SARTORIUS

Sartorius Stedim Biotech GmbH, 37070 Göttingen

Changenotification_ab@sartorius.com

March 10th, 2023

Expected implementation date	Customer action required by Sartorius	Type of action
April 2023	No	NA

Notification Letter

ECR: 33619 ST Certificates - Removal of cGMP Claim:

Dear Valued Customer,

This letter is to inform you about the removal of the cGMP claim on the quality assurance certificates for Sartorius Separation Technology products.

Change Description

Since Sartorius Separation Technology products are not pharmaceutical goods or drugs themselves, the cGMP claim on our QA certificates might be misleading.
Sartorius hereby confirms that the basis for ensuring product quality and safety is the full compliance with our implemented and certified ISO 9001 QM system. And that within this quality management system, a risk-based approach comparable to the cGMP requirements is implemented for the development and control of processes and quality measures. The overall goal, independent of using ISO 9001 or cGMP requirements, is a safe and regulated product life cycle, including:

- Corrective and preventive actions
- Non-conformance management
- Engineering change request management
- Training of employees
- Design and development controls and outputs
- Document control
- Control of production and service provision, including in-process control

Additional agreements with an individual scope of quality requirements can be defined in the respective quality agreements.

Sartorius Stedim Biotech GmbH
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www.sartorius.com

Sitz der Gesellschaft:
Göttingen
Registergericht:
Amtsgericht Göttingen
HRB-Nr. 200266

Geschäftsführer:
Michaela Pischke,
Dr. Helge Henning

Vorsitzender des Aufsichtsrates:
Dr. Joachim Kreuzburg

As a customer, you will not notice any changes to the product safety and quality, or on our service resulting from the QA certificate adaptation.

This change has no impact on fit, form or function and safety of all our Separation Technology products.

It should be noted that this change will also be successively adapted in other documents, such as Validation Guides.

Impacted Products

This change impacts all products manufactured at the following sites:

Sartorius Stedim Biotech GmbH, Göttingen, Germany
Sartorius Stedim Plastics GmbH, Göttingen, Germany
Sartorius Stedim Filters, Inc., Yauco, USA
Sartorius Stedim Lab Ltd., Stonehouse; UK.
Sartorius Stedim India Pvt. Ltd., Bangalore, India

Change Implementation

This change is controlled internally in accordance with Sartorius change management procedures.

This change will be implemented from April 2023 onwards.

We continuously strive to implement solutions to our products and services to enable you to get your treatments to patients faster. We thank you for your trust and continued use of Sartorius products, and we look forward to assisting you in managing this change.

Sincerely,

DocuSigned by:
Davy de Wilde
Signer Name: Davy de Wilde
Signing Reason: I approve this document
Signing Time: 2023-03-16 | 16:49:48 CET
B96FB7BA8D5F40F5B8C73D70C479435E

Davy de Wilde
Head of Product Management FMT
Sartorius Stedim Belgium S.A

DocuSigned by:
Claire Michiels
Nom du signataire : Claire Michiels
Motif de la signature : J'approuve ce document
Heure de signature : 2023-03-20 | 10:34:06 CET
EBF66771F50C40C982FAF5AE17273355

Claire Michiels
Head of Quality Assurance &
Quality Control FMT, ST
Sartorius Stedim FMT S.A.S.

DocuSigned by:
Louis Villain
Name des Unterzeichners: Louis Villain
Signiergrund: Ich genehmige dieses Dokument
Signierzeit: 2023-03-17 | 08:23:22 MEZ
22EDCAB37AF14C11BB76AEFA64D0094D

Louis Villain
Head of Product Group
Separation Consumables
Sartorius Stedim Biotech GmbH

Note: List of affected manufacturing sites:
Sartorius Stedim Biotech GmbH, Göttingen, Germany
Sartorius Stedim Plastics GmbH, Göttingen, Germany
Sartorius Stedim Filters, Inc., Yauco, USA
Sartorius Stedim Lab Ltd., Stonehouse; UK
Sartorius Stedim India Pvt. Ltd., Bangalore, India

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Attachment 1

Sartorius QA certificate before change – cGMP claim is marked yellow

SARTORIUS

Quality Assurance Certificate

Sartopore® 2 300
Sterile Capsule

Order no.	5441307H5--OO--B
Use before	01 / 2026
Pore size	0.45 + 0.2 µm
Lot no.	2303000203

Max. operating pressure 4 bar
Sterilization: Autoclaving at max. 134 °C, no in-line steaming

This document certifies that the designated product was manufactured by Sartorius in conformance with established Current Good Manufacturing Practice (cGMP) standards.

This product is developed, produced and distributed according to a Quality Management System that is certified for compliance with DIN/ISO 9001.

This filter capsule was sterilized using a validated process following DIN/EN ISO 17665-1 regulations, pertaining to "Sterilization of Medical Products".

This product is registered with the Food and Drug Administration (FDA). The DMF number is available upon request.

This product has passed Sartorius' inhouse tests and thus meets Sartorius' stringent quality control standards.

Integrity test values: Each membrane filter element has been individually tested for integrity by means of diffusion and bubble point testing. These tests have been performed according to the procedures stated in the corresponding Validation Guide.

For this filter element the bubble point measured was ≥ 3.2 bar/ 46 psi.

Diffusion rate measured for this filter was found to be ≤ 2.0 ml/min, at a test pressure of 2.5 bar/ 36 psi.

For sterilizing - grade filters, these integrity test values have been fully correlated to the ASTM F 838 Bacteria Challenge test, using a challenge level ≥ 1 x 10^7 CFU/cm^2 of *Brevundimonas diminuta*. For filters with 0.45 µm pore size, these integrity test values have been fully correlated to the retention of *Serratia marcescens* using a challenge level ≥ 1 x 10^7 CFU/cm^2.

Biosafety: All materials of this filter element meet the requirements of the current USP Biological Reactivity tests <88> for plastics Class VI, (Systemic Injection, Intracutaneous and Implantation tests).

Non fibre releasing: This filter product complies with the title21 of the Code of Federal Regulations (CFR), section 210.3(b)(6) and 211.72.

In addition to these main tests, the following is checked on a regular basis:

Bacterial Retention: Quantitative retention of *Brevundimonas diminuta* (*Serratia marcescens*) is checked for every 0.2 µm (0.45 µm) membrane lot. Additionally, the retention of *B. diminuta* (*S. marcescens*) is checked by regular sampling of all sterilizing grade (0.45 µm rated) filter elements.

Oxidizable Substances: The filtrate of these filter elements shows a negative reaction when tested according to the current USP.

Extractable Substances: The total amount of extractables is well below the limits established by the current USP under "Sterile Water for Injection".

Bacterial Endotoxins: An endotoxine free water extract of this filter product contains less than 0.25 EU/ml, which was determined by using the Limulus Amebocyte Lysate (LAL) test.

Particulate Matter: This product releases particulate matter in quantities well below the requirements established in the current USP in "Large Volume Injections for Single Dose Infusion".

Thermal Stability: Capsules that underwent multiple (25) autoclaving cycles at 134 °C showed no loss of integrity.

Note: Details of the methodologies used in the tests mentioned above as well as more detailed test results are given in the respective Validation Guide.

2023-01-24
Date

Dr. Anna Vreemann
Site Quality Manager

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SARTORIUS

Attachment 2

Sartorius sample QA certificate after change

SARTORIUS

Quality Assurance Certificate

Sartopore® 2 300
Sterile Capsule

Order no.	5441307H5--OO--B
Use before	09 / 2025
Pore size	0.45 + 0.2 µm
Lot no.	SAMPLE

Max. operating pressure 4 bar
Sterilization: Autoclaving at max. 134 °C, no in-line steaming

This product is developed, produced and distributed according to a Quality Management System that is certified for compliance with DIN/ISO 9001.

This filter capsule was sterilized using a validated process following DIN/EN ISO 17665-1 regulations, pertaining to "Sterilization of Medical Products".

This product is registered with the Food and Drug Administration (FDA).
The DMF number is available upon request.

This product has passed Sartorius' inhouse tests and thus meets Sartorius' stringent quality control standards.

Integrity test values: Each membrane filter element has been individually tested for integrity by means of diffusion and bubble point testing. These tests have been performed according to the procedures stated in the corresponding Validation Guide.

For this filter element the bubble point measured was ≥ 3.2 bar/ 46 psi.

Diffusion rate measured for this filter was found to be ≤ 2.0 ml/min, at a test pressure of 2.5 bar/ 36 psi.

For sterilizing - grade filters, these integrity test values have been fully correlated to the ASTM F 838 Bacteria Challenge test, using a challenge level ≥ 1 x 10^7 CFU/cm^2 of *Brevundimonas diminuta*. For filters with 0.45 µm pore size, these integrity test values have been fully correlated to the retention of *Serratia marcescens* using a challenge level ≥ 1 x 10^7 CFU/cm^2.

Biosafety: All materials of this filter element meet the requirements of the current USP Biological Reactivity tests <88> for plastics Class VI, (Systemic Injection, Intracutaneous and Implantation tests).

Non fibre releasing: This filter product complies with the title21 of the Code of Federal Regulations (CFR), section 210.3(b)(6) and 211.72.

In addition to these main tests, the following is checked on a regular basis:

Bacterial Retention: Quantitative retention of *Brevundimonas diminuta* (*Serratia marcescens*) is checked for every 0.2 µm (0.45 µm) membrane lot. Additionally, the retention of *B. diminuta* (*S. marcescens*) is checked by regular sampling of all sterilizing grade (0.45 µm rated) filter elements.

Oxidizable Substances: The filtrate of these filter elements shows a negative reaction when tested according to the current USP.

Extractable Substances: The total amount of extractables is well below the limits established by the current USP under "Sterile Water for Injection".

Bacterial Endotoxins: An endotoxine free water extract of this filter product contains less than 0.25 EU/ml, which was determined by using the Limulus Amebocyte Lysate (LAL) test.

Particulate Matter: This product releases particulate matter in quantities well below the requirements established in the current USP in "Large Volume Injections for Single Dose Infusion".

Thermal Stability: Capsules that underwent multiple (25) autoclaving cycles at 134 °C showed no loss of integrity.

Note: Details of the methodologies used in the tests mentioned above as well as more detailed test results are given in the respective Validation Guide.

SAMPLE
Date

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Site Quality Manager

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