Microsart® @Filter and Microsart® @Media

Validation Guide

SARTORIUS

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1. Introduction

Pharmaceutical products, as well as water for injections (WFI) and raw materials (especially water), must conform to defined quality standards and regulations. The desired quality of the final product can be ensured only if the entire production process is adequately monitored and controlled. Microbiological in-process and final product quality control tests of non-sterile pharmaceuticals are performed according to the following Pharmacopoeia regulations.

- EP 2.6.12, EP 2.6.13 and USP <61> and <62> on Microbiological Examination of Non-sterile Products
- EP 5.1.4 and USP 2021 on Microbiological Quality of Non-sterile Pharmaceutical Preparations and Substances for Pharmaceutical Use
- EP and USP chapters concerning water (USP 1231, EP and USP Purified Water, Highly Purified Water and Water for Injection)

Even more important than testing is the mitigation of any risks of secondary contamination, particularly at critical manufacturing points where the product is exposed to the environment. The lower the bioburden of raw materials used and the better the analysis of critical control points, the easier a final product can be released following final quality control testing. The process and the methods used for quality control must be validated and need to take all aspects of the product characteristics and of the production process into account.

Validation is indispensable for confirming the safety of any pharmaceutical product. Therefore, it is a logical supplement to and a significant part of the cGMP regulations. Guidelines for validation are given in the U.S. Code of Federal Regulations Title 21 and in various Pharmacopoeias, such as the USP and EP. In addition, guidelines have been jointly established by the Committee for Laboratories and Official Drug Product Inspection Services as well as the Department of Industrial Pharmacists of the Fédération Internationale Pharmaceutique (F.I.P.). These guidelines define validation as follows: "Validation, as used in these guidelines, comprises the systematic testing of essential production steps and equipment in R & D and production departments, including testing and inspection of pharmaceutical products, with the goal of ensuring that the finished products can be manufactured reliably and reproducibly and in the desired quality in keeping with the established production and quality control procedures."

Sartorius follows the "EEC guide to good manufacturing practice" published by the Commission of the European Communities.

This Validation Guide is a compilation of the qualification and validation procedures performed at Sartorius for the combined use of Microsart® @Filter and Microsart® @Media. The detailed information provided is intended to give you guidance on planning, implementing and documenting your own validation procedures for bioburden testing and|or microbial limit testing. Such information covers the test methods used by Sartorius during product development and quality assurance (QA) and|or quality control (QC), ranging from inspection of raw materials to the final release of Microsart® products. In addition, Sartorius can design and perform such validation procedures according to your specific requirements.

Because the Microsart® system constituted by the combination of Microsart® @Filter and Microsart® @Media is designed for touch-free membrane transfer, it reduces the risk of secondary contamination to an absolute minimum. This convenient Quality by Design product will not only save you work, but will also give you confidence in the reliability of the results of your validation testing procedures.

2. Quality and Its Assurance

2.1 Quality Assurance

The consistently high quality of Sartorius products is assured by careful selection of all raw materials in accordance with current regulations, such as FDA, CFRs and cGMP in-house standards; well-planned and validated production technologies; and an exceptionally efficient Quality Assurance Department. All of these measures together result in excellent batch-to-batch reproducibility.

Documentation begins with the inspection of incoming raw materials, including in-process materials, molded parts, glue, etc., for the manufacturing process. Suppliers of these materials and parts are audited regularly. At Sartorius, compliance with cGMP requirements – for example, on cleanroom conditions, gowning and personnel hygiene standards – is monitored by documented in-process quality control tests, ensuring optimal quality control in standard operating procedures for manufacture.

Final Microsart® @Filter and Microsart® @Media products undergo strict final quality control testing, which entails individual tests that are carried out on a representative number of samples. A lot is released only if all in-process and final quality control data are available and confirmed to be within the specifications.

2.2 Complete Traceability

The type, lot number, sterilization and expiration date are printed on each Microsart® @Media dish as well as on the label on each bag and on each box of the product. For Microsart® @Filter this information is given on each bag|tray of Microsart® @Filter (depending on which packaging type is being used) as well as on the outer box of the products. The traceable lot numbers allow convenient retrieval of all data compiled on the materials, production steps and QC tests used.

2.3 DIN EN ISO Certificates

The quality management system of Sartorius AG has been certified for compliance by SQS International Certification Service GmbH with the following standards: the DIN EN ISO 9001 series on quality management systems; DIN EN ISO 14001 on environmental management systems; and DIN EN ISO 50001 on energy management systems. These International Standards have been adopted by the European Standards EN and transposed into national law by German Industrial Standards, DIN.

All certificates can be downloaded from our website at:

https://www.sartorius.com/en/legal-documents

2.4 Product Quality Certificates

The certificates of Microsart® @Filter are enclosed in each package of this product. The certificates of Microsart® @Media can be downloaded from the BD website at:

http://regdocs.bd.com/regdocs/regDocsHomePage.do

2.5 Requirements to Be Fulfilled

2.5.1 General Requirements

Requirements	Steps Needed for Compliance	Tests Completed
A reliable and significant product quality needs to be assured.	Effective quality control procedures must be determined and performed.	QC lot release tests (see Sections 5.1, 5.2)
The products may not deteriorate during transport and storage.	The integrity of the packaging must be maintained up to the time of use. No aging that could affect the function may occur, at least up to the indicated expiration date.	QC lot release tests (see Sections 5.1, 5.2) Shelf life tests (see Sections 4.5, 4.6)
The system must allow the shortest possible test time.	Quick filtration of the sample has to be ensured.	Flow rate for water Wetting time Drop adsorption test (see Section 5.1)
The system must be practical.	Graduated marks to simplify filling. Easy and contamination-free transfer of Microsart® @Filter to Microsart® @Media.	Validation tests (see Section 4.1)
User|environmental safety must be ensured.	The membrane may not burst. Touch-free contamination to prevent bacterial contamination.	Burst pressure test (see Section 5.1) Validation tests (see Section 4.3.2)

2.5.2 Requirements for Microbiological Examination of Non-sterile Products and of Pharmaceutical Water (EP 2.6.12, 2.6.13, 5.1.4, Chapter on Water for Injection; USP 61, 62, 2021, 2022)

Requirements	Steps Needed for Compliance	Tests Completed
Testing has to be carried out under conditions designed to avoid extrinsic microbial contamination of the product to be examined.	The product must be sterile and fully functional. The product design and handling enable customers to avoid extrinsic contamination.	Sterilization validation (see Section 4.4) Validation tests (see Section 4.3)
Membrane filtration method: The method chosen must allow testing of a sufficient sample size. The suitability of the method selected must be verified.	The product design and handling enable customer to use different filtration volumes. Products used for membrane filtration are suitable for this application.	Validation tests (see Sections 4.1.3, 4.3.1, 4.3.2) QC lot release tests (see Section 5)
The ability of the test system to detect microorganisms must be demonstrated.	Perform growth promotion tests with using a sterility test system.	Validation tests (see Sections 143.2.1, 143.2.2) QC lot release tests (see Section 305)
The media must pass growth promotion tests.	Test each batch of medium for growth-promoting ability.	Validation tests (see Section 143.2.1) QC lot release tests (see Section 305)
The enumeration method must be suitable for testing the product.	Perform growth promotion tests using the product.	To be done by the customer.

3. Technical Specifications

3.1 Product Description

Microsart® @Filter units are used for microbial enumeration. They enable reliable detection and enumeration of microorganisms in pharmaceuticals, cosmetics, beverages, water and other liquids. The devices are sterile, ready to use and combine a funnel and a gridded membrane filter all into one unit. The optimized design of Microsart® @Filter permits thorough rinsing of the system after filtration to remove inhibitors; no liquid is retained in the filter funnel.

Microsart® @Media are dishes prefilled with different types of agar medium, sterile-packaged and ready to use. Together with the Microsart® @Filter units, they introduce a brand-new membrane transfer and agar media concept for microbial limit testing. The "active" lid of Microsart® @Media allows touch-free membrane transfer from the Microsart® @Filter base, thus reducing the risk of secondary contamination to an absolute minimum.

Both products have been specifically developed for microbial limit testing according to the USP (Chapter <61>) and EP (Chapter 2.6.12).

3.2 Ordering Information

3.2.1 Microsart® @Filter

Microsart® @Filter 100 with CN membrane (= cellulose mixed ester), sterile single-use filter units with lid, 47 mm, 100 mL, packaged on trays, ideal for use in clean benches, 24 units.

Pore Size [µm]	Membrane Filter* Color | Grid Color	Order No.
0.2	White | Black	16D01--10-07--TG
0.45	White | Black	16D01--10-06--TG
0.45, High Flow	White | Black	16D01--10-H6--TG
0.45, High Flow	Gray | White*	16D03--10-H6--TG
0.45	Green | Dark green	16D02--10-06--TG

Microsart® @Filter 250 with CN membrane (= cellulose mixed ester), sterile single-use filter units with lid, 47 mm, 250 mL, packaged on trays, ideal for use in clean benches, 16 units.

Pore Size [µm]	Membrane Filter* Color | Grid Color	Order No.
0.2	White | Black	16D01--25-07--TF
0.45	White | Black	16D01--25-06--TF
0.45, High Flow	White | Black	16D01--25-H6--TF
0.45, High Flow	Gray | White*	16D03--25-H6--TF
0.45	Green | Dark green	16D02--25-06--TF
0.65	Gray | White*	16D03--25-05--TF

Microsart® @Filter 100 with CN membrane (= cellulose mixed ester), sterile single-use filter units, 47 mm, 100 mL, stacked and packaged in bags, ideal for use with Microsart® Funnel Dispenser, 60 units

Pore Size [µm]	Membrane Filter* Color | Grid Color	Order No.
0.2	White | Black	16D01--10-07--BL
0.45	White | Black	16D01--10-06--BL
0.45, High Flow	White | Black	16D01--10-H6--BL
0.45, High Flow	Gray | White*	16D03--10-H6--BL
0.45	Green | Dark green	16D02--10-06--BL

Microsart® @Filter 250 with CN membrane (= cellulose mixed ester), sterile single-use filter units, 47 mm, 250 mL, stacked and packaged in bags, ideal for use with Microsart® Funnel Dispenser, 48 units

Pore Size [µm]	Membrane Filter* Color | Grid Color	Order No.
0.2	White | Black	16D01--25-07--BK
0.45	White | Black	16D01--25-06--BK
0.45, High Flow	White | Black	16D01--25-H6--BK
0.45, High Flow	Gray | White*	16D03--25-H6--BK
0.45	Green | Dark green	16D02--25-06--BK
0.65	Gray | White*	16D03--25-05--BK

* Gray membranes; black after wetting

Microsart® @Filter 100 with CN membrane (= cellulose mixed ester), individually sterile-packaged, 100 mL capacity, with covers, 27 units

Pore Size [µm]	Membrane Filter* Color | Grid Color	Order No.
0.45, High Flow	White | Black	16D01--10-H6--ACG
0.45, High Flow	Gray | White*	16D03--10-H6--ACG
0.2	White | Black	16D01--10-07--ACG

Microsart® @Filter 250 with CN membrane (= cellulose mixed ester), individually sterile-packaged, 250 mL capacity, with covers, 18 units

Pore Size [µm]	Membrane Filter* Color | Grid Color	Order No.
0.45, High Flow	White | Black	16D01--25-H6--ACF
0.45, High Flow	Gray | White*	16D03--25-H6--ACF
0.2	White | Black	16D01--25-07--ACF

* Gray membranes; black after wetting

Microsart® @Filter 100 with PVDF membrane, sterile single-use filter units, 47 mm, 100 mL, stacked and packaged in bags, ideal for use with Microsart® Funnel Dispenser, 60 units

Pore Size [µm]	Membrane Filter* Color | Grid Color	Order No.
0.45	White | no grid	16D04--10-06--BL

Microsart® @Filter 100 with PVDF membrane, sterile single-use filter units with lid, 47 mm, 100 mL capacity, packed in trays, ideal for use in clean benches, 24 units

Pore Size [µm]	Membrane Filter* Color | Grid Color	Order No.
0.45	White | no grid	16D04--10-06--TG

Microsart® @Filter 100 with PVDF membrane, individually sterile packed, 47 mm, 100 mL capacity, with covers, 27 units

Pore Size [µm]	Membrane Filter* Color | Grid Color	Order No.
0.45	White | no grid	16D04--10-06-ACG

3.2.2 Microsart® @Media

Microsart® @Media prefilled agar media dishes, sterile-double-packaged and ready-to-use, quantity of 100 per box, 10 bags, each containing 10 media dishes.

Media Type	Target Microorganism	Order No.	Typical Incubation Time and Temperature
Microsart® @Media TSA (Tryptic Soy Agar)	Total count	14313–47----ACN	1 to 5 days (EP) or 48 to 72 hrs (USP) at 30 °C to 35 °C
Microsart® @Media SDA (Sabouraud Dextrose Agar)	Yeasts and molds	14314--47----ACN	5 to 7 days at 20 °C to 25 °C
Microsart® @Media R2A	Total count	14322--47----ACN	5 to 7 days at 20 °C to 28 °C

3.3 Technical Specifications

3.3.1 Microsart® @Filter

Materials	Funnel: Polypropylene Base: ABS (acrylonitrile butadiene styrene) Membrane filter: cellulose nitrate (cellulose mixed ester); choice of various colors and grids Bacterial recovery testing has shown that the grid lines do not enhance or inhibit the growth of microorganisms.
Capacity	100 mL; graduated marks at 20, 50 and 100 mL 250 mL; graduated marks at 50, 100, 200 and 250 mL
Filter diameter	47 mm
Filtration area	13.2 cm^2
Pore size	0.2, 0.45, 0.45 High Flow or 0.65 µm The pore size of the 0.2 µm membrane filters is determined by quantitative retention of *Brevundimonas diminuta* in accordance with the ASTM document F838-05 (2005) standard test method for determining the bacterial retention of membrane filters utilized for liquid filtration. The pore size of the 0.45 µm and 0.45 µm High Flow membrane filters is determined by retention of *Serratia marcescens* in accordance with the standard methods of water and wastewater. All membrane filters with a pore size of 0.45 µm meet the requirements of international standards, such as the European Drinking Water Directive 98|83|EC, the European Pharmacopoeia (EP), the U.S. Pharmacopoeia and the American Standard Methods for the Examination of Water and Wastewater (APHA).
Max. operating pressure	Vacuum only
Sterilization	Gamma-irradiation; units have been irradiated to a safety assurance level (SAL) of 10^{-5} The sterilization process does not enhance or inhibit subsequent growth of microorganisms.
pH of filter extract	< 8.3
Thermal resistance	130 °C max.
Thickness acc. to DIN 53105	> 110 µm
Chemical compatibility	Aqueous solutions (pH 4 – 8), hydrocarbons and several other organic solvents
Extractable content in water	< 1 %
Wetting time	< 5 s
Area weight	47.5 g/m^2
Growth promotion test	All the membrane filters tested exhibited excellent growth properties and typical colony morphology when challenged with a solution of approx. 100 colony-forming units (cfu). Recovery rates of total and coliform bacteria show that there is no influence on bacterial growth or development due to chemical extractables. *Escherichia coli* ATCC 8739: recovery ≥ 90 % vs. control lot filter tested according to ISO 7704. *Pseudomonas aeruginosa* ATCC 9027: recovery ≥ 90 % vs. control lot filter tested according to ISO 7704.

Bubble Point with Water (Visual Method acc. to DIN 58355)

Pore Size	0.2 µm	0.45 µm	0.45 µm High Flow	0.65 µm
Bubble point	> 3.5	> 2.0	> 2.0	> 1.8
Burst pressure	0.5 – 0.6 bar			
Typical flow rate for water [mL/(min + cm^2 + bar)]	20	70	100	130

3.3.2 Microsart® @Media

Dimensions	Dish diameter Dish height Agar area	68.8 mm 14.9 mm 13.2 cm^2
Materials		
Lid and base Membrane ring Adhesive	Polystyrene Polypropylene Acrylate Agar media: R2A, TSA, SDA Inhibitor-free glue	
Sterilization	Gamma-irradiation within a range of 11.8 kGy to 25.0 kGy	
Plate appearance	R2A TSA SDA	Pale to light tan and clear to trace hazy Light to medium tan yellow and clear to trace hazy Light tan cream to tan yellow and trace hazy
Fill	8.0 – 9.5 mL	
Gel strength	Firm	
pH at 25 °C	R2A TSA SDA	7.0 – 7.4 7.1 – 7.5 5.4 – 5.8
Animal source	See lot-specific certificates of analysis	

3.3.2.1 Biological Performance of Microsart® @Media

The tests for biological performance were performed with spread plates and membrane filtration versus a reference agar. The inoculum was 10 cfu to 100 cfu for all test strains. TSA with 5 % sheep blood was used as control for all tests.

Specification:
The recovery rate of the test strains must be satisfactory (= 50 % – 200 % compared to the control) and must be comparable to a previously released batch. If the recovery rate cannot be quantified, there must be fair to heavy growth that has to be comparable to the control and to a previously released batch.

Biological Performance for R2A

Strain	ATCC No.	Incubation Temperature	Incubation Time	Results
Bacillus subtilis	6633	30 – 35 °C	3 days	Satisfactory
Candida albicans	10231	35 – 37 °C	18 – 48 hrs	Satisfactory
Escherichia coli	8739	35 – 37 °C	18 – 48 hrs	Satisfactory
Kocuria rhizophila	9341	35 – 37 °C	18 – 48 hrs	Satisfactory
*Pseudomonas aeruginosa**	9027	30 – 35 °C	3 days	Satisfactory
Staphylococcus aureus	6538	35 – 37 °C	18 – 48 hrs	Satisfactory
Staphylococcus epidermidis	12228	35 – 37 °C	18 – 48 hrs	Satisfactory

Biological Performance for TSA

Strain	ATCC No.	Incubation Temperature	Incubation Time	Results
Aspergillus brasiliensis	16404	30 – 35 °C	Up to 5 days	Satisfactory
Aspergillus brasiliensis	16404	20 – 25 °C	Up to 5 days	Satisfactory
Bacillus subtilis	6633	30 – 35 °C	Up to 3 days	Satisfactory
Bacillus subtilis	6633	20 – 25 °C	Up to 3 days	Satisfactory
Candida albicans	10231	30 – 35 °C	Up to 5 days	Satisfactory
Candida albicans	10231	20 – 25 °C	Up to 5 days	Satisfactory
Escherichia coli	8739	30 – 35 °C	Up to 3 days	Satisfactory
Kocuria rhizophila	9341	30 – 35 °C	Up to 3 days	Satisfactory
*Pseudomonas aeruginosa**	9027	30 – 35 °C	Up to 3 days	Satisfactory
Staphylococcus aureus	6538	30 – 35 °C	Up to 3 days	Satisfactory
Staphylococcus epidermidis	12228	30 – 35 °C	Up to 3 days	Satisfactory

* This strain has also been tested using the membrane filtration method.

Biological Performance SDA

Strain	ATCC No.	Incubation Temperature	Incubation Time	Results
Aspergillus brasiliensis	16404	20 – 25 °C	5 days	Satisfactory
Aspergillus fumigatus	26934	20 – 25 °C	5 days	Fair to heavy growth
*Candida albicans**	10231	20 – 25 °C	5 days	Satisfactory
Candida albicans	10231	30 – 35 °C	5 days	Satisfactory
Candida albicans	60193	20 – 25 °C	5 days	Fair to heavy growth
Escherichia coli	8739	30 – 35 °C	18 – 48 hrs	Satisfactory
Trichophyton mentagrophytes	8739	20 – 25 °C	5 days	Fair to heavy growth

* This strain has also been tested using the membrane filtration method.
The inoculum of the tests strains that are not counted is taken directly from plates and, therefore, not quantified.

4. Validation Tests

4.1 Visual Tests

Background
Microsart® @Filter and Microsart® @Media are manufactured under controlled conditions. All parts are treated with care so there are no scratches or any other visible damage. The agar has to be smooth and homogeneous and does not contain any particles or air bubbles. The methods and results are described in the following sections.

For testing the Microsart® @Filter product group, Microsart® @Filter 16D01--10-H6--BL was chosen as representative of this group. The packaging in bags was selected as the type of packaging to provide the worst-case scenario in comparison with the tray version.

4.1.1 Microsart® @Filter

Method
The Microsart® @Filter products containing cellulose nitrate filters were inspected visually for the following:

- Dimensions of the base and funnel match tolerances specified on the drawing
- Volumetric accuracy:
  graduated marks within a tolerance range of ± 10 %
- Base-to-manifold fit (using manual force for attachment):
  bases must engage in|disengage from manifold using the appropriate manual force.
- Base-to-manifold fit (vacuum automatically created):
  bases should fit on the manifold so that a sufficient vacuum can be created to enable rapid filtration.
- Funnel-to-base fit (using manual force for attachment):
  appropriate manual force required for device assembly
- Membrane flatness after assembly:
  membrane must lie flat within a tolerance of 2 mm
- Leak-tightness with 114H6 CN
  (cellulose nitrate = cellulose mixed ester) membrane:
  units leak-tight after 1 min.
- Hold-up volume:
  < 1 mL residual volume after filtration
- The labels of the products and their packaging have to be accurate, complete and identical to the reference photographs of labels.
- There may be no visible scratches or any other damage ≥ 1 cm.

Results

Test	Product Order No.	Lot No.	No. of Samples Tested (per Product | Lot)	Passed* Yes | No
Dimensions match tolerances	V2-00764 1000005669 1000005116	1303005M T15.3.13 T52	8	Yes
Volumetric accuracy	100 mL funnel 250 mL funnel	151033M 1501021M	24	Yes
Base-to-manifold fit (man. force)	16D01--10-H6--BL 16D01--25-H6--BK	1303024RD 1306002RD	180	Yes
Base-to-manifold fit (auto. vacuum)	16D01--10-H6--BL 16D01--25-H6--BK	1303024RD 1306002RD	96	Yes
Funnel-to-base fit (man. force)	16D01--10-H6--BL 16D01--25-H6--BK	1303024RD 1306002RD	96	Yes
Membrane flatness after assembly	16D01--10-H6--BL 16D01--25-H6--BK	1303024RD 1306002RD	180	Yes
Leak-tightness	16D01--10-H6--BL 16D01--25-H6--BK	1303024RD 1306002RD	180	Yes
Hold-up volume	16D01--10-H6--BL 16D01--25-H6--BK	1303024RD 1306002RD	180	Yes
Labeling is accurate, complete and identical to reference photographs.	16D01--10-H6--BL	1303024RD 1305002RD 1305003RD	20	Yes
No visible damage or scratches ≥ 1 cm	16D01--10-H6--BL	1303024RD 1305002RD 1305003RD	20	Yes

* All samples have to be within the specifications to pass.

4.1.2 Microsart® @Media

Method
The Microsart® @Media products were inspected visually for the following:

- Correct labeling of the outer and inner package (tested against reference photographs of labels)
- Visible damage to the packaging: The packaging must be intact; in particular, the inner packaging (bag) must be intact to ensure the sterility of the product.
- Visible damage to Microsart® @Media: There may be no visible scratches or any other damage ≥ 1 cm. No plastic dishes may be broken. The agar must be homogeneous and of uniform color, and not contain any particles.

The visual inspections further included testing of the color and consistency of the agar for a period of 38 weeks, with inspections after 8, 12, 18, 20, 26, 28, 32 and 38 weeks. The samples were stored at 2 °C – 8 °C before testing. The consistency was tested by running a finger over the agar surface by applying slight pressure.

Results

Test	Product Order No.	Lot No.	No. of Samples Tested (per Product | Lot)	Passed* Yes | No
Inspection of labeling of outer and inner packaging	TSA: 14313--47----ACN	3070098 3112270 3170348	20	Yes
	SDA: 14314--47----ACN	3070100 3112269	20	Yes
	R2A: 14322--47----ACN	3070103	20	Yes
The packaging is intact and free of visible damage	TSA: 14313--47----ACN	3070098 3112270 3170348	20	Yes
	SDA: 14314--47----ACN	3070100 3112269	20	Yes
	R2A: 14322--47----ACN	3070103	20	Yes
No visible scratches or any other damage ratches or and free of visible damage agar is homogeneous and of uniform color and does not contain any particles.	TSA: 14313--47----ACN	3070098 3112270 3170348	20	Yes
	SDA: 14314--47----ACN	3070100 3112269	20	Yes
	R2A: 14322--47----ACN	3070103	20	Yes
The agar is firm to the touch, pale to light tan and clear to trace hazy.	R2A: 14322--47----ACN	3283226 3283228 3283236	1 per lot and point in time	Yes
The agar is firm to the touch, light to medium tan yellow and clear to trace hazy	TSA: 14313--47----ACN	3281360 3281364 3282242	1 per lot and point in time	Yes
The agar is firm to the touch, light tan cream to tan yellow and trace hazy	SDA: 14314--47----ACN	3282239 3282240 3282241	1 per lot and point in time	Yes

* All samples have to be within the specifications to pass.

4.1.3 Microsart® @Filter in Combination with Microsart® @Media

For testing of the Microsart® @Filter product group, Microsart® @Filter 16D01--10-H6--BL was chosen as representative of this group. The packaging in bags was selected as the type of packaging to provide the worst-case scenario in comparison with the tray version.

Membrane transfer from Microsart® @Filter base to Microsart® @Media:

- The membrane must be easily transferred to Microsart® @Media. There may be no visible bubbles, pleats or waviness of the membrane on the agar.
- There may be no glue sticking to the underside of the membrane.
- The membrane is glued correctly and uniformly to fit concentrically over the ring of medium in Microsart® @Media.

Results

Test	Product Order No.	Lot No.	No. of Samples Tested (per Product | Lot)	Passed* Yes | No
The membrane can be easily transferred to Microsart® @Media. No visible bubbles, no pleats or waviness of the membrane on the agar.	16D01--10-H6--BL	1303024RD 1305002RD 1305003RD	20	Yes
No glue sticks to the underside of the membrane.	16D01--10-H6--BL	1303024RD 1305002RD 1305003RD	20	Yes
The membrane is glued correctly and uniformly to fit concentrically over the ring of medium in Microsart® @Media	16D01--10-H6--BL	1303024RD 1305002RD 1305003RD	20	Yes

* All samples have to be within the specifications to pass.

4.2 Analytical Tests

4.2.1 pH Measurement of Microsart® @Media

Background
The Microsart® @Media products have a specified pH (see Section 3.3.2). The pH must remain stable throughout the shelf life of the products. The pH of the media was measured by BD in its validation study and is required to be within the specified range (see Section 3.3.2).

Method
The method used is described in the validation report issued by BD.

Results
The results of the pH measurement are documented in the validation report issued by BD. All products passed the test. For further information, please contact BD.

4.2.2 Fill Weight and Media Shrinkage of Microsart® @Media

Background
The Microsart® @Media products have a specified fill volume (see Section 3.3.2) that has to remain stable throughout the shelf life of the products. Measurements of the fill weight and media shrinkage were performed by BD in their validation study. The fill weight and media shrinkage must be within the specified range (see Section 3.3.2).

Method
The method used is described in the validation report issued by BD.

Results
The results of the fill weight and media shrinkage measurements are documented in the validation report issued by BD. All products passed the test. For further information, please contact BD.

4.3 Microbiological Tests

4.3.1 Growth Promotion Tests of Microsart® @Media

Background
For the method according to EP 2.6.12 and USP 61, each lot of growth media must be tested for its growth-promoting ability throughout its shelf life. Therefore, growth promotion of Microsart® @Media has been validated by BD. The products have to be within the specified range (3.3.2.1).

Method
The method used is described in the validation report issued by BD.

Results
The results of growth promotion tests are documented in the validation report issued by BD. All products passed the test. For further information, please contact BD.

4.3.2 Microbial Recovery from Microsart® @Filter and Microsart® @Media

Background
Microsart® @Filter and Microsart® @Media were tested in their intended use to demonstrate their ability to promote the growth of microorganisms. The strains specified by the EP 2.6.12 and USP 61 for the growth promotion tests based on membrane filtration were used in the present validation study.

For testing the Microsart® @Filter product group, Microsart® @Filter 16D01--10-H6--BL was chosen as representative of this product group. The packaging in bags was selected as the type of packaging to provide the worst-case scenario in comparison with the tray version. For the validation tests, 3 lots of Microsart® @Filter were tested in combination with at least one lot of Microsart® @Media with the microorganisms shown below.

Strain	ATCC No.	Manufacturer	Lot Number
Aspergillus brasiliensis	16404	Microbiologics	392-152-1
Bacillus subtilis	6633	LGC Promochem	59138416
Candida albicans	10231	LGC Promochem	Q A 6904
Escherichia coli	8739	LGC Promochem	59740475
Pseudomonas aeruginosa	9027	Microbiologics	484-232-7
Salmonella enterica subsp. enterica serovar typhimurium	14028	Microbiologics	363-123-13
Staphylococcus aureus	6538	LGC Promochem	58834359

Tests were performed per Microsart® @Filter lot according to the validation matrix below.

	Samples to be Plated on Agar					
Test Organism	TSA Merck	TSA Microsart® @Media	Sabouraud Dextrose Merck	Sabouraud Dextrose Microsart® @Media	R2A Oxoid	R2A Microsart® @Media
Bacillus subtilis	20	20			20	20
Escherichia coli	20	20				
Pseudomonas aeruginosa	20	20			20	20
Salmonella enterica subsp. Enterica serovar typhimurium	20	20				
Staphylococcus aureus	20	20				
Aspergillus brasiliensis	20	20	20	20		
Candida albicans	20	20	20	20		

	Filters of Reference Lot (conventional filtration in stainless steel devices)					
Test Organism	TSA Merck	TSA Microsart® @Media	Sabouraud Dextrose Merck	Sabouraud Dextrose Microsart® @Media	R2A Oxoid	R2A Microsart® @Media
Bacillus subtilis	20	20			20	20
Escherichia coli	20	20				
Pseudomonas aeruginosa	20	20			20	20
Salmonella enterica subsp. Enterica serovar typhimurium	20	20				
Staphylococcus aureus	20	20				
Aspergillus brasiliensis	20	20	20	20		
Candida albicans	20	20	20	20		

	Filters per Product Lot					
Test Organism	TSA Merck	TSA Microsart® @Media	Sabouraud Dextrose Merck	Sabouraud Dextrose Microsart® @Media	R2A Oxoid	R2A Microsart® @Media
Bacillus subtilis	20	20			20	20
Escherichia coli	20	20				
Pseudomonas aeruginosa	20	20			20	20
Salmonella enterica subsp. Enterica serovar typhimurium	20	20				
Staphylococcus aureus	20	20				
Aspergillus brasiliensis	20	20	20	20		
Candida albicans	20	20	20	20		

A total of 60 filters per test organism and growth medium were tested, resulting in 440 filters per Microsart® @Filter lot and an overall sample size of 1,320 filters. For robustness testing, *P. aeruginosa* was tested on all three Microsart® @Filter lots with R2A in Goettingen, Germany, and with TSA in India.

Acceptance criteria: the mean recovery of all test organisms by the filters and by Microsart® @Media must be ≥ 70 % compared to reference agar plates (spread plates) and ≥ 80% compared to the reference membrane on reference agar, with confidence intervals of 95 %.

Method

Preparation of the Test Microorganisms (Working Cultures)

For filtration, cells from the cryo-cultures were transferred into 10 mL of liquid TSA medium. Bacteria were incubated at 30 °C – 35 °C for 24 hours. Candida albicans was incubated at 20 °C – 24 °C for 3 – 5 days. These precultures were stored for 1 – 7 days at 4 °C – 8 °C for use in filtration trials.

Aspergillus brasiliensis was purchased in predetermined titers and was suspended according to the suppliers' instructions directly before filtration.

Test Protocol

1. Prepare a serial dilution of the culture to a final concentration of 100 cfu/50 µL.
2. Prepare a spread plate with 50 µL of the cell suspension (100 cfu/50 µL) onto 1 plate of reference agar.
3. Prepare a spread plate with 50 µL of the cell suspension (100 cfu/50 µL) onto 1 plate of Microsart® @Media.
4. Place 2 reference filters and 2 Microsart® @Filter units into the corresponding filtration units (if all 3 validation lots of Microsart® @Filter are tested, use 2 Microsart® @Filter units of each validation lot → 6 filters total).
5. Prefill all 4 funnels with 10 mL of phosphate buffer (all organisms except *B. subtilis*) or peptone buffer (*B. subtilis*) each (with the vacuum tap closed).
6. Add 50 µL of the cell suspension (100 cfu/50 µL) to each funnel, mix gently and filter.
7. Place reference filters onto 1 reference agar plate and 1 Microsart® @Media plate.
8. Place Microsart® @Filter onto 1 reference agar plate and 1 Microsart® @Media plate.
9. Repeat steps 1 – 7 nineteen times (to have 20 samples each).
10. Incubate all agar plates upside down for 24 – 48 h at 30 °C – 35 °C (bacteria) or 1 – 5 days at 20 °C – 24 °C (molds).
11. Check colony morphology and record the cell count; take photos of each plate.
12. Document results and photos.

Only plate counts of 30 to 250 cfu/plate (bacteria) or 15 to 150 cfu/plate (yeasts/molds) were used in this validation. If the titer of more than 3 plates per sample (of 20 samples) was out of this range, the entire test was repeated.

Results

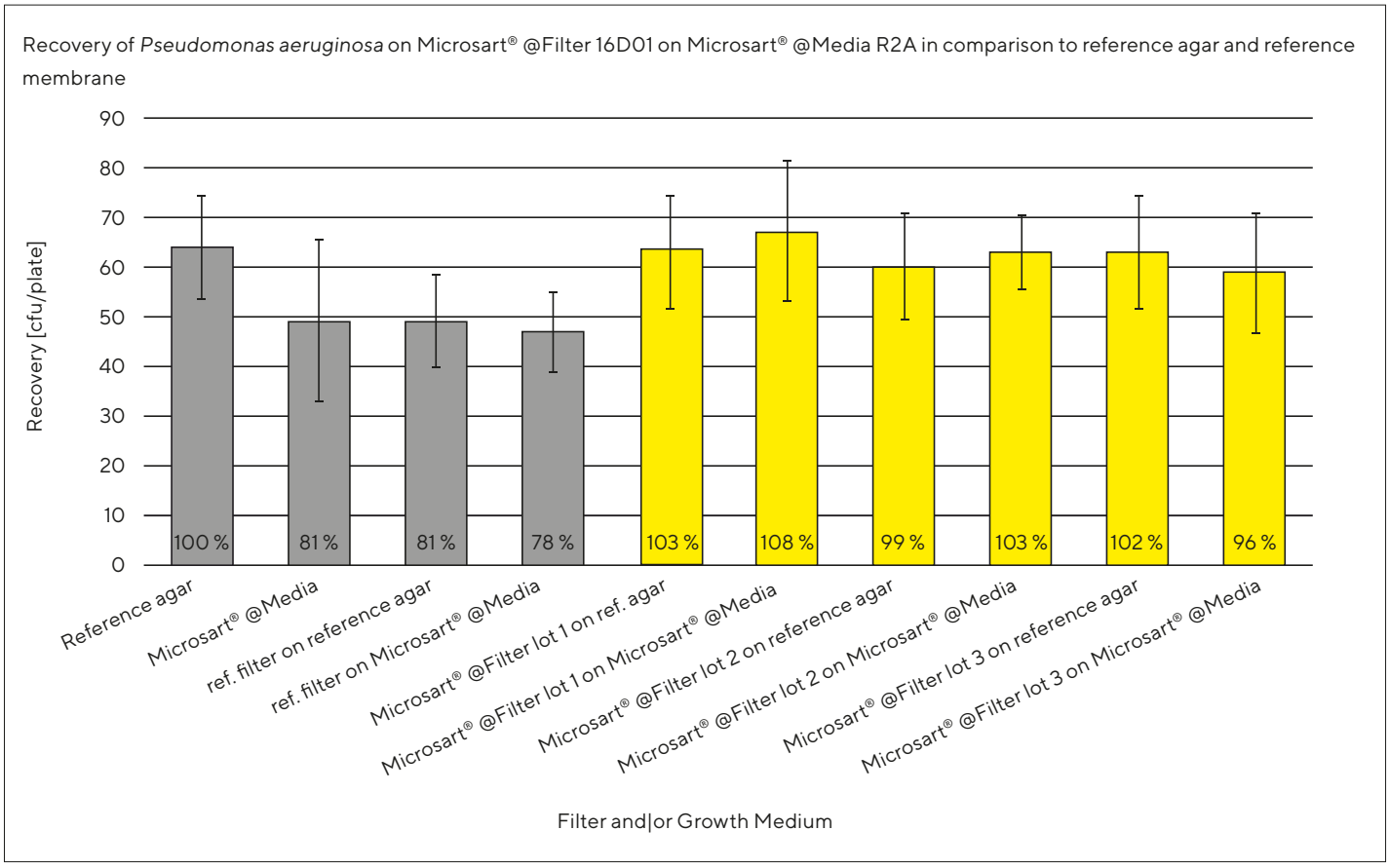
Test Strain|Media Type	Acceptance Criteria	Lot No. Microsart® @Filter	Lot No. Microsart® @Media	No. of Samples Tested (per Product | Lot)	Passed* Yes | No
Bacillus subtilis with TSA	≥ 70 % recovery compared to reference agar	1303024RD 1305002RD 1305003RD	3112270	20	Yes
	≥ 80 % recovery compared to reference filter			20	Yes
Bacillus subtilis with R2A	≥ 70 % recovery compared to reference agar	1303024RD 1305002RD 1305003RD	3070103	20	Yes
	≥ 80 % recovery compared to reference filter			20	Yes
Escherichia coli with TSA	≥ 70 % recovery compared to reference agar	1303024RD 1305002RD 1305003RD	3070098	20	Yes
	≥ 80 % recovery compared to reference filter			20	Yes
Pseudomonas aeruginosa with TSA	≥ 70 % recovery compared to reference agar	1303024RD 1305002RD 1305003RD	3112270	20	Yes
	≥ 80 % recovery compared to reference filter			20	Yes
Pseudomonas aeruginosa with R2A	≥ 70 % recovery compared to reference agar	1303024RD 1305002RD 1305003RD	3070103	20	Yes
	≥ 80 % recovery compared to reference filter			20	Yes
Salmonella enterica with TSA	≥ 70 % recovery compared to reference agar	1303024RD 1305002RD 1305003RD	3070098	20	Yes
	≥ 80 % recovery compared to reference filter			20	Yes
Staphylococcus aureus with TSA	≥ 70 % recovery compared to reference agar	1303024RD 1305002RD 1305003RD	3070098	20	Yes
	≥ 80 % recovery compared to reference filter			20	Yes
Aspergillus brasiliensis with TSA	≥ 70 % recovery compared to reference agar	1303024RD 1305002RD 1305003RD	3170348	20	Yes
	≥ 80 % recovery compared to reference filter			20	Yes
Aspergillus brasiliensis with SDA	≥ 70 % recovery compared to reference agar	1303024RD 1305002RD 1305003RD	3112269	20	Yes
	≥ 80 % recovery compared to reference filter			20	Yes
Candida albicans with TSA	≥ 70 % recovery compared to reference agar	1303024RD 1305002RD 1305003RD	3112270	20	Yes
	≥ 80 % recovery compared to reference filter			20	Yes
Candida albicans with SDA	≥ 70 % recovery compared to reference agar	1303024RD 1305002RD 1305003RD	3070100	20	Yes
	≥ 80 % recovery compared to reference filter			20	Yes

* All samples have to be within the specifications to pass.

Microsart® @Filter validation lots were labeled as:
Lot 1302024RD = validation lot 1; lot 1305002RD = validation lot 2; lot 1305003 RD = validation lot 3

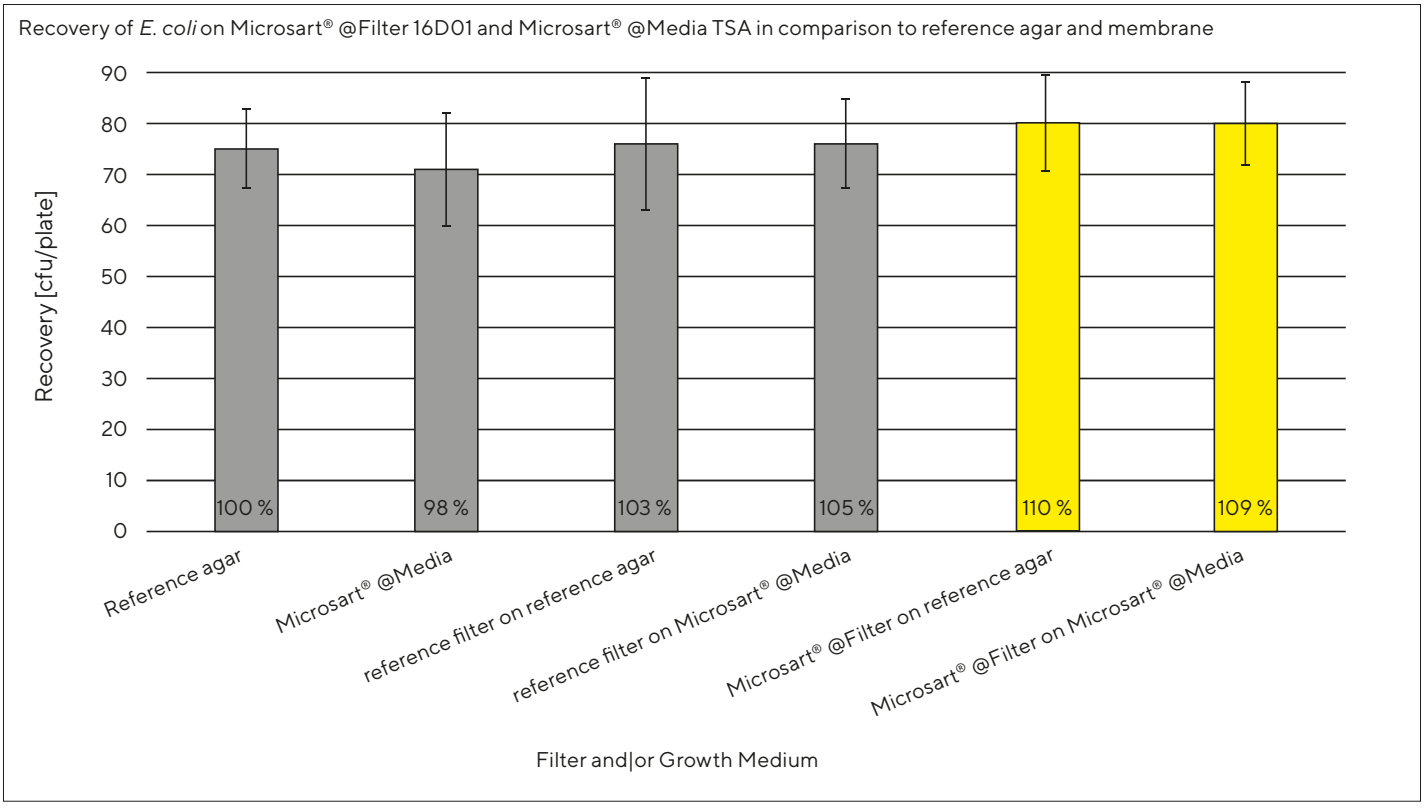
In the following graphs (Figs. 1–3), exemplary validation results are shown for all three validation lots of Microsart® @Filter with each Microsart® @Media type and three different microorganisms.

Fig. 1: Validation Results for Pseudomonas aeruginosa on R2A



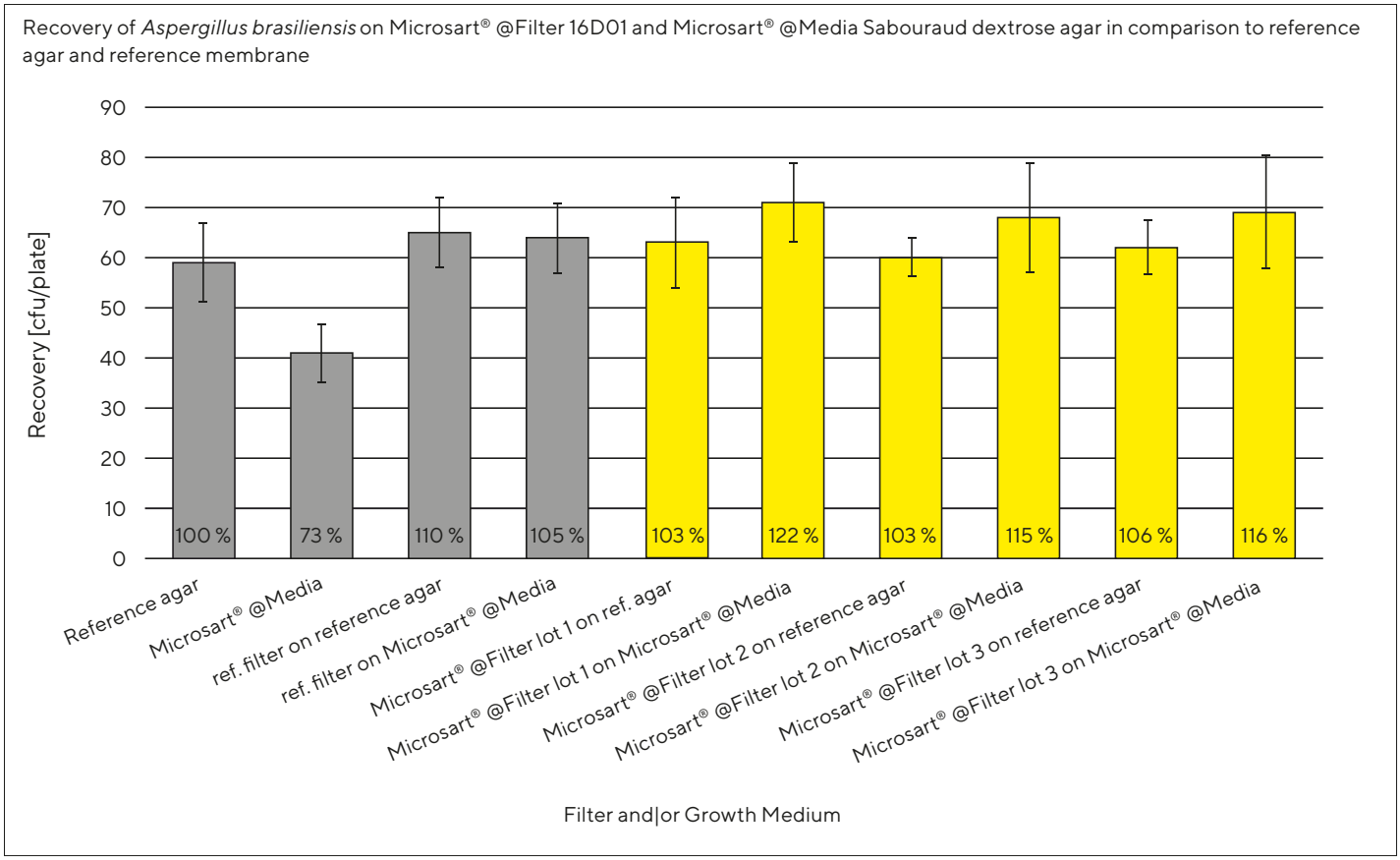
The recovery is shown in cfu/plate and in percent (with the reference agar as 100 %).

Fig. 2: Validation Results for *Escherichia coli* on TSA with Validation Lot 1303024RD



The recovery is shown in cfu/plate and in percent (with the reference agar as 100 %).

Fig. 3: Validation Results for *Aspergillus brasiliensis* on SDA



The recovery is shown in cfu/plate and in percent (with the reference agar as 100 %).

4.4 Sterilisation Validation

The Microsart® @Filter products were sterilized using a validated process in accordance with DIN EN ISO 11137 regulations.

The Microsart® @Filter products are gamma-irradiated to reach a Safety Assurance Level (SAL) of 10^{-5} using a dose of min. 15 kGy.

The Microsart® @Media products are sterilized at BD by gamma-irradiation. For further information on the sterilization validation of Microsart® @Media, please contact BD accordingly.

4.5 Shelf Life Tests Performed on Microsart® @Filter

The shelf life of Microsart® @Filter was tested after 1 month as well as after 3, 12 and 24 months.

Devices tested after 1 month

Test	Product Order No.	Lot No.	No. of Samples Tested (per Product | Lot)	Passed* Yes | No
Visual inspection			30	Yes
Base-to-manifold fit (manual force)	16D01--10-H6--BL 16D01--25-H6--BK	1303024RD 1306002RD	30	Yes
Base-to-manifold fit (automatic vacuum)	16D01--10-H6--BL 16D01--25-H6--BK	1303024RD 1306002RD	30	Yes
Funnel-to-base fit (manual force)	16D01--10-H6--BL 16D01--25-H6--BK	1303024RD 1306002RD	30	Yes
Leak-tightness	16D01--10-H6--BL 16D01--25-H6--BK	1303024RD 1306002RD	30	Yes
Membrane flatness after assembly	16D01--10-H6--BL 16D01--25-H6--BK	1303024RD 1306002RD	30	Yes

Devices tested after 3 months

Test	Product Order No.	Lot No.	No. of Samples Tested (per Product | Lot)	Passed* Yes | No
Visual inspection			30	Yes
Base-to-manifold fit (manual force)	16D01--10-H6--BL 16D01--25-H6--BK	1303024RD 1306002RD	30	Yes
Base-to-manifold fit (automatic vacuum)	16D01--10-H6--BL 16D01--25-H6--BK	1303024RD 1306002RD	30	Yes
Funnel-to-base fit (manual force)	16D01--10-H6--BL 16D01--25-H6--BK	1303024RD 1306002RD	30	Yes
Leak-tightness	16D01--10-H6--BL 16D01--25-H6--BK	1303024RD 1306002RD	30	Yes
Membrane flatness after assembly	16D01--10-H6--BL 16D01--25-H6--BK	1303024RD 1306002RD	30	Yes

* All samples have to be within the specifications to pass.

Devices tested after 12 months

Test	Product Order No.	Lot No.	No. of Samples Tested (per Product | Lot)	Passed* Yes | No
Visual inspection			30	Yes
Base-to-manifold fit (manual force)	16D01--10-H6--BL 16D01--25-H6--BK	1303024RD 1306002RD	30	Yes
Base-to-manifold fit (automatic vacuum)	16D01--10-H6--BL 16D01--25-H6--BK	1303024RD 1306002RD	30	Yes
Funnel-to-base fit (manual force)	16D01--10-H6--BL 16D01--25-H6--BK	1303024RD 1306002RD	30	Yes
Leak-tightness	16D01--10-H6--BL 16D01--25-H6--BK	1303024RD 1306002RD	30	Yes
Membrane flatness after assembly	16D01--10-H6--BL 16D01--25-H6--B	1303024RD 1306002RD	30	Yes

Devices tested after 24 months

Test	Product Order No.	Lot No.	No. of Samples Tested (per Product | Lot)	Passed* Yes | No
Visual inspection			30	Yes
Base-to-manifold fit (manual force)	16D01--10-H6--BL 16D01--25-H6--BK	1303024RD 1306002RD	30	Yes
Base-to-manifold fit (automatic vacuum)	16D01--10-H6--BL 16D01--25-H6--BK	1303024RD 1306002RD	30	Yes
Funnel-to-base fit (manual force)	16D01--10-H6--BL 16D01--25-H6--BK	1303024RD 1306002RD	30	Yes
Leak-tightness	16D01--10-H6--BL 16D01--25-H6--BK	1303024RD 1306002RD	30	Yes
Membrane flatness after assembly	16D01--10-H6--BL 16D01--25-H6--B	1303024RD 1306002RD	30	Yes

* All samples have to be within the specifications to pass.

4.6 Shelf Life Tests Performed on Microsart® @Media

BD tested the shelf life of Microsart® @Media in its validation study (see Sections 4.1, 1.1, 4.3). Please contact BD for more information.

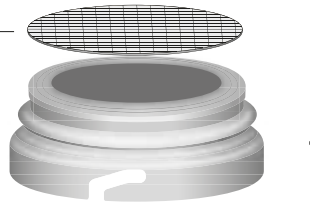
5. Test Parameters for Quality Assurance

5.1 Test Parameters for Microsart® @Filter

5.1.1 Test Scheme

Funnel and base
- Injection molding flaws and residues
- No particles > 1 mm
- Damage
- Water leak test of base and funnel

Membrane filter
- Bacteria challenge test with 10^{-7} cfu/cm^2 *Brevundimonas diminuta* (0.2 µm pore size) or *Serratia marcescens* (0.45 µm pore size)
- Growth promotion test with *Escherichia coli* and *Pseudomonas aeruginosa*
- Bubble point
- Burst pressure
- Flow rate for water
- Thickness
- Mass per unit area
- Extractables for water
- Wetting time for water
- Drop adsorption time with NaCl



Filtration device
- Visual inspection of packaging

5.1.2 Quality Control Tests

Test Type	Reference and Test Method Equipment	Reference to Method Description	Measuring Unit
Membrane Filter Bacteria challenge test with *Brevundimonas diminuta*	Acc. to DIN 58355; suspension of *B. diminuta* (filters with 0.2 µm pore size)	Internal SOP	Number of filtrates, sterile | non-sterile
Bacteria challenge test with *Serratia marcescens*	Acc. to standard methods of water and wastewater; suspension of *S. marcescens* (filters with 0.45 µm pore size)	Internal SOP	Number of filtrates, sterile | non-sterile
Growth promotion test for CN membrane filters	Acc. to DIN EN ISO 7704; suspensions of *Escherichia coli* and *Pseudomonas aeruginosa*	Internal SOP	In % recovery compared to reference filter
Growth promotion test for PVDF membrane filter	Acc. to EP|USP	Internal SOP	In % recovery compared to reference filter
Bubble point test	Visual test acc. to DIN 58355, compressed air, calibrated measuring device	Internal SOP	In bar (~14.5 psi)
Burst pressure test	Compressed air, calibrated measuring device	Internal SOP	In bar
Flow rate for water	Acc. to DIN 58355; water, pressure gauge, stop watch, balance	Internal SOP	In mL/(min × cm^2 × bar)
Thickness	Acc. to DIN 53105; thickness gauge	Internal SOP	In µm
Mass per unit area	Balance	Internal SOP	In g/m^2
Extractables for water	Boiled water, moisture analyzer, balance	Internal SOP	In %
Wetting time for water	Water, stopwatch	Internal SOP	Seconds (sec.)
Drop adsorption time with NaCl	Pipet, stopwatch, NaCl solution	Internal SOP	Seconds (sec.)
Base | Funnel Visual inspections	Task lighting, inspection lamp with magnifier	Internal SOP	Number of rejected devices
Water leak tests	Vacuum pump, filtration equipment, water	Internal SOP	Percentage of rejected devices
Device Assembly | Packaging Visual inspections	Task lighting, inspection lamp with magnifier	Internal SOP	Percentage of rejected devices

5.2 Test Parameters for Microsart® @Media

5.2.1 Test Scheme

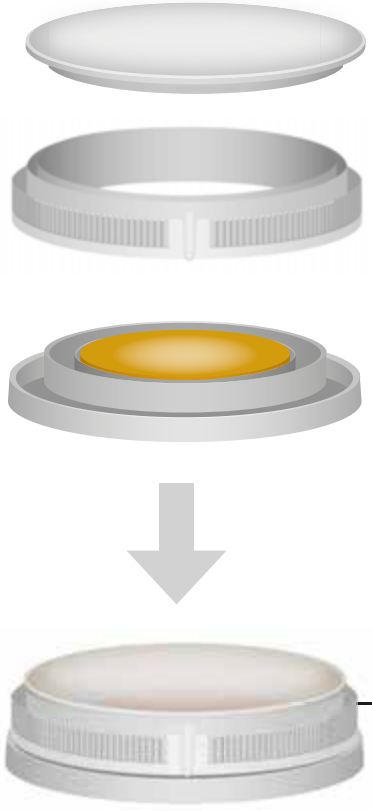
Plastic parts

Visual inspections:

- Absence of damage
- No flash
- No sink holes
- Clarity of base and lid
- Ring correctly glued

Fit and function:

- All parts fit



Agar media

- Agar fill volume
- pH
- Biological performance

5.2.2 In-Process Quality Control Tests

Test Type	Reference and Test Method Equipment	Reference to Method Description	Measuring Unit
Plastic Parts Visual inspections ■ No flash ■ No sink holes ■ Clarity of base and lid ■ Gluing of ring	Inspection lamp with magnifier	Internal SOP	Percentage of rejected devices
Fit and function ■ Ring must fit base and lid ■ Lid must fit ring ■ Base must fit ring	None	Internal SOP	Percentage of rejected devices

5.2.3 Final Product Quality Control Tests

Test Type	Reference and Test Method Equipment	Reference to Method Description	Measuring Unit
Agar fill volume	Please refer to BD site for further information	BD‘s internal SOP	In mL
Correct pH	Please refer to BD site for further information	BD‘s internal SOP	pH
Biological performance	8 microbial strains (3.3.2.1)	BD‘s internal SOP	Growth|percentage of recovery

6. Microsart® @Filter Version (16D04--10-06-xxx)

6.1 Technical Specifications

Materials	Funnel: Polypropylene Base: ABS (acrylonitrile butadiene styrene) Filter support: PET nonwoven (polyester) Membrane filter: PVDF (polyvinylidenfluorid)
Capacity	100 mL; graduation marks at 20, 50 and 100 mL
Filter diameter	47 mm
Filtration area	13.2 cm^2
Pore size	0.45 µm The pore size is determined by retention of *Serratia marcescens* in accordance with ASTM D3863-87. The PVDF membrane filter meets the requirements of the European Pharmacopoeia (EP) and the US Pharmacopoeia (USP).
Typical flow rate for water	> 22 mL/(min × cm^2) at -0.93 bar
Max. operating pressure	Vacuum only
Sterilisation	Gamma-irradiation, units have been irradiated to a safety assurance level (SAL) of 10^{-5} The sterilisation process does not enhance or inhibit subsequent growth of microorganisms.
Thermal resistance	150 °C max.
Thickness acc. to DIN 53105	> 100 µm
Chemical compatibility	Aqueous solutions (pH 1–12), hydrocarbons and several other organic solvents, alcoholic solvents
Wetting time	< 10 s
Growth promotion test	PVDF membrane filters provide good growth and typical colony aspects. Recovery rates indicate that there is no influence on bacterial growth. PVDF membrane filters are tested according to EP/USP.

6.2 Qualification Tests

6.2.1 Visual Inspection

The Microsart® @Filter PVDF product was visually inspected for:

Test	Article No.	Lot No.	No. of Samples Tested (per article | lot)	Passed Yes | No
Smooth side of PVDF filter facing upwards	16D04--10-06--BL	1709008RD 1709009RD 1711016RD	20	Yes
All plastic parts clean and acceptable quality to use	16D04--10-06--BL	1805040VS	20	Yes

6.2.2 Functionality of Microsart® @Filter PVDF Version in Combination with Microsart® Manifolds

Test	Article No.	Lot No.	No. of Samples Tested (per article | lot)	Passed Yes | No
Graduation accuracy	16D04--10-06--BL	1805040VS	3	Yes
Fit of base to manifold	16D04--10-06--BL	1805040VS	20	Yes
Leak tightness	16D04--10-06--BL	1709008RD 1709009RD 1711016RD	20	Yes
Liquid hold up in funnel	16D04--10-06--BL	1805040VS	20	Yes
Membrane flatness	16D04--10-06--BL	1805040VS	20	Yes
Removal of funnel from base	16D04--10-06--BL	1805040VS	20	Yes
Filter does not adhere to the removed funnel	16D04--10-06--BL	1709008RD 1709009RD 1711016RD	20	Yes
Filter support is fixed to filtration base	16D04--10-06--BL	1709008RD 1709009RD 1711016RD	20	Yes
Membrane flatness (after transfer to agar)	16D04--10-06--BL	1709008RD 1709009RD 1711016RD	20	Yes
Liquid hold up in base	16D04--10-06--BL	1805040VS	20	Yes
Removal of base from manifold	16D04--10-06--BL	1805040VS	20	Yes

6.2.3 Microbial Recovery with Microsart® @Filter PVDF Version

Microsart® @Filter were tested in their intended use to demonstrate their ability to promote growth of microorganisms. EP 2.6.12 and USP <61> specify strains to be used for growth promotion tests in membrane filtration. These were used in the qualification study.

For the qualification tests, 3 lots of Microsart® @Filter PVDF version (16D04--10-06--BL) were tested with one lot of reference agar (Tryptic Soy Agar and Sabouraud Dextrose Agar) using the microorganisms shown below.

Test strain	ATCC No.
Bacillus subtilis	6633
Pseudomonas aeruginosa	9027
Staphylococcus aureus	6538
Aspergillus brasiliensis	16404
Candida albicans	10231

The testing was performed according to the qualification matrix below. In this table, the number of tests per Microsart® @Filter lot is shown.

	Spread Plates		16D04--10-06--BL units/ lot	
Test Microorganism	**TSA reference agar**	**SDA reference agar**	**TSA reference agar**	**SDA reference agar**
Bacillus subtilis	10	–	10	–
Pseudomonas aeruginosa	10	–	10	–
Staphylococcus aureus	10	–	10	–
Aspergillus brasiliensis	10	10	10	10
Candida albicans	10	10	10	10

Acceptance criteria:
According to EP 2.6.12/USP <61> the recovery of all test organisms must be ≥ 50 % and ≤ 200 % compared to reference agar plates (spread plate method).

Results

Test Strain|Media Type	Acceptance Criteria	Lot No. Microsart® @F ilter	No. of Samples Tested (per lot)	Passed Yes | No
Bacillus subtilis on TSA reference agar	≥ 50 % recovery compared to reference agar	1709008RD 1709009RD 1711016RD	20	Yes
Pseudomonas aeruginosa on TSA reference agar	≥ 50 % recovery compared to reference agar	1709008RD 1709009RD 1711016RD	20	Yes
Staphylococcus aureus on TSA reference agar	≥ 50 % recovery compared to reference agar	1709008RD 1709009RD 1711016RD	20	Yes
Aspergillus brasiliensis on TSA reference agar	≥ 50 % recovery compared to reference agar	1709008RD 1709009RD 1711016RD	20	Yes
Aspergillus brasiliensis on SDA reference agar	≥ 50 % recovery compared to reference agar	1709008RD 1709009RD 1711016RD	20	Yes
Candida albicans on TSA reference agar	≥ 50 % recovery compared to reference agar	1709008RD 1709009RD 1711016RD	20	Yes
Candida albicans on SDA reference agar	≥ 50 % recovery compared to reference agar	1709008RD 1709009RD 1711016RD	20	Yes

7. Conclusion

With the qualification and quality assurance measures presented in this validation guide, it could be verified that the Microsart® @Filter and Microsart® @Media products are in accordance to various relevant national and international standards (e.g. DIN EN ISO 7704, all applicable standards are listed in the individual chapters of this document) and to the European and US Pharmacopoeia. This validation guide should assist Sartorius customers to perform their own product specific validation with these products and may help reduce their validation effort.

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