

Changenotification_AB@sartorius.com

January 27, 2025

Sartorius Stedim FMT S.A.S.
 Zone Industrielle Les Paluds
 Avenue de Jouques - CS 91051
 13781 Aubagne Cedex, France

t:+33.(0)4.42.84.5600
 f:+33.(0)4.42.84.5619
www.sartorius.com

Expected implementation date	Customer action required by Sartorius	Type of action
March 2025	No	N/A

Notification Letter

ECR 45638_A: Change in the Biosafety Claim Strategy for FMBT

Dear Valued Customer,

This change notification is to inform you of a new strategy of biosafety claim for Fluid Management & Bioreactor Technologies (FMBT) single use systems.

Change Description

Sartorius has updated its biosafety strategy for the FMBT SUS product families, with a focus on two major aspects: in vitro Cytotoxicity testing and Extractable data.

Since the quality of plastics does not change, the pharmaceutical industry and regulatory bodies are now questioning the long-held notion that USP <88> Class VI testing is necessary for a material to be considered well characterized as the use of disposable plastic manufacturing systems matures.

Sartorius adopts a risk-based strategy for evaluating the safety of SUS by combining extractables with suitable in vitro biological reactivity (USP<87>/ISO10993-5). Given the wealth of information on widely used plastics, it is considered unnecessary to keep testing for biocompatibility as mandated by USP <88> Class VI regulation. In alignment with European legislation, public concerns, and animal welfare, Sartorius strategy will no longer require animal testing.

The updated strategy aligns with market demands and BioPhorum recommendations¹. Sartorius will continue to require biocompatibility tests (ISO 10993-5, USP<87>, USP<88>) from suppliers, but USP <88> testing will no longer be necessary if components comply with USP <87> or ISO 10993-5 after processing and irradiation.

The strategy is developed in the Appendix 1 "Sartorius Stedim FMBT Single Use Biosafety Strategy".

The biosafety claim is mentioned on the certificate of release, ensuring transparency and compliance with the updated strategy.

¹ Bioreactivity testing in single-use system biomanufacturing: industry position paper.

We maintain our commitment to biosafety and make the necessary adjustments to our documentation to reflect the intended use of our products

To ensure full alignment and consistency with our biosafety claim, we will be removing on the certificate of release (CoR) the mention of 21 CFR part 177 for the film contact layer. This reference was initially included during the qualification phase for characterization purposes only. The manufacturing processes and raw materials used in our products are not intended for food contact use.

We would like to remind you that our FMBT product is specifically designed for use in biotechnology applications.

Equally, the term "current" from the sentence "SARTORIUS STEDIM Biotech bags pass current USP <661> for plastic Containers. The contact layer of the SXX* film passes current EP 3.1. X*" will be removed as these tests were performed during the qualification phase.
(*specific to film material)

This change has not impact on the, fit, form or function of the finished product.
There are no modifications to testing, or release criteria resulting from the updated certificate content.

Product Compliance statements will be updated on March 31, 2025.

This change will lead to a revision of the certificate of release, as described below and in Appendix 2:

- Finished product with bag:

Section Biological Reactivity Tests in vitro and in vivo:

"Bags and representative fluid contact components have been tested and passed one or a set of biocompatibility/biological reactivity tests USP <88> class VI, ISO 10993 -5, USP <87>"

Section Physicochemical Test:

"SARTORIUS STEDIM Biotech bags pass USP <661> for plastic Containers. The contact layer of the SXX* film passes EP 3.1. X.*"

(*specific to film material)

- Finished product without bag:

Section Biological Reactivity Tests in vitro and in vivo:

"Representative fluid contact components have been tested and passed one or a set of biocompatibility/biological reactivity tests USP <88> class VI, ISO 10993 -5, USP <87>"

Impacted Products

The list of impacted products can be found in Appendix 3_Impacted Products List.
This change will extend its benefits to future references.

Change Implementation

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

This change will be implemented on March 31, 2025.

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,

Signiert von:
Thorsten Adams
Name des Unterzeichners: Thorsten Adams
Signiergrund: Ich genehmige dieses Dokument
Signierzeit: 2025-01-28 | 16:27:13 MEZ
6B8812D7C0C74CCD8EE86997783AFD0E

Signé par :
Jonas Lejeune
Nom du signataire : Jonas Lejeune
Motif de la signature : J'approuve ce document
Heure de signature : 2025-01-28 | 09:30:22 CET
4E190FC098A54650A1D7C762C6CF7663

Thorsten Adams
Head of Product Group Fluid
Management Technologies
Fluid Management & Bioreactor Technologies
Sartorius Stedim Biotech GmbH

Jonas Lejeune
Manager of Quality Engineering
OU Consumables Technologies
Sartorius Stedim FMT S.A.S.

Note: List of affected manufacturing site(s) / manufacturing site(s) of impacted products

- Sartorius Stedim FMT S.A.S., Aubagne, France
- Sartorius Stedim Biotech, Beijing, China
- Sartorius Stedim Filters Inc., Yauco, Puerto Rico
- Sartorius Stedim Bioprocess, M'Hamdia, Tunisia

Appendix 1: Statement Update of Sartorius Stedim FMT Single Use Biosafety Strategy – see document attached

Appendix 2: Example of a Revised Template with Updated Claims – see below

Appendix 3: List of Impacted Products – see document attached

Appendix 2 - Example of a Revised Template with Updated Claims

Finished products with bags:

SPECIMEN NOT SUBMITTED TO NOTIFICATION		SARTORIUS	
Certificate of Release			
Product Description:			
Product description:	Description	Quantity:	99999
Reference:	REFERENCE	Revision level:	NN
Batch number:	XXXXXXXX		
Expiry date:	YYYY - MM		
Customer part number:	CUSTOMER PART NUMBER		
Irradiation batch (cert. enclosed):	IRRADIATION BATCH NUMBER		
=====			
Specifications:	STERILE PRODUCT		
STATEMENTS			
Biological Reactivity Tests in vitro and in vivo:	Bags and representative fluid contact components have been tested and passed one or a set of biocompatibility/biological reactivity tests USP <88> class VI, ISO 10993 -5, USP <87>.		
Physicochemical Test:	SARTORIUS STEDIM Biotech bags pass USP <861> for plastic Containers. EVAM®, the contact layer of the S71 film passes EP 3.1.7 (Polyethylene-Vinyl-Acetate).		
TSE-BSE status:	Conform to the European Guidance EMA /410/01 rev 3 and the European Pharmacopoeia (EP) 5.2.8.		
MONITORING			
Endotoxins:	Representative product has been tested according to current USP <85> Bacterial Endotoxins test by LAL and current EP 2.6.14. Passes the acceptance criteria of < 0.125 EU/mL.		
Subvisible Particles:	Representative product has been tested according to current USP <788> and current EP 2.9.19. Passes the acceptance criteria according to the product nominal capacity.		
Bioburden:	Representative product has been tested according to current ISO 11737 method by filtration. Passes the acceptance limits determined by validation.		
Sterility:	According to current ISO 11137: Sterilization of health care products - Radiation with a 10 ⁻⁶ Sterility Assurance Level (SAL).		
BATCH TESTING			
Visual Inspection:	100% of these bags are inspected and pass the SARTORIUS STEDIM Biotech specifications.		
Leak testing:	100% of these bags are leak tested.		
Product Conformity:	Technical drawing compliance and Batch record review.		
Irradiation:	25 kGy minimum. The Certificate of Irradiation from the approved sub-contractor is enclosed.		
=====			
PARTICLES PREVENTION PROGRAM			
Visible Particles:	Representative product has been analyzed for particles with sizes ≥ 100 µm according to internally developed and validated method. Results are monitored.		
=====			
<i>We certify that this batch has been manufactured in compliance with our internal procedures and that all the test results conform to our specifications.</i>			
<small>Ref: GAMFLEXBO Rev02*</small>			
Note: Comment			
<u>09.09.9999</u>	<u>Quality Specialist</u>		
Date of Release	QUALITY DEPARTMENT		
Certification	Manufactured by Legal Entity	Address	Phone Fax Mail

*Revision number can differ according to the template

Finished products without bags:

SPECIMEN NOT SUBMITTED TO NOTIFICATION		SARTORIUS	
Certificate of Release			
Product Description:			
Product description:	Description	Quantity:	99999
Reference:	REFERENCE	Revision level:	NN
Batch number:	XXXXXXXX		
Expiry date:	YYYY - MM		
Customer part number:	CUSTOMER PART NUMBER		
Irradiation batch (cert. enclosed):	IRRADIATION BATCH NUMBER		
Specifications: STERILE PRODUCT			
STATEMENTS			
Biological Reactivity Tests in vitro and in vivo:	Representative fluid contact components have been tested and passed one or a set of biocompatibility/biological reactivity tests USP <88> class VI, ISO 10993 -5, USP <87>.		
TSE-BSE status:	Conform to the European Guidance EMA/410/01 rev 3 and the European Pharmacopoeia (EP) 5.2.8.		
MONITORING			
Endotoxins:	Representative product has been tested according to current USP <85> Bacterial Endotoxins test by LAL and current EP 2.6.14. Passes the acceptance criteria of <0.125 EU/mL.		
Subvisible Particles:	Representative product has been tested according to current USP <788> and current EP 2.9.19. Passes the acceptance criteria according to the product nominal capacity.		
Bioburden:	Representative product has been tested according to current ISO 11737 method by filtration. Passes the acceptance limits determined by validation.		
Sterility:	According to current ISO 11137: Sterilization of health care products - Radiation with a 10 ⁻⁶ Sterility Assurance Level (SAL).		
BATCH TESTING			
Visual Inspection:	100% of these assemblies are inspected and pass the SARTORIUS STEDIM Biotech specifications.		
Product Conformity:	Technical drawing compliance and Batch record review.		
Irradiation:	25 kGy minimum. The Certificate of Irradiation from the approved sub-contractor is enclosed.		
PARTICLES PREVENTION PROGRAM			
Visible Particles:	Representative product has been analyzed for particles with sizes ≥ 100 µm according to internally developed and validated method. Results are monitored.		
<i>We certify that this batch has been manufactured in compliance with our internal procedures and that all the test results conform to our specifications.</i> Ref: GAMLIGNE Rev02*			
Note: Comment			
09.09.9999		Quality Specialist	
Date of Release		QUALITY DEPARTMENT	
Certification	Manufactured by Legal Entity	Address	Phone Fax Mail

*Revision number can differ according to the template