bottle closure only and does not consider properties of tubing, fittings, container or other components that may be included in the fluid management system with Mycap® bottle closure.

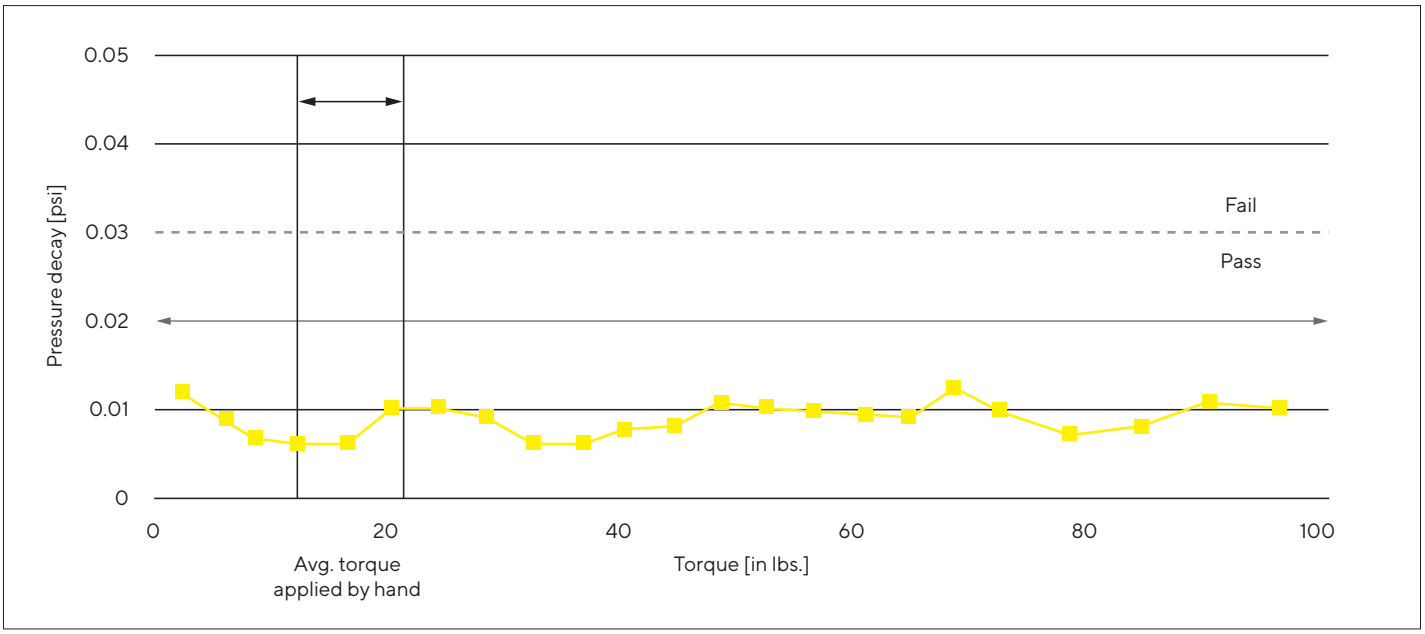
Cap Material (non-fluid contact)	Polycarbonate
Seal material	Platinum-cured silicone
Appearance	Translucent
Maximum use temperature	138 °C
Minimum use temperature	-65 °C
Brittleness temperature (of cap material)	-135 °C
Heat deflection temperature (of cap material)	138 °C
TSE | BSE	Animal derived component free
Container closure by immersion	Pass
USP <87>	Pass
USP <88>	Pass
USP <788>	Pass
USP <85>	Pass
USP <381>	Pass
USP <661>	Pass
21CFR 177.2600	Pass
Melamine content	Melamine free
Bisphenol-A content	Bisphenol-A free
Pthalate content	Pthalate free

4.3.1 Torque Specification

Sartorius considers torque specification provided by a container manufacturer important but not applicable.
The dimensions and materials of the Sartorius Mycap® cap may be different from the cap supplied by the container manufacturer and Mycap® bottle closure includes the robust platinum-cured silicone seal. Silicone has low stress-to-seal properties and provides a leak-free seal across a wide range of torque.

A study was executed to affirm Mycap® bottle closures are easily and appropriately installed.

A torque wrench was used to install Mycap® bottle closures precise torque application for Mycap® closure testing.
Once a closure was torqued to a known value, the vessel was pressure decay tested using TME Worker, Model W-L-015.
Passing criteria is less than 0.03 psi, in accordance with the Mycap® bottle closure pressure decay test. Torque values and corresponding pressure decay results are shown below:



An acceptable pressure decay rate was observed with minimal torque applied, 2 in.-lbs., to material failure at 64 and 100 in.-lbs.

Allowing for a torque error margin, Sartorius recommends a minimum | maximum closure torque of 6 – 40 in.-lbs.

Torque is not measured during Mycap® bottle closure system assembly. Tools are not used in manufacturing to install Mycap® bottle closure. Instead, Sartorius relies on passing pressure decay test results to confirm correct assembly and installation.

A second study was performed to measure torque applied during installation of Mycap® bottle closure to containers by Sartorius manufacturing personnel.

The torque applied by a sampling of operators was measured using torque wrench. The data table is shown on the preceeding graph.

Torque values confirm operators are able to consistently apply closures within the recommended range of 6 – 40 in.-lbs.

4.3.2 Microbial Container Closure

A study to evaluate the barrier properties of Mycap® bottle closures was performed. Barrier properties are measured by immersing the containers into a solution containing a microbial challenge for a specified time, pressure and vacuum.

Tested containers with Mycap® bottle closure were assembled according the Sartorius operating procedures. All containers passed the pressure decay test release criteria. Containers were gamma irradiated and shipped to Nelson Laboratories for test.

Test articles were aseptically filled with soybean casein digest broth (SCDB). The test articles were immersed in a microbial challenge of *Brevundimonas diminuta,* American type culture collection (ATCC) #19146. Vacuum pressure of 5 ± 1 inHg was applied for 10 ± 1 minutes. Pressure is applied to the vessel at 5 ± 0.5 psig for 5 ± 1 minutes.

Containers are removed from the challenge solution inverted so the medium is in contact with the cap and incubated at 30 ± 2 °C for seven days. Containers are inverted at least once during the incubation.

After incubation, each container was observed for growth. All test articles were negative for *Brevundimonas diminuta*a indicating Mycap® bottle closures are a microbial barrier.

The test included positive and negative controls.

Positive controls were aseptically filled with SCDB, punctured with a 22 gauge needle and treated in the same manner as test articles. Positive controls were positive for growth of *Brevundimonas diminuta*.

Negative controls were aseptically filled with SCDB, but not exposed to the challenge solution and instead treated incubated at 30 ± 2 °C for seven days. Negative controls were negative for growth of *Brevundimonas diminuta*.

4.4 Biocompatibility

4.4.1 USP <87>

The purpose of this test is to determine if any chemicals that leach or may be extracted from the Mycap® bottle closure are cytotoxic. The study is conducted in accordance with United States Pharmacopoeia (USP) Section 87.

A 5.9 gram sample of article was extracted in 29.5 mL of 1X minimum essential media (MEM) with 5% bovine serum for 24 - 25 hours at 37 ± 1 °C, with agitation.

Multiple well cell culture plates were seeded with L-929 mouse cells and incubated until 80% confluent. Extract solution was added to the wells. Observations for reactivity were made after incubation for 72 hours at 37 ± 1 °C with 5 ± 1% CO_2.

The requirements of USP Cytotoxicity Test have been met.

4.4.2 USP <88>

Intracutaneous reactivity
The purpose of this test is to determine if any chemicals that leach or may be extracted from the Mycap® bottle closure cause local irritation in the dermal tissue of rabbits. The study is conducted in accordance with United States Pharmacopoeia (USP) Section 88.

A 4 gram test article was placed into 20 mL of extraction solution. Extraction of test articles was performed for 72 ± 2 hours at 50 ± 2 °C. Extract solutions are: normal saline, cottonseed oil, 5% ethanol in saline, polyethylene glycol.

Observations of reactivity in the rabbits were made at 24, 48 and 72 hours after intracutaneous injection of test extracts.

The requirements of USP Intracutaneous Reactivity Test have been met.

Acute systemic injection test
The purpose of this test is to screen extracts from Mycap® bottle closure for potential toxic effects. The study is conducted in accordance with United States Pharmacopoeia (USP) Section 88.

A 4 gram test article was placed into 20 mL of extraction solution. Extraction of test articles was performed for 72 ± 2 hours at 50 ± 2 °C. Extract solutions are: normal saline, cottonseed oil, 5% ethanol in saline, polyethylene glycol.

Observations for biological reaction in rabbits were made at 0, 24, 48 and 72 hours after intravenous and intraperitoneal administration of test extracts.

The requirements of USP Acute Systemic Injection Test have been met.

Intramuscular implant test
The purpose of this test is to study local effects of Mycap® bottle closure when in direct contact with living skeletal muscle tissue of rabbits. The study is conducted in accordance with United States Pharmacopoeia (USP) Section 88.

Test articles were cut into 3 mm × 10 mm pieces. Test articles were surgically implanted into the paravertebral. After seven days, tissue containing the implant was observed for hemorrhage, film, encapsulation, necrosis, discoloration or infections, and recorded.

The requirements of USP Intramuscular Implant Test have been met.

4.5 Particulates

4.5.1 USP <788>

The purpose of this test is to detect and quantify particulate matter in Mycap® bottle closure systems. Particulate matter is defined as extraneous, mobile, undissolved substances, other than gas bubbles unintentionally present in the device.

The USP <788> test is a destructive test and is done as part of product validation. The study is conducted in accordance with United States Pharmacopoeia (USP) Section 788.

Validation testing referred to in this guide was performed on assemblies constructed in the New Oxford site clean-room. The tested assembly was selected because it represents the worse case of facility handling, transport and operator manipulation. The assembly included components from a variety of suppliers and types including: different bottle containers, hose barbed connectors, aseptic connecting devices, vent filters and different tubing sizes with and without Quickseal® aseptic disconnect.

The fluid pathway, including each container of the test article, is filled with low particulate water. Fluid held in each container was pooled for analysis. Particulate from three aliquots from the pooled samples was measured and enumerated using the HIAC Royco Liquid Particle Counting System. The values obtained were averaged.

Acceptance criteria is ≤ 25 particles per mL which are ≥ 10 µm and ≤ 3 particles per mL which are ≥ 25 µm.

The requirement for USP <788> has been met.

Particulate testing is done routinely on products manufactured at Sartorius's New Oxford facility, including Mycap® bottle closure systems to maintain data on particulate manifested on products.

4.6 Endotoxins

4.6.1 USP <85>

The purpose of this test is to detect and quantify bacterial endotoxins in Mycap® bottle closure systems. The Limulus Amebocyte Lysate (LAL) test is an in-vitro, destructive test and is done as part of product validation. The study is conducted in accordance with United States Pharmacopoeia (USP) Section 85 and ANSI | AAMI ST72.

Endotoxins are lipopolysaccharides from the cell wall of micro-organisms. In some cases, endotoxins from gram-negative bacteria may be pyrogenic (fever inducing). Clean-room management procedures described in the New Oxford site quality system include strategies to reduce, control and monitor viable organisms.

Validation testing referred to in this guide was performed on assemblies constructed in the New Oxford site clean-room. The tested assembly was selected because it represents the worse case of facility handling, transport and operator manipulation. The assembly included components from a variety of suppliers and types including: different bottle containers, hose barbed connectors, aseptic connecting devices, vent filters and different tubing sizes with and without Quickseal® aseptic disconnect.

LAL testing is done routinely on products manufactured at Sartorius's New Oxford facility, including Mycap® bottle closure systems to maintain data on endotoxin manifested on products.

The fluid pathway of the test article is flushed with LAL reagent water heated to 37 ± 1 °C. Fluid was kept in contact with the fluid pathway for >1 hour at 18 – 25 °C. The extract solution was then analyzed for endotoxin units (EU). Detected endotoxin was below detection limits of 0.0050 EU/mL.

Sartorius's acceptance criteria is less than 0.25 EU/mL. The requirement for USP <85> has been met.

4.7 Physicochemical and Extractables

4.7.1 USP <381>

This test measures the physicochemical properties of impurities extracted from elastomeric closures. The extract solution is analyzed for acidity | alkalinity, reducing substances, heavy metals and optical absorbance.

A sample of Mycap® silicone closure was extracted in purified water in autoclave at 121°C. The extracted solution is tested per USP <381>.

The acceptance criteria for USP <381> has been met.

4.7.2 21 CFR 177.2600

This test measures the extractable content from a sample of the silicone closure of Mycap® extracted in distilled water for the first seven hours and next two hours of extraction time. Extractable limits are < 20 mg/sq-in for the first seven hours and < 1 mg/sqin for the next two hours.

The acceptance criteria for 21CFR 177.2600 has been met.

5. Leachables and Extractables

Extractables are compounds that have the potential to leach from the materials of the fluid handling system into the solution. The conditions and solvents used in a study of extractables are more extreme than normal process conditions. Aside from the intrinsic properties of the solvent, exposure time and temperature are manipulated in order to extract the most compounds.

Leachables are the compounds that will actually leach from the materials of the fluid handling system into the process fluid. It is important to understand leachables effect on the security, identity, strength, purity or quality of the drug product. Sartorius is not able to provide applicable leachable studies because the conditions and solutions of our customers' processes are unknown.

A risk assessment is advised to determine the extent of leachable and extractable studies required. Considerations should include the production stage, exposure time and temperature, exposure surface area, and the process fluid pH and polarity.

Testing for low-risk profiles may be adequately met by USP <87> and USP <88>, which are leachable and extractable studies. These studies do not identify or quantify compounds leaching the materials. Instead, these studies measure biologic and cytotoxic effects of leachables from the materials under the defined extraction parameters. Per guidelines, extractions are performed using:

Extract solvent	Extraction Time [h]	Extraction Temperature [°C]
Normal saline	72	50
Cottonseed oil	72	50
5% ethanol in saline	72	50
Polyethylene glycol	72	50
1 × minimum essential media (MEM) with 5% bovine serum	24	37

Extracts for all fluid-contact materials of fluid management systems with Mycap® bottle closures are found to have no cytotoxic or adverse biological effect.

Further leachables and extractables data may be necessary for components with high-risk profiles. Confidential information about additional leachable and extractable studies may be available from our component manufacturers.

Sartorius's Confidence® Service is available to perform customized and confidential extractable and leachable studies on polymer-based process components.

6. Gamma Sterilization Validation

6.1 Purpose

A sterilization validation study has been performed to validate sterility assurance level (SAL) 10^{-6} for the fluid pathway fluid management systems with Mycap® bottle closures after gamma irradiation to 25 kGy. The method follows the current ISO 11137 guideline.

6.2 Method

VD_{max}^{25} for multiple production batches procedure described by the ISO 11137 has been selected for this study. The method for 25 kGy as routine minimum dose is applicable to product having an average bioburden less or equal to 1,000 CFU.

6.2.1 Bioburden Evaluation

Nature of raw material, type of components, product design and size, manufacturing process, manufacturing equipment and manufacturing environment have been considered to define the representative product.

The bioburden study is performed on 3 × 10 units of representative products. Samples have been manufactured from 3 batches and packaged under normal production conditions. The bioburden is evaluated according to ISO 11737-1 requirements.

6.2.2 Verification Dose Experiments

The verification dose is determined to produce a SAL 10^{-1} according to the rules defined in the ISO 11137 for method VD_{max}^{25}. It is characteristic of both the bioburden level and the associated maximal resistance. Ten units of representative products have been manufactured and packaged under normal production conditions. They are then irradiated at the selected dose experiment ± 10% according to the ISO 11137-2 recommendations.

6.2.3 Sterility Testing

Individual sterility testing has been performed on these ten irradiated samples. Sterility test meets the criteria: not more than one positive.

6.2.4 Conclusion

The verification dose experiment is accepted as no growth has been observed on the 10 units tested. Therefore, 25 kGy is substantiated as the minimum sterilization dose for Mycap® to obtain SAL of 10^{-6}.

6.2.5 Maintenance of Sterility

Dose audits verifications are performed quarterly on representative products in order to confirm the validity of the 25 kGy minimum dose according to the ISO 11137-2 requirements.

Conclusion
The validation of the sterilization process conducted on Mycap® has met the standard ISO 11137 requirements. Sterility of Mycap® is validated with a SAL of 10^{-6}.

An irradiation certificate, in addition to the certificate of release, is provided with each released batch.

7. Shelf Life

Fluid management systems with Mycap® bottle closures are validated for a two-year shelf life post gamma sterilization, using accelerated aging conditions. If a new component with a shorter shelf life is used in a fluid management system with Mycap® bottle closure, the whole fluid management system will receive the shortest shelf life. Design rules control fluid management systems with Mycap® bottle closures designs.

The critical performance properties and bioburden of the fluid management systems with Mycap® bottle closures is assessed and compared with original properties after a two-year storage in accelerated conditions.

7.1 Bioburden Maintenance

Samples of representative product were gamma irradiated and aged for two years. At the conclusion of the aging, a bioburden evaluation was performed for the fluid pathway.

The fluid pathway was found to be free from bioburden, affirming sterility was maintained after aging.

7.2 Verification of Critical Performance Properties

7.2.1 Container Closure

Samples of representative product were gamma irradiated and aged for two years. At the conclusion of the aging, a container closure study by immersion was conducted, as per section 4.3.2 Microbial Container Closure.

The samples passed the container closure test affirming closure integrity is maintained after aging.

7.2.2 Pressure Decay Test

Samples of representative product were gamma irradiated and aged for two years. At the conclusion of the aging, a pressure decay test was performed as per section 3.5.1 Pressure Decay Test.

The samples passed the release criteria established for newly constructed systems, thus affirming the closure integrity after aging.

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Publication No.: SP-5701-e
Status 11|2024