Millipore®
Preparation, Separation,
Filtration & Monitoring Products

EZ-Fit® filtration unit validation summary

Introduction

This guide is designed to provide a basic understanding of the methods used to qualify the newly launched product EZ-Fit® filtration unit.

Section 1 of this guide provides an introduction, a product description, a set of catalog numbers, internal documentation, regulatory information and our quality standards.

Section 2 of this guide provides a summary of test methods and test results used to qualify the EZ-Fit® filtration unit.

This validation summary shows that the performance of EZ-Fit® filtration unit is in accordance with the specified acceptance criteria.

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Product summary

1 Product description

EZ-Fit® filtration unit components

The EZ-Fit® filtration unit is a disposable filtration device for bioburden testing of liquid samples including water, process samples, or final products. It is designed for optimizing and securing the laboratory workflow to provide time-saving and reliable microbiological results. After the filtration of the sample, the membrane can be transferred for microbial culture on an agar plate. Using the blue EZ-Fit® filtration unit with pad, liquid media can alternatively be added after the filtration, and the device converts into a petri dish.

1.1 Technical specifications

Unit technical specifications

Material of construction	**Cover**	Polystyrene
	Funnel	Styrene-butadiene copolymer (SBC)
	Membrane	Mixed cellulose esters, PVDF
	Support pad	Cellulose
	Base	Acrylonitrile butadiene styrene
	Plug	Low-density polyethylene
Dimensions	**Height**	100 mL: 66.5 mm (2.6 in.) 250 mL: 108.5 mm (4.3 in.)
	Largest diameter	75.8 mm (3.0 in.)
Filtration Surface	12,56 cm^2	
Sterilization method [1]	Irradiation (e-beam)	
Maximum temperature	45 °C	

[1] The sterilization process is validated following ISO 11137 (E-beam) guidelines. The pink base filtration units are sterilized by E-beam and the blue base units are sterilized using ethylene oxide. Each lot meets the respective acceptance criteria for the controlled and validated sterilization cycle parameters. Internal sterility tests performed during sterilization validation have shown negative results.

Membrane technical specifications

	HA	GS	AA	HV
Material of construction	Mixed cellulose esters (MCE)	Mixed cellulose esters (MCE)	Mixed cellulose esters (MCE)	Polyvinylidene Fluoride (PVDF)
Membrane pore size	0.45 µm	0.22 µm	0.8 µm	0.45 µm
Property	Hydrophilic	Hydrophilic	Hydrophilic	Hydrophilic
Average thickness	150 µm	150 µm	150 µm	115 µm
Water bubble point	22–34 psi	50–60 psi	12–20 psi	22 –28 psi

Note: the membranes used in the EZ-Fit® filtration unit are the same as the ones used in the Microfil® V/S device

1.2 Catalog numbers

PINK base – no pad			
EZ-Fit® filtration unit, white plain PVDF membrane, 0.45 µm, 100 mL	48	Single	**EFHVW10IS**
EZ-Fit® filtration unit, white gridded MCE membrane, 0.45 µm, 100 mL	48	Multipack of 4 units	**EFHAW10MS**
EZ-Fit® filtration unit, white gridded MCE membrane, 0.45 µm, 250 mL	48	Bulk with protective bag	**EFHAW25BS**
EZ-Fit® filtration unit, black gridded MCE membrane, 0.45 µm, 100 mL	48	Multipack of 4 units	**EFHAB10MS**
EZ-Fit® filtration unit, black gridded MCE membrane, 0.45 µm, 250 mL	48	Bulk with protective bag	**EFHAB25BS**
EZ-Fit® filtration unit, white gridded MCE membrane, 0.22 µm, 100 mL	48	Multipack of 4 units	**EFGSW10MS**
EZ-Fit® filtration unit, white gridded MCE membrane, 0.22 µm, 100 mL	48	Single	**EFGSW10IS**
EZ-Fit® filtration unit, white gridded MCE membrane, 0.8 µm, 100 mL	48	Bulk with protective bag	**EFAAW10BS**
EZ-Fit® filtration unit, white gridded MCE membrane, 0.45 µm, 100 mL	48	Bulk, with protective bag	**EFHAW10BS**
EZ-Fit® filtration unit, black gridded MCE membrane, 0.45 µm, 100 mL	48	Bulk, with protective bag	**EFHAB10BS**
EZ-Fit® filtration unit, white gridded MCE membrane, 0.45 µm, 100 mL	48	Single	**EFHAW10IS**
EZ-Fit® ® filtration unit, white gridded MCE membrane, 0.22 µm, 100 mL	48	Single	**EFGSW25IS**
BLUE base – with pad			
EZ-Fit® filtration unit, white gridded MCE membrane, 0.45 µm, 100 mL	48	Bulk	**EFHAW100B**
EZ-Fit® filtration unit, white gridded MCE membrane, 0.45 µm, 100 mL	48	Single	**EFHAW100I**
EZ-Fit® filtration unit, white gridded MCE membrane, 0.45 µm, 250 mL	48	Bulk	**EFHAW250B**
EZ-Fit® filtration unit, white gridded MCE membrane, 0.45 µm, 250 mL	48	Single	**EFHAW250I**
EZ-Fit® filtration unit, black gridded MCE membrane, 0.45 µm, 100 mL	48	Bulk	**EFHAB100B**
EZ-Fit® filtration unit, black gridded MCE membrane, 0.45 µm, 100 mL	48	Single	**EFHAB100I**
EZ-Fit® filtration unit, black gridded MCE membrane, 0.45 µm, 250 mL	48	Bulk	**EFHAB250B**
EZ-Fit® filtration unit, black gridded MCE membrane, 0.45 µm, 250 mL	48	Single	**EFHAB250I**
EZ-Fit® filtration unit, white gridded MCE membrane, 0.45 µm, 100 mL, with plug	48	Single	**EFHAW100IP**
EZ-Fit® filtration unit, white gridded MCE membrane, 0.45 µm, 100 mL	48	Multipack of 3 units	**EFHAW100M3**
EZ-Fit® filtration unit, black gridded MCE membrane, 0.45 µm, 100 mL	48	Multipack of 3 units	**EFHAB100M3**

2 Validation references

2.1 Internal documentation references

The following qualification documents which support this validation summary may be consulted during a scheduled audit:

Document Number	Title
Initial EZ-Fit® filtration unit blue validation	
FRP128-VQ1	EZ-Fit® filtration unit and EZ-Fit® manifold validation master plan
FRP128-PQP5	Product and process performance qualification Protocol of EZ-Fit® filtration unit, cat. numbers EFHAW100I, EFHAW100B, EFHAB100I, EFHAB100B, EFHAW250I, EFHAW250B, EFHAB250I, EFHAB250B
FRP128-PQR5 **FRP128-PQR5-ADD1**	Product and process performance qualification Reports of EZ-Fit® filtration unit, cat. numbers EFHAW100I, EFHAW100B, EFHAB100I, EFHAB100B, EFHAW250I, EFHAW250B, EFHAB250I, EFHAB250B
FRP128-SLP1	Shelf life protocol for EZ-Fit® filtration unit, cat. numbers EFHAW100I, EFHAW100B, EFHAB100I, EFHAB100B, EFHAW250I, EFHAW250B, EFHAB250I, EFHAB250B
FRP128-SLR1 **FRP128-SLR1-ADD1** **FRP128-SLR1-ADD2** **FRP128-SLR1-ADD3** **FRP128-SLR1-ADD4** **20118324** **20200025** **20292916**	Shelf life reports for EZ-Fit® filtration unit, cat. numbers EFHAW100I, EFHAW100B, EFHAB100I, EFHAB100B, EFHAW250I, EFHAW250B, EFHAB250I, EFHAB250B
Initial EZ-Fit® filtration unit pink validation	
20190201	FRP160-VQ1 – Validation Master Plan for EZ-Fit® blue and pink filtration unit
20209677	FRP160-PQP1 Process and product performance qualification protocol for EZ-Fit® extension units
20226430	FRP160-PQR1 Process and product performance qualification report for EZ-Fit® extension units
20227307	FRP160-PQP1-ADD1 Process and product performance qualification protocol for EZ-Fit® extension units – 250 mL version
20232373	FRP160-PQP1-ADD1 Process and product performance qualification report for EZ-Fit® extension units – 250 mL version
20199578	FRP160-SLP1 Rhino development and PQ shelf life protocol for EZ-Fit® extension units
20226087	FRP160-SLR1 Rhino development and PQ shelf life report for EZ-Fit® extension units
EZ-Fit® filtration units harmonization: switch of EZ-Fit® filtration unit blue to e-beam sterilization and packaging rationalization	
20443815	FRPPI019-DVR1: report for the design verification of the EZ-Fit® filtration units blue sterilized with e-beam
20417119	FRPPI019-PQP1 – Product qualification protocol of the EZ-Fit® filtration units with pad e-beam sterilized
20455165	FRPPI019-PQR1 – Product qualification report of the EZ-Fit® filtration units with pad e-beam sterilized
20369323	Shelf life protocol for EZ-Fit® filtration units harmonization
20447241	Shelf life report for EZ-Fit® filtration units harmonization PQ

2.2 Regulations

Standard or regulation	Chapter	Title
European Pharmacopoeia 10th Edition	**2.6.12**	Non-sterile microbial products enumeration test
	2.6.13	Microbiological examination of non-sterile products: Test for specified micro-organisms
USP 42-NF 37, second supplement	**61**	Microbiological examination of non-sterile products: Microbial enumeration test
	62	Microbiological examination of non-sterile products: Tests for specified microorganisms
Japanese Pharmacopeia 17th Edition	**12**	Microbial attributes of non-sterile pharmaceutical products
	21	Quality control of water for pharmaceutical use
ISO 7704:1985	**All**	Water quality - Evaluation of membrane filters used for microbiological analyses
ISO 11133-A1:2018	**All**	Microbiology of food, animal feed and water — Preparation, production, storage and performance testing of culture media
ASTM	**Part 9000**	Standard Methods for the Examination of Water and Wastewater, Microbiological examination
	D4169	Standard practice for performance testing of shipping containers and systems, ASTM International, West Conshohocken, PA, 2016, www.astm.org

3 Standard for Quality assurance and environment

The EZ-Fit® filtration units are manufactured in our facility in Millipore SAS, France, which is certified by an accredited registering body to ISO 9001 Quality Management System standards.

3.1 Quality Assurance

The EZ-Fit® quality program and manufacturing process follow cGMP requirements. Millipore SAS, France has determined an effective and efficient process which leads to a consistent high quality for each batch of product.

Standard operating and testing procedures are precisely defined to closely monitor the process and to ensure the product compliance to the specifications.

We follow the recommendations from the United States, European and Japanese Pharmacopeia to ensure a consistent performance of the product.

3.2 Traceability

Batch records are made during each EZ-Fit® filtration unit manufacturing run. There is traceability for all raw materials used for the production, and demonstration that all the steps are followed as defined in the internal procedures. Verification that the defined controls are performed accurately ensure that the products comply with the specifications.

The products are identified by reference, lot number and expiration date.
Batch records are reviewed for compliance and released by Quality Assurance.

3.3 Process change control

Any change to the EZ-Fit® filtration unit manufacturing process or product is evaluated to avoid any impact on the product quality, requirements and safety for the users.

Changes are validated as necessary and appropriately communicated to customers according our internal policy.

3.4 Environmental

The EZ-Fit® filtration units are manufactured in an environment controlled according to internal specification, including microbiological and particulate monitoring.

Furthermore, internal procedures describe the general rules, restrictions and cleaning instructions to be followed by all employees working in the manufacturing area

4 Validation purpose

The goal of the validation was to ascertain the performance of all references listed in §1.2 in terms of physical and microbiological properties according to internal requirements and regulations.

To achieve this objective, the following validation tests have been conducted:

4.1 Internal documentation references

Nominal volume
The purpose of this test is to verify that the nominal volume graduation is accurate, for both 100 mL and 250 mL funnels.

Wettability Test
The purpose of this test is to determine the wetting time of filter sample and also the absence of any hydrophobic spots on the membrane.

Assembly Test
The purpose of this water tightness test is to check the assembly of the filtration unit.

Water flow time
The purpose of this test is to determine the time needed to filter a specific volume of purified water through the filter.

Residual water on the funnel
The purpose of this test is to determine the quantity of residual water on the funnel wall after filtration.

Shipping packaging qualification to transport hazards
The objective of this test is to challenge the capability of the packaging to withstand transport hazards.

4.2 Microbiological features of the product

Growth Promotion Test/ Suitability of the counting method

The purpose of this study is to prove the ability of microorganisms to grow on the filter from EZ-Fit® filtration unit.

The growth promotion tests were conducted by membrane filtration with spread plate controls to be in compliance with the US / EP / JP Pharmacopeias, ISO 7704 and ASTM related to potable water regulations.

During the growth promotion test, visual aspect and EZ-Fit® device functionality, including membrane wettability, were also verified.

5 Validation test summary

This section of the validation summary describes the validation lots, validation tests, the objectives, methods, acceptance criteria and test results.

5.1 Validation lot numbers

Qualification was conducted with the following catalog numbers which are representative of the EZ-Fit® filtration unit product range.

Catalog Number	Product Description	Qualification Lot Numbers
EZ-Fit® filtration unit, blue base		
EFHAW100I	EZ-Fit® filtration unit, 100 mL, white MCE membrane 0,45µm, gridded, individual packaging	F3JA59933Q
EFHAW100B	EZ-Fit® filtration unit, 100 mL, white MCE membrane 0,45µm, gridded, bulk packaging	F3MA27859
EFHAB100I	EZ-Fit® filtration unit, 100 mL, black MCE membrane 0,45µm, gridded, individual packaging	F3JA59934Q
EFHAW250B	EZ-Fit® filtration unit, 250 mL, white MCE membrane 0,45µm, gridded, bulk packaging	F3JA59939Q
EFHAW250I	EZ-Fit® filtration unit, 250 mL, white MCE membrane 0,45µm, gridded, individual packaging	F3NA42998Q F3NA43000Q F3JA59937Q
EFHAB250B	EZ-Fit® filtration unit, 250 mL, black MCE membrane 0,45µm, gridded, bulk packaging	F3JA59940Q
EFHAB250I	EZ-Fit® filtration unit, 250 mL, black MCE membrane 0,45µm, gridded, individual packaging	F3NA42999Q F3NA43001Q F3JA59938Q
EZ-Fit® filtration unit harmonization, switch to e-beam sterilization		
EFHAW100M3	EZ-Fit® filtration unit, 100 mL, white MCE membrane 0,45µm, gridded, Multipack	F0AB86392Q
EFHAB100B	EZ-Fit® filtration unit, 100 mL, black MCE membrane 0,45µm, gridded, bulk packaging	F0AB86345Q
EFHAW250B	EZ-Fit® filtration unit, 100 mL, white MCE membrane 0,45µm, gridded, bulk packaging	SAMPLE
EFHAW250I	EZ-Fit® filtration unit, 100 mL, white MCE membrane 0,45µm, gridded, individual packaging	F0AB83962Q
EFHAW100I	EZ-Fit® filtration unit, 100 mL, white MCE membrane 0,45µm, gridded, individual packaging	F8NA47547T
EFHAB100I	EZ-Fit® filtration unit, 100 mL, black MCE membrane 0,45µm, gridded, individual packaging	F9DA19773T F8NA47549T F9DA19775T

Rationale of qualification lot composition

The objective was to have a representative for each filtration unit format (100 mL and 250 mL) and cover the three packaging types (individual, bulk, multipack), and 3 different lots of the critical components: membrane, funnel, base, cover. As all the raw material components are similar for both the 100 mL and 250 mL versions and as the sterilization cycle is the same, the composition of the lots shown above covers inter-lot variability. 2 batches in 100 mL format covering the membranes range were made for feasibility step. The PVDF membrane component is covered in the pink base unit tested references.

EZ-Fit® filtration unit, pink base

Catalog Number	Product Description	Qualification Lot Numbers
EFHVW10IS	EZ-Fit® filtration unit, white plain PVDF membrane, 0,45µm, 100 mL, single	SAMPLE
EFGSW10MS	EZ-Fit® filtration unit, white gridded MCE membrane, 0,22µm, 100 mL, multipack	F6JA782248Q
EFAAW10BS	EZ-Fit® filtration unit, white gridded MCE membrane, 0,8µm, 100 mL, bulk with protective bag	F6JA782250Q
EFHAB10MS	EZ-Fit® filtration unit, black gridded MCE membrane, 0,45µm, 100 mL, multipack	F6JA782247Q
EFAAB10BS	EZ-Fit® filtration unit, black gridded MCE membrane, 0,8µm, 100 mL, bulk with protective bag	F6JA782251Q
EFHAW10MS	EZ-Fit® filtration unit, white gridded MCE membrane, 0,45µm, 100 mL, multipack	F6JA782246Q
EFAAW25BS	EZ-Fit® filtration unit, white gridded MCE membrane, 0,8µm, 250 mL, bulk with protective bag	F6NA15714Q
EFHAB25BS	EZ-Fit® filtration unit, black gridded MCE membrane, 0,45µm, 250 mL, bulk with protective bag	F6NA15715Q
EFAAB250BS	EZ-Fit® filtration unit, black gridded MCE membrane, 0,8µm, 250 mL, bulk with protective bag	SAMPLE

Rationale of qualification lot composition

The molded component variability is covered within the blue base unit validation, the funnels and cover are the same those used for the pink base unit.

The objective was to use all the types and colors of membranes (HA white and black, GS white, AA white and black, HV white), and to cover the four different types of packaging (100 mL single, 100 mL multipack of 4 units, 100 mL bulk with protective bag, 250 mL bulk with protective bag).

5.2 Nominal volume test

Test Summary

The objective of this test was to verify the accuracy of the nominal volume graduation: 100 mL or 250 mL, for both blue and pink versions of EZ-Fit® filtration devices.

The test was carried out by weighing the volume of purified water in a EZ-Fit® device when filled up to the funnel's nominal volume graduation.

Test Specification

Volume measured is within 5 % of the nominal volume:

- 100 mL: 95 to 105 mL
- 250 mL: 237.5 to 262.5 mL

Test Results

EZ-Fit® filtration unit, blue base

Funnel volume	Test Result
100 mL	**Pass**
250 mL	**Pass**

EZ-Fit® filtration unit, pink base

Funnel volume	Test Result
100 mL	**Pass**
250 mL	**Pass**

Conclusion

All tested EZ-Fit® filtration units match the nominal volume acceptance criteria.

5.3 Wettability test

Test Summary

The objective of this test was to determine the wetting times of filter samples and the absence of any hydrophobic spots on the membrane.

A petri dish was filled with a sufficient volume of purified water at 25 °C to cover bottom of dish. A 47 mm filter disc is placed on the surface of the test liquid. At the same time, the timer was started, and then stopped when the filter is completely wet.

Test Specification

According to our internal test method (005189TM): EZ-Fit® filtration unit: ≤5 seconds.

Test Results

EZ-Fit® filtration unit, blue base

EZ-Fit® filtration units, 100 mL

Catalog Number	Lot Number	Test Result
EFHAW100I	F3JA59933Q	**Pass**
EFHAB100I	F3JA59934Q	**Pass**

EZ-Fit® filtration units, 250 mL

Catalog Number	Lot Number	Test Result
EFHAW250I	F3JA59937Q F3NA42998Q F3NA43000Q	**Pass**
EFHAB250I	F3JA59938Q F3NA42999Q F3NA43001Q	**Pass**
EFHAW250B	F3JA59939Q	**Pass**
EFHAB250B	F3JA59940Q	**Pass**

EZ-Fit® filtration unit, pink base

EZ-Fit® filtration units, 100 mL

Catalog Number	Lot Number	Test Result
EFHAW10MS	F6JA782246Q	**Pass**
EFHAB10MS	F6JA782247Q	**Pass**
EFGSW10MS	F6JA782248Q	**Pass**
EFAAW10BS	F6JA782250Q	**Pass**
EFAAB10BS	F6JA782251Q	**Pass**
EFHVW10IS	F6JA782245Q	**Pass**

EZ-Fit® filtration units, 250 mL

Catalog Number	Lot Number	Test Result
EFHAB25BS	F6NA15715Q	**Pass**
EFAAW25BS	F6NA15714Q	**Pass**

Conclusion

All tested EZ-Fit® filtration units match the wettability testing acceptance criteria. The EZ-Fit® filtration unit offers equivalent wettability performance to the Microfil® V/S device. The test has not been documented for EZ-Fit® filtration unit harmonization as the membrane was not changed compared to initial validation, and performance after irradiation demonstrated during pink unit validation.

5.4 Assembly test

Test Summary

The purpose of the assembly test is to check the absence of unit leakage. The sampling unit was filled with the appropriate volume (100 mL or 250 mL) of purified water colored with methylene blue dye. The filtration was started, and the device was observed for leak detection.

Test Specification

According to our validation protocols (00082480TM and 0005249TM). EZ-Fit® filtration unit: no leakage, equivalent to Microfil® V/S criteria

Test Results

EZ-Fit® filtration unit, blue base

EZ-Fit® filtration units, 100 mL

Catalog Number	Lot Number	Test Result
EFHAW100I	F3JA59933Q	**Pass**
EFHAB100I	F3JA59934Q	**Pass**

EZ-Fit® filtration units, 250 mL

Catalog Number	Lot Number	Test Result
EFHAW100I	F3NA42998Q F3NA43000Q	**Pass**
EFHAB100I	F3NA42999Q F3NA43001Q	**Pass**

EZ-Fit® filtration unit, pink base

EZ-Fit® filtration units, 100 mL

Catalog Number	Lot Number	Test Result
EFHAW10MS	F6JA782246Q	**Pass**
EFHAB10MS	F6JA782247Q	**Pass**
EFGSW10MS	F6JA782248Q	**Pass**
EFAAW10BS	F6JA782250Q	**Pass**
EFAAB10BS	F6JA782251Q	**Pass**
EFHVW10IS	F6JA782245Q	**Pass**

EZ-Fit® filtration units, 250 mL

Catalog Number	Lot Number	Test Result
EFHAB25BS	F6NA15715Q	**Pass**
EFAAW25BS	F6NA15714Q	**Pass**

Conclusion

All tested EZ-Fit® filtration units match the assembly testing acceptance criteria.

5.5 Water flow time test

Test Summary

The purpose of this test was to determine the time needed to filter an appropriate volume (100 mL or 250 mL) of purified water through the unit filter with a vacuum of -10 psi ±1 psi.

Test Specification

- 100 mL HA (white gridded and black gridded membranes): maximum 15 sec
- 100 mL GS (white gridded membrane): maximum 36 sec
- 100 mL AA (white gridded and black gridded membranes): maximum 9 sec
- 100 mL HV (white plain membrane): maximum 20 sec
- 250 mL HA (white gridded and black gridded membranes): maximum 38 sec
- 250 mL AA (white gridded and black gridded membranes): maximum 23 sec

Test Results

EZ-Fit® filtration unit, blue base

EZ-Fit® filtration units, 100 mL

Catalog Number	Lot Number	Test Result
EFHAW100I	F3JA59933Q	**Pass**
EFHAB100I	F3JA59934Q	**Pass**

EZ-Fit® filtration unit, pink base

EZ-Fit® filtration units, 100 mL

Catalog Number	Lot Number	Test Result
EFHAW10MS	F6JA782246Q	**Pass**
EFHAB10MS	F6JA782247Q	**Pass**
EFGSW10MS	F6JA782248Q	**Pass**
EFAAW10BS	F6JA782250Q	**Pass**
EFAAB10BS	F6JA782251Q	**Pass**
EFHVW10IS	F6JA782245Q	**Pass**

Conclusion

All tested EZ-Fit® filtration units match the water flow time acceptance criteria. EZ-Fit® filtration unit offers equivalent or better water flow time performance, compared to the Microfil® V/S device.

5.6 Residual water on the funnel

Test Summary

The purpose of this test is to determine the quantity of residual water on the funnel wall after filtration, by weighing the funnel before and after filtration of the appropriate sample volume (100 or 250 mL).

Test Specification

According to our validation protocol, remaining water in the funnel after filtration:

- For 100 mL version: < 0.1 mL
- For 250 mL version, < 0.25 mL

Test Results

EZ-Fit® filtration unit, blue base

EZ-Fit® filtration units, 100 mL

Catalog Number	Lot Number	Test Result
EFHAW100I	F3JA59933Q	**Pass**
EFHAB100I	F3JA59934Q	**Pass**

EZ-Fit® filtration units, 250 mL

Catalog Number	Lot Number	Test Result
EFHAW250I	F3NA42998Q F3NA43000Q	**Pass**
EFHAB250I	F3NA42999Q F3NA43001Q	**Pass**

EZ-Fit® filtration unit, pink base

As the funnels of the EZ-Fit® filtration unit with pink base are the same as the blue base unit, this test has not been repeated.

Conclusion

All tested EZ-Fit® filtration units match the acceptance criteria. The test has not been repeated during EZ-Fit® filtration unit harmonization as product design was not changed.

5.7 Growth promotion test

Test Summary

The purpose of this study is to determine the microbiological performance of the unit versus a panel of representative microorganisms from pharmacopeia and regulation requirements.

Test Specification

Some plastic material could be contaminated by bacteriostatic or fungistatic agents that may inhibit the growth of viable microorganisms contained in the product being filtered. This can produce false negative results.

The recovery test is performed to ensure the ability of the EZ-Fit® filtration units to promote the growth of specific test microorganisms. Each EZ-Fit® device is inoculated with one type of microorganism at a concentration below 100 CFU per device.

EZ-Fit® filtration unit, blue base: test specifications and results

Rationale and acceptance criteria according to our validation protocol.

The acceptance criteria set up for qualification was 50%≤ Recovery % ≤200 % versus spread plate according to USP/EP/JP Pharmacopeia for the following strains:

- *Staphylococcus aureus* ATCC® 6538
- *Aspergillus brasiliensis* ATCC® 16404
- *Bacillus subtilis* ATCC® 6633
- *Candida albicans* ATCC® 10231
- *Pseudomonas aeruginosa* ATCC® 9027
- *Escherichia coli* ATCC® 8739
- *Methylobacterium extorquens* ATCC® 43645

For the strains listed below, related to ISO 7704 and ASTM for potable water, the acceptance criteria was ≥ 80% on agar versus spread plate:

- *Escherichia coli* ATCC® 8739
- *Klebsiella aerogenes* ATCC® 49701
- *Saccharomyces cerevisiae* ATCC® 7754

Additional strains were tested as they are commonly found in industrial beverage & pharmaceutical manufacturing processes.

The acceptance criteria were set up as follows

For solid non-selective media: ≥70% versus spread plate or Microfil® control
For solid selective media: ≥50% versus spread plate or Microfil® control
For liquid media: ≥50% versus Microfil® control

- *Ralstonia pickettii* ATCC® 27511
- *Enterococcus faecalis* ATCC® 19433
- *Kocuria rhizophila* ATCC® 9341
- *Lactobacillus brevis* ATCC® 8287
- *Pichia membranifaciens* ATCC® 16046
- *Dekkera naardenensis* ATCC® 22075

During the growth promotion test, visual aspect and EZ-Fit® device functionality, including membrane wettability, were also verified.

Growth promotion summary table for EZ-Fit® filtration unit with White MCE membrane on solid media:

Strain tested	Incubation media and temperature	Acceptance criterion	Results				
			EFHAW250I F3JA59937Q	EFHAW100I F3JA59933Q F8NA47547T F9DA19773T	EFHAW250B F3JA59939Q	EFHAW100M3 F0AB86392Q	EFHAW250I F0AB83962Q
Aspergillus brasiliensis ATCC® 16404	SDA 22.5 °C ± 2.5 °C	Recovery between 50 and 200% versus spread plate	**Pass**	**Pass**	**Pass**	**Pass**	**Pass**
Bacillus subtilis ATCC® 6633	TSA 32.5 °C ± 2.5 °C		**Pass**	**Pass**	**Pass**	**Pass**	**Pass**
Pseudomonas aeruginosa ATCC® 9027	TSA 32.5 °C ± 2.5 °C		**Pass**	**Pass**	**Pass**	**Pass**	**Pass**
Candida albicans ATCC® 10231	SDA 22.5 °C ± 2.5 °C		**Pass**	**Pass**	**Pass**	**Pass**	**Pass**
Staphylococcus aureus ATCC® 6538	TSA 32.5 °C ± 2.5 °C		**Pass**	**Pass**	**Pass**	**Pass**	**Pass**
Escherichia coli ATCC 8739	TSA 32.5 °C ±2.5 °C		**Pass**	**Pass**	**Pass**	**Pass**	**Pass**
Escherichia coli ATCC® 8739	m-FC with rosolic acid 44.5 °C ± 2.5 °C	Recovery ≥ 80% versus spread plate	**Pass**	**Pass**	**Pass**	**Pass**	**Pass**
Klebsiella aerogenes ATCC® 49701	m-Endo 35 °C ± 2.5 °C		**Pass**	**Pass**	**Pass**	Not tested[2]	Not tested[2]
Methylobacterium extorquens ATCC® 43645	R2A 32.5 °C ± 2.5 °C		**Pass**	**Pass**	Not tested[1]		
Ralstonia pickettii ATCC® 27511	R2A 32.5 °C ± 2.5 °C		**Pass**	**Pass**	Not tested[1]	Not tested[2]	Not tested[2]
Enterococcus faecalis ATCC® 19433	TSA 37 °C ± 2.5 °C		**Pass**	**Pass**	Not tested[1]	Not tested[2]	Not tested[2]
Kocuria rhizophila ATCC® 9341	TSA 32.5 °C ± 2.5 °C		**Pass**	**Pass**	Not tested[1]	Not tested[2]	Not tested[2]

[1] The 3rd lot was not tested as extensively as the 2 first lots: only the pharmacopeia and regulations strains were tested.
[2] Not tested on performance qualification batches, tested and pass on the design verification batch F9DA19773T.

Growth promotion summary table for EZ-Fit® filtration unit with White MCE membrane on liquid media:

Strain tested	Incubation media and Temperature	Acceptance criterion	Results			
			EFHAW250I F3JA59937Q	EFHAW100I F3JA59933Q	EFHAW250B F3JA59939Q	EFHAW100I F9DA19773T
Escherichia coli ATCC® 8739	m-FC Broth with Rosolic Acid 44.5 °C ±2.5°C	Average recovery between 50 % and 200% versus Microfil® V	**Pass**	**Pass**	**Pass**	**Pass**
Klebsiella aerogenes ATCC® 49701	m-Endo Broth 35 °C ±2.5 °C		**Pass**	**Pass**	**Pass**	**Pass**
Lactobacillus brevis ATCC® 8387	De Man, Rogosa and Sharpe (MRS) Broth 32.5 °C ±2.5 °C Anaerobic		**Pass**	**Pass**	Not tested (1)	**Pass**
Saccharomyces cerevisiae ATCC® 7754	m-Green Broth 30°C±2.5°C		**Pass**	**Pass**	Not tested (1)	**Pass**
Pichia membranifaciens ATCC® 16046	m-Green Broth 30 °C ±2.5 °C		**Pass**	**Pass**	Not tested (1)	Not tested (1)
Dekkera naardenensis ATCC® 22075	Brettanomyces Selective Broth 22.5 °C ±2.5 °C		**Pass**	**Pass**	Not tested (1)	Not tested (1)

(1) The 3rd lot was not tested as extensively as the 2 first lots: only the pharmacopeia and regulation strains were tested.

Growth promotion summary table for EZ-Fit® filtration unit with White MCE membrane on solid media:

Strain tested	Incubation media and Temperature	Acceptance criterion	Results			
			EFHAB250I F3JA59938Q	F8NA47549T F9DA19775T	EFHAB250B F3JA59940Q	EFHAB100B F0AB86345Q
Escherichia coli ATCC® 8739	TSA 32.5 °C±2.5 °C	Recovery between 50 and 200% versus spread plate	**Pass**	**Pass**	Not tested (1)	Not tested
Staphylococcus aureus ATCC® 6538			**Pass**	**Pass**	Not tested	**Pass**
Bacillus subtilis ATCC® 6633			**Pass**	**Pass**	Not tested	**Pass**
Pseudomonas aeruginosa ATCC® 9027			**Pass**	**Pass**	Not tested	**Pass**
Candida albicans ATCC® 10231	SDA 22.5 °C±2.5 °C		**Pass**	**Pass**	Not tested	**Pass**
Aspergillus brasiliensis ATCC® 16404			**Pass**	**Pass**	Not tested	**Pass**
Saccharomyces cerevisiae ATCC® 7754		Recovery ≥ 80 versus spread plate	**Pass**	**Pass**	**Pass**	**Pass**
Escherichia coli ATCC® 8739	m-FC 44.5 °C ±2.5 °C		**Pass**	**Pass**	**Pass**	**Pass**

(1) The 3rd lot was not tested as extensively as the 2 first lots: only the pharmacopeia and regulations strains were tested.

Growth promotion summary table for EZ-Fit® filtration unit with White MCE membrane on liquid media:

Strain tested	Incubation media and Temperature	Acceptance criterion	Results			
			EFHAB250I F3JA59938Q	EFHAB100I F3JA59934Q	EFHAB250B F3JA59940Q	EFHAB100I F8NA47549T
Escherichia coli ATCC® 8739	m-FC Broth with Rosolic Acid 44.5 °C ±2.5 °C	Average recovery between 50 % and 200% versus Microfil® V	**Pass**	**Pass**	**Pass**	Not tested
Saccharomyces cerevisiae ATCC® 7754	m-Green Broth 30 °C ±2.5 °C		**Pass**	**Pass**	**Pass**	**Pass**

(1) The 3rd lot was not tested as extensively as the 2 first lots: only the pharmacopeia and regulations strains were tested.

Conclusion

All tested EZ-Fit® filtration units match the acceptance criteria. EZ-Fit® filtration unit offers equivalent microbiological performances to the Microfil® V/S device.

EZ-Fit® filtration unit, pink base: test specifications and results

Microorganisms' rationale and acceptance criteria according to our validation protocols.

The acceptance criteria set up for USP/EP/JP Pharmacopeia strains qualification was: Recovery ≥ 70% versus spread plate, investigate if > 150%:

- *Staphylococcus aureus* ATCC® 6538
- *Aspergillus brasiliensis* ATCC® 16404
- *Bacillus subtilis* ATCC® 6633
- *Candida albicans* ATCC® 10231
- *Pseudomonas aeruginosa* ATCC® 9027

For the strains listed on the COQ of EZ-Fit® filtration unit with 0.45 µm or 0.8 µm membranes, related to ISO 7704 and ASTM for potable water, the acceptance criteria was: Recovery ≥ 80% versus spread plate, investigate if > 150%:

- *Escherichia coli* ATCC® 8739
- *Klebsiella aerogenes* ATCC® 49701
- *Saccharomyces cerevisiae* ATCC® 7754
- *Candida albicans* ATCC® 10231
- *Pseudomonas aeruginosa* ATCC® 9027

For the strains listed on the COQ of EZ-Fit® filtration unit with 0.22 µm membranes, the acceptance criteria was: Recovery ≥ 50% versus spread plate, investigate if > 150%:

- *Pseudomonas aeruginosa* ATCC® 9027
- *Brevundimonas diminuta* ATCC® 19146

Additional strains were tested as they are commonly found in industrial beverage & pharmaceutical manufacturing processes.

– When a selective media was used: the acceptance criteria was: ≥ 50% versus spread plate, investigate if > 150%.

– When a non-selective media was used: the acceptance criteria was: ≥ 70% versus spread plate, investigate if > 150%:

- *Methylobacterium extorquens* NBRC 15911
- *Ralstonia pickettii* ATCC® 27511
- *Enterococcus faecalis* ATCC® 19433
- *Kocuria rhizophila* ATCC® 9341
- *Lactobacillus brevis* ATCC® 8287
- *Pichia membranifaciens* ATCC® 16046
- *Dekkera naardenensis* ATCC® 22075
- *Staphylococcus epidermidis* ATCC® 12228

During the growth promotion test, visual aspect and EZ-Fit® device functionality, including membrane wettability, were also verified.

Growth promotion summary table for EZ-Fit® filtration unit with white 0.45 µm MCE membrane on solid media:

Strain tested	Incubation media and Temperature	Acceptance criterion	Results
			EFHAW10MS F6JA782246Q
Aspergillus brasiliensis ATCC® 16404	SDA 22.5 °C ±2.5 °C	Recovery ≥ 70% versus spread plate	**Pass**
Bacillus subtilis ATCC® 6633	TSA 32.5 °C ±2.5 °C		**Pass**
Pseudomonas aeruginosa ATCC® 9027	TSA 32.5 °C ±2.5 °C		**Pass**
Candida albicans ATCC® 10231	SDA 22.5 °C ±2.5 °C		**Pass**
Staphylococcus aureus ATCC® 6538	TSA 32.5 °C ±2.5 °C		**Pass**
Escherichia coli ATCC® 8739	m-FC with rosolic acid 44 °C ±2.5 °C	Recovery ≥ 80% versus spread plate	**Pass**
Klebsiella aerogenes ATCC® 49701	m-Endo 36 °C ±2 °C		**Pass**
Escherichia coli ATCC® 8739	CCA 36 °C ±2 °C	Recovery ≥ 50% versus spread plate	**Pass**
Methylobacterium extorquens NRBC 15911	R2A 32.5 °C ±2.5 °C	Recovery ≥ 70% versus spread plate	**Pass**
Ralstonia pickettii ATCC® 27511	R2A 32.5 °C ±2.5 °C		**Pass**
Enterococcus faecalis ATCC® 19433	TSA 37 °C ±2.5 °C		**Pass**
Kocuria rhizophila ATCC® 9341	TSA 32.5 °C ±2.5 °C		**Pass**
Lactobacillus brevis ATCC® 8287	MRS 30 °C ±1 °C		**Pass**
Staphylococcus epidermidis ATCC® 12228	TSA 32.5 °C ±2.5 °C		**Pass**

Growth promotion summary table for EZ-Fit® filtration unit with white 0.45 µm MCE membrane on solid media:

Strain tested	Incubation media and Temperature	Acceptance criterion	Results	
			EFHAB10MS 100 mL F6JA782247Q	EFHAB25BS 250 mL F6NA15715Q
Aspergillus brasiliensis ATCC® 16404	SDA 22.5 °C ±2.5 °C	Recovery ≥ 70% versus spread plate	**Pass**	**Pass**
Bacillus subtilis ATCC® 6633	TSA 32.5 °C ±2.5 °C		**Pass**	**Pass**
Pseudomonas aeruginosa ATCC® 9027	TSA 32.5 °C ±2.5 °C		**Pass**	**Pass**
Candida albicans ATCC® 10231	SDA 22.5 °C ±2.5 °C		**Pass**	**Pass**
Staphylococcus aureus ATCC® 6538	TSA 32.5 °C ±2.5 °C		**Pass**	**Pass**
Escherichia coli ATCC® 8739	m-FC with rosolic acid 44 °C ±2.5 °C	Recovery ≥ 80% versus spread plate	**Pass**	**Pass**
Saccharomyces cerevisiae ATCC® 7754	SDA 22.5 °C ±2.5 °C		**Pass**	**Pass**
Pichia membranifaciens ATCC® 16046	SDA 22.5 °C ±2.5 °C	Recovery ≥ 70% versus spread plate	**Pass**	**Pass**

Growth promotion summary table for EZ-Fit® filtration unit with both white and black 0.8 µm MCE membrane on solid media:

Strain tested	Incubation media and Temperature	Acceptance criterion	Results		
			EFAAW10BS 100 mL F6JA782250Q	EFAAB10BS 100 mL F6JA782251Q	EFAAW25BS 250 mL F6NA15714Q
Aspergillus brasiliensis ATCC® 16404	SDA 22.5 °C ±2.5 °C	Recovery ≥ 70% versus spread plate	**Pass**	**Pass**	**Pass**
Candida albicans ATCC® 10231	SDA 22.5 °C ±2.5 °C	Recovery ≥ 80% versus spread plate	**Pass**	**Pass**	**Pass**
Saccharomyces cerevisiae ATCC® 7754	SDA 22.5 °C ±2.5 °C		**Pass**	**Pass**	**Pass**

Growth promotion summary table for EZ-Fit® filtration unit with white 0.22 µm MCE membrane on solid media:

Strain tested	Incubation media and Temperature	Acceptance criterion	Results
			EFGSW10MS 100 mL F6JA782248Q
Aspergillus brasiliensis ATCC® 16404	SDA 22.5 °C ±2.5 °C	Recovery ≥ 70% versus spread plate	**Pass**
Bacillus subtilis ATCC® 6633	TSA 32.5 °C ±2.5 °C		**Pass**
Candida albicans ATCC® 10231	SDA 22.5 °C ±2.5 °C		**Pass**
Staphylococcus aureus ATCC® 6538	TSA 32.5 °C ±2.5 °C		**Pass**
Pseudomonas aeruginosa ATCC® 9027	TSA 32.5 °C ±2.5 °C	Recovery ≥ 50% versus spread plate	**Pass**
Brevundimonas diminuta ATCC® 19146	TSA 32.5 °C ±2.5 °C		**Pass**

Growth promotion summary table for EZ-Fit® filtration unit with White 0.45 µm PVDF membrane on solid media:

Strain tested	Incubation media and Temperature	Acceptance criterion	Results
			EFHVW10IS 100 mL F6JA782245Q
Aspergillus brasiliensis ATCC® 16404	SDA 22.5 °C ±2.5 °C	Recovery ≥ 70% versus spread plate	**Pass**
Bacillus subtilis ATCC® 6633	TSA 32.5 °C ±2.5 °C		**Pass**
Candida albicans ATCC® 10231	SDA 22.5 °C ±2.5 °C		**Pass**
Staphylococcus aureus ATCC® 6538	TSA 32.5 °C ±2.5 °C		**Pass**
Pseudomonas aeruginosa ATCC® 9027	TSA 32.5 °C ±2.5 °C	Recovery ≥ 80% versus spread plate	**Pass**
Escherichia coli ATCC® 8739	TSA 32.5 °C ±2.5 °C		**Pass**

Conclusion

All tested EZ-Fit® filtration units match the acceptance criteria for the growth promotion test.

5.8 Packaging qualification to transport hazards

Test Summary

The objective of this test is to challenge the capability of the packaging, including individual and bulk versions, to withstand transport hazards

Test Specification

Tests were carried out according to the specifications of ASTM D4169 cycle 13, criticality level 2, which is a distribution simulating test used to release high performance packaging system designs for pharmaceutical, medical device and consumer product manufacturers.

This is accomplished by subjecting the packaged product to a sequence of representative, anticipated hazards: shock/drop (manual handling), compression (vehicle stacking), vibration (loose load), low pressure exposure (high altitude), random vibration (truck vehicle), and shock drop (handling).

No functional defect must be observed on the filtration unit after the test sequence by visual inspection.

Test Results

EZ-Fit® filtration unit, blue base

EZ-Fit® filtration units, 100 mL

Catalog Number	Lot Number	Test Result
EFHAW100I EZ-Fit® filtration unit, 100 mL, White MCE 0.45µm, Individual	F3JA59933Q	**Pass**
EFHAW100B EZ-Fit® filtration unit, 100 mL, White MCE 0.45 µm, Bulk	F3MA27859	**Pass**
EFHAW100M3 EZ-Fit® filtration unit, 100 mL, white MCE 0.45µm, multipack	F0AB86392Q	**Pass**

EZ-Fit® filtration units, 250 mL

Catalog Number	Lot Number	Test Result
EFHAW250I EZ-Fit® filtration unit, 250 mL, White MCE 0.45µm, Individual	F3NA42998Q	**Pass**
EFHAB250B EZ-Fit® filtration unit, 250 mL, Black MCE 0.45 µm, Bulk	F3NA42999Q[(1)]	**Pass**
EFHAW250B	SAMPLE	**Pass**

[(1)]The boxes used for these tests are composed of units from lot F3NA42299Q repackaged in bulk version.

EZ-Fit® filtration unit, pink base

EZ-Fit® filtration units, 100 mL

Catalog Number	Lot Number	Test Result
EFGSW10MS Multipack of 4 units	F6JA82248Q	**Pass**
EFHVW10IS Single-packed	F6JA82245Q	**Pass**
EFAAW10BS Bulk with protective bag	F6JA82250Q	**Pass**

EZ-Fit® filtration units, 250 mL

Catalog Number	Lot Number	Test Result
EFAAW25BS Bulk with protective bag	F6NA15714Q	**Pass**

Conclusion

All tested EZ-Fit® units packaging versions match the acceptance criteria.

5.9 Product shelf life

Test Summary

Shelf life studies ensure that the devices are still within the specifications until a given expiry date.

An accelerated shelf life (equivalent of 2 years) was performed. For accelerated aging study, testing is performed on devices exposed at 45°C, 60% humidity after determined period of time in order to simulate 2 years (based on accelerated aging model).

Real time testing is also performed in parallel, at room temperature for 2 years.

Test performed:

- Assembly test
- Residual water on the funnel (only for blue base units)
- Water flow time
- Growth Promotion test
- Wettability and use tests (on final product = membrane + funnel)

Test Specification

According to our internal test method (00083167SO).
The acceptance criteria are the same as explained in previous paragraphs.

Test Results

EZ-Fit® filtration unit, blue base

Test Time Point	Results for EZ-Fit® filtration units, 100 mL		Results for EZ-Fit® filtration units, 250 mL	
Shelf life type	**Accelerated**	**Real time**	**Accelerated**	**Real time**
3 months	**Pass**	**Pass**	**Pass**	**Pass**
6 months	**Pass**	**Pass**	**Pass**	**Pass**
13 months	**Pass**	**Pass**	**Pass**	**Pass**
30 months	**Pass**	**Pass**	**Pass**	**Pass**

EZ-Fit® filtration unit, pink base

Test Time Point	Results for EZ-Fit® filtration units, 100 mL		Results for EZ-Fit® filtration units, 250 mL	
Shelf life type	**Accelerated**	**Real time**	**Accelerated**	**Real time**
3 months	**Pass**[(1)]	**Pass**	**Pass**	**Pass**
13 months	**Pass**	**Pass**	**Pass**	**Pass**
25 months	**Pass**	**Pass**	**Pass**	**Pass**

[(1)]The product's shelf life is based on an accelerated ageing study, correlated with one real time test point: three months. The results of the accelerated ageing met the specification for 25 months, thus enabling a two year expiry claim.

Conclusion

All tested EZ-Fit® units packaging versions match the acceptance criteria.

6 Glossary

AA	MCE membrane with 0.8 µm porosity
ASTM	American Standard Methods
ATCC	American Type Culture Collection
cGMP	current Good Manufacturing Practice
CCA	Chromogenic Coliform Agar
CFU	Colony Forming Unit
COQ	Certificate of Quality
EO	Ethylene Oxide
EP	European Pharmacopeia
GS	MCE membrane with 0.22 µm porosity
HA	MCE membrane with 0.45 µm porosity
HV	PVDF membrane with 0.45 µm porosity
ISO	International Organization for Standardization
JP	Japanese Pharmacopeia
MCE	Mixed Cellulose Esters
MP	Management Procedure
MRS	de Man, Rogosa and Sharpe
NBRC	NITE Biological Resource Center
PVDF	Polyvinylidene Fluoride
R2A	Reasoner’s 2A agar
SDA	Sabouraud Dextrose Agar
TBP	To Be Performed
TM	Test Method
TSA	Trypticase Soy Agar
USP	United States Pharmacopeia

7 Conclusion

This validation summary shows that the performances of the 100 mL and 250 mL EZ-Fit® filtration units meet all the specified acceptance criteria.

EZ-Fit® filtration units offer equivalent performances to the Microfil® V/S device.

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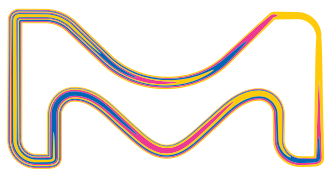

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