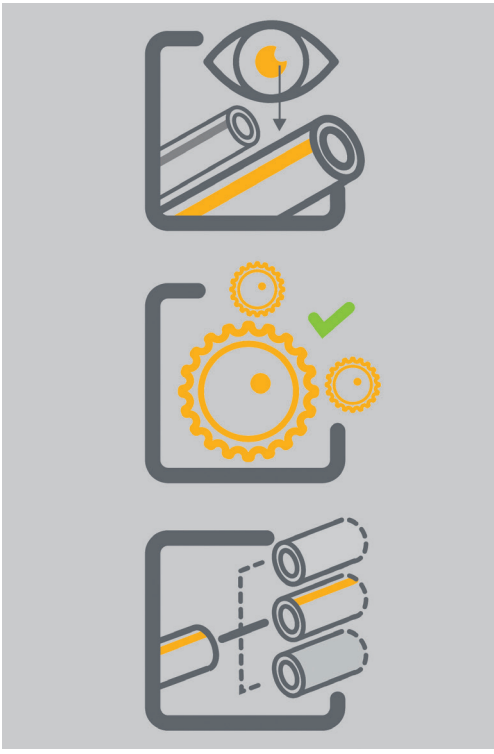
sartorius stedim biotech

Validation Guide
TuFlux® TPE – Thermoplastic Elastomer Tubing



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1. Introduction

Sartorius Stedim Biotech bags and systems are widely used in biopharmaceutical processes for a variety of unit operations of the commercial production of drug products such as vaccines, recombinant proteins and monoclonal antibodies and for the development of future biomolecules in clinical phases.

Buffers and media are increasingly formulated, sterile filtered and stored in single-use Fluid Management Systems (FMS) that involve Flexel®, Flexsafe® and Flexboy® Bags integrated with filters, impeller mixers, tubing, connectors and monitoring tools, as well as transfer sets. Product intermediates are also filtered and stored between UF|DF and chromatography purification steps in gamma sterile Fluid Management Systems.

Fluid Management Systems are also adopted for the formulation, filtration and aseptic processing of final drug products.

From buffer media preparation, cell culture operations, purification operations up to final formulation, filtration and transfer, the thermoplastic tubing TuFlux® TPE is a key element for the successful implementation of disposable manufacturing processes.

The TuFlux® TPE, Sartorius Stedim Biotech Thermoplastic tubing, is qualified, manufactured and released according to stringent product validation protocols and Quality Control testing to offer safe and robust single-use processes to the end users of the biopharmaceutical industry.

The qualification of the tubing includes testing and inspection set up at supplier site with the goal of ensuring that tubing can be reliably and reproducibly manufactured.

We have compiled this validation guide so that users of TuFlux® TPE can plan, implement and document their own validation procedures.

This validation guide is applicable for both TuFlux® TPE sold as a stand-alone product and pre-assembled on Sartorius Stedim Biotech single-use systems.

1.1. Security of Supply

Sartorius Stedim Biotech offers the most secured manufacturing resources and capabilities on the market to ensure the strongest security of supply. We hold the most modern facilities in Europe, America, North Africa for production of pharmaceutical and medical plastic Fluid Management Systems with a total of 6.200 m^2 (67.000 sq.ft) of controlled clean environment of minimum ISO 8 Class.

Our manufacturing plants operate under a common information system in order to offer flexibility and reliable product transfer from one location to the other. Consistent process performance is ensured by the on-going qualification of all components and assemblies, manufacturing processes and personnel.

1.2 cGMP Quality Assurance from Sartorius Stedim Biotech

Consistent high quality of the TuFlux® TPE tubing is assured by careful selection of the raw material by Raumedic, well planned and validated production technologies and an efficient Quality Assurance Department, all of which result in high batch-to-batch reproducibility.

1.3 Quality Assurance

For quality assurance, all materials are carefully selected and validated in accordance with Sartorius Stedim Biotech in-house guidelines and the specifications of our Research and Development Department including product performance and security of supply. TuFlux® TPE as a component undergoes quality controls. This involves 100 % batch testings. A lot release is based on in-process control and final control of the data. A lot is not released until all in-process and final quality control data are available.

1.4 Complete Traceability

The product reference and lot number are printed on the label of the protective plastic bag and on the label of the box in which the TuFlux® TPE Thermoplastic tubing is packed. The traceable lot number allows convenient retrieval of all data compiled on the materials used, production steps and QC tests.

1.5 Quality Management System

Sartorius Stedim Biotech has a Quality Management System in place to assure consistent high quality of the TuFlux® TPE tubing.

Sartorius Stedim Biotech Quality Systems for single-use products follow applicable ISO 9001, FDA regulations and ISO 13485 for Medical Devices1.***

The complete Quality Systems Certificates are continuously updated and can be downloaded on our website www.sartorius-stedim.com.

- Raumedic is also certified according to ISO 13485

1.6 Human Resources

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

1.7 Infrastructure

The buildings, equipment and work environment at Sartorius Stedim Biotech have been designed to maximize employee comfort and safety while responding to current GMP requirements for the manufacture of single-use FMS destined to the pharmaceutical industry and medical applications. All infrastructure (equipment, utilities, etc.) that has an impact on the product quality is inventoried and undergoes an appropriate qualification.

*** ISO13485 certificate for the sites of Aubagne, France and M'Hamdia, Tunisia

1.8 Purchasing Supplier and Raw Material Qualification

All our suppliers are carefully selected according to internal standards and applicable regulations. Each raw material and|or component used in FMS is put through prior qualification. This qualification includes a list of required statements from the supplier that is dependent on the final use of the component and|or raw material. Typical requirements for components that are in contact with the product flow are the following (not exhaustive list):

- USP <88> Class VI and|or ISO10993-6,-10, and -11 conformity
- TSE|BSE statement EP conformity (if applicable)

Change notification agreement with supplier in order to ensure the security of supply.

Beyond these requirements, Sartorius Stedim Biotech performs a qualification of the proposed component and|or raw material internally. For components, beside other tests shown in the following chapters which detailed the characteristics of the tubing material, the qualification will be centered around the testing of the assembly of the new component with other components and|or bags that will be attached.

Disclaimer

TuFlux® TPE has not been tested and approved for patient cure and hospital, such as for temporary insertion or any in vivo procedure.

TuFlux® TPE is intended to be used in the biopharmaceutical industry but not tested for implantable medical devices.

Supplier Evaluation

Suppliers are periodically evaluated on the basis of the following performance metrics:

- Delivery conformity.
- Conformity of products on reception
- Compliance with delivery deadlines
- Suppliers audit is performed periodically based on criticality.

1.9 Verification of Purchased Product (Incoming QC)

Tubing products are inspected upon arrival at Sartorius Stedim Biotech against approved control specifications. Typical testing requirements applied at incoming quality inspection are listed below:

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

Only approved materials will be allowed to be used in production of single-use FMS manufactured by Sartorius Stedim Biotech.

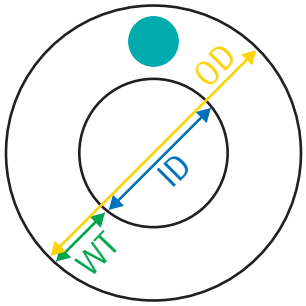
2. Technical Specifications

2.1 Tubing Manufacturing

TuFlux® TPE is produced by Raumedic (Germany) under clean room conditions according to ISO 14644, ISO class 7. The production site of Raumedic is certified according to ISO 13485:2003.

2.2 Tubing Dimensions

Dimensions [mm] (ID × OD)	Dimensions [inch] (ID × OD)	Color Stripe	RAL Code
3.2 × 6.4	1/8 × 1/4	Yellow	1018
6.4 × 9.5	1/4 × 3/8	Orange	1028
6.4 × 11.1	1/4 × 7/16	Red	3020
9.5 × 15.9	3/8 × 5/8	White	9003
12.7 × 19.1	1/2 × 3/4	Grey	7046
19.1 × 25.4	3/4 × 1	Blue	5012
19.1 × 28.6	3/4 × 1 1/8	Black	9005



Color Stripes

Every dimension has a dedicated unique color within the standard range of TuFlux® TPE for a clear identification.

This color stripe is fully embedded into the tubing wall and has neither contact to the inner-, nor the outer surface of the tubing. All tests results shown in this Validation Guide (if not specified) include the color stripes in their specific dimensions.

2.3 Type and Part Numbers Overview

Tubing coils made of TuFlux® TPE are of dimensions between 1/8" × 1/4" (ID × OD) and 3/4" × 1 1/8" (ID × OD). Tubing coils are provided in a double PE bags and single packaged in a cardboard box.

Part Number	Dimensions [mm] (ID × OD)	Dimensions [inch] (ID × OD)	Tubing Coil Length [m|ft]
FSA121869	3.2 × 6.4	1/8 × 1/4	200|656
FSA121870	6.4 × 9.5	1/4 × 3/8	125|410
FSA121871	6.4 × 11.1	1/4 × 7/16	100|328
FSA121872	9.5 × 15.9	3/8 × 5/8	50|164
FSA121873	12.7 × 19.1	1/2 × 3/4	30|98
FSA121874	19.1 × 25.4	3/4 × 1	20|66
FSA121875	19.1 × 28.6	3/4 × 1 1/8	20|66

2.4 Material of Construction

The generic raw materials entering in the TPE formulation from the TPE compounder are described below.

The TPE formulation is composed of:

- Styrenic Bloc Copolymer (SBC)
- Mineral oil
- Polyolefin
- Additives
- Pigments for colored stripes

According to the current state-of-the-art individual fisheyes due to raw material and processing, foreign material, dirt inclusions and air bubbles as well as contamination on the tubing surface, like intrinsic particles and fluff, cannot be completely excluded.

TuFlux® TPE is delivered to customers within the following dimensions specifications:

SSB PN#	RM Description	SSB Product Description	Tube Diameter (ID × OD)	ID [mm]	WT [mm]	Color Stripe
FSA121869	TuFlux® TPE 1/8" × 1/4" Yellow	TuFlux® TPE 1/8" ID × 1/4" OD Yellow stripe (200 m)	1/8" × 1/4"	3.10–3.30	1.50–1.70	Yellow
FSA121870	TuFlux® TPE 1/4" × 3/8" Orange	TuFlux® TPE 1/4" ID × 3/8" OD Orange stripe (125 m)	1/4" × 3/8"	6.25–6.55	1.50–1.70	Orange
FSA121871	TuFlux® TPE 1/4" × 7/16" Red	TuFlux® TPE 1/4" ID × 7/16" OD Red stripe (100 m)	1/4" × 7/16"	6.25–6.55	2.25–2.45	Red
FSA121872	TuFlux® TPE 3/8" × 5/8" White	TuFlux® TPE 3/8" ID × 5/8" OD White stripe (50 m)	3/8" × 5/8"	9.35–9.65	3.05–3.35	White
FSA121873	TuFlux® TPE 1/2" × 3/4" Grey	TuFlux® TPE 1/2" ID × 3/4" OD Grey stripe (30 m)	1/2" × 3/4"	12.40–12.80	3.05–3.35	Grey
FSA121874	TuFlux® TPE 3/4" × 1" Blue	TuFlux® TPE 3/4" ID × 1" OD Blue stripe (20 m)	3/4" × 1"	18.75–19.25	3.05–3.35	Blue
FSA121875	TuFlux® TPE 3/4" × 1 1/8" Black	TuFlux® TPE 3/4" ID × 1 1/8" OD Black stripe (20 m)	3/4" × 1 1/8"	18.75–19.25	4.55–5.05	Black

Contamination with asbestos particles is excluded due to purity of raw materials used and due to manufacturing process.

TuFlux® TPE is free from any substances defines as SVHC – Substances of Very High Concern – by the European REACH regulation, Annex XIV.

The material grade meets the requirements of heavy metals limits according to European directive 2011/65/EC.

2.5 Physical Properties

2.5.1 USP <661> - Containers, Physicochemical Tests – Plastic

Purpose
Physicochemical tests are designed to determine physical and chemical properties of TuFlux® TPE tubing and their extracts. They are performed on TuFlux® TPE samples before and after irradiation, autoclaving and accelerated ageing conditions.

Test Method
Samples of the TuFlux® TPE cut in small portions previously gamma irradiated (50 kGy) were extracted in ultrapure water at 70 °C (158 °F) for 30 hours. The tests are conducted in order to determine physical and chemical properties of the test article and its extracts. The same test have been performed on non-sterile (5 years shelf life) or autoclaved (30 minutes at 123 °C) tubing and stored during a period corresponding to a shelf life of 3 years (accelerated ageing conditions).

	Condition	Norm	Conclusion
TuFlux® TPE	50 kGy/t = 0	USP 37 – NF32 <661>	Compliant
	50 kGy/t = 3 y	USP 37 – NF32 <661>	Compliant
	AC/t = 0	USP 37 – NF32 <661>	Compliant
	AC/t = 3 y	USP 37 – NF32 <661>	Compliant
	NS/t = 5 y	USP 37 – NF32 <661>	Compliant

2.5.2 Material Hardness

Purpose and Test Method
A measure of the indentation resistance of elastomeric or soft plastic materials based on the depth of penetration of a conical indentor. Hardness values range from 0 (for full penetration) to 100 (for no penetration).

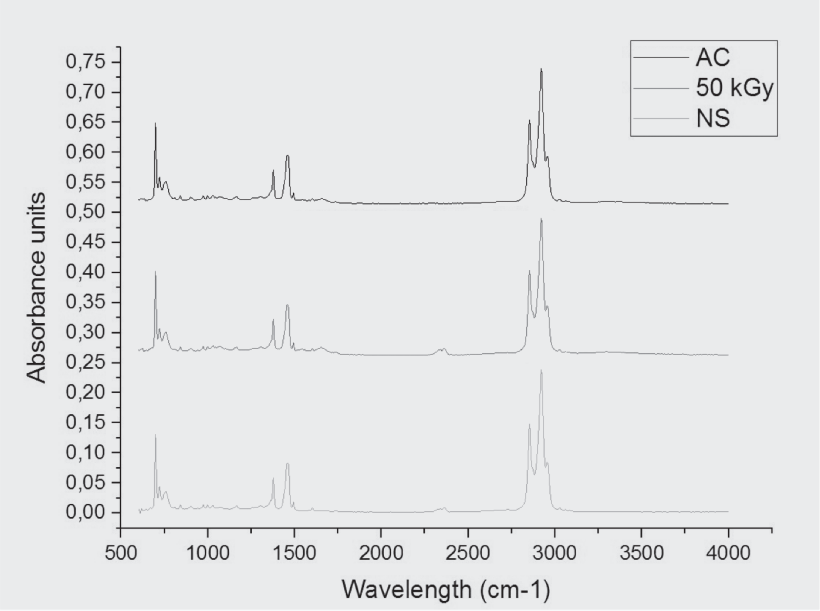
For each TPE plate, the hardness has been measured according to ISO 868 (Plastics - Determination of indentation hardness by means of a durometer (Shore hardness, 3s)) after different treatments (50 kGy or AC) and up to 5 years shelf life.

Test Results

	Condition	Time	Standards	Units	Value
TuFlux® TPE	NS	t = 0 & t = 5 y	ISO 868	Shore A	60 ± 5
	50 kGy	t = 0 & t = 5 y	ISO 868	Shore A	60 ± 5
	AC	t = 0 & t = 5 y	ISO 868	Shore A	60 ± 5

2.5.3 FT-IR

Purpose
FT-IR analysis has been conducted in order to highlight the chemical fingerprint of the polymer including additives.



No difference (no new peaks between the 2 spectra) is observed between the FT-IR spectra for the TuFlux® TPE tubes after the different treatments. (50 kGy or AC). The spectra are equivalent whatever is the treatment meaning that no physico-chemical modifications are detected with the FT-IR analytical technique.

2.5.4 Thermal Stability

The operational temperature range (ie. the temperature range where there are no transition phase like melting or glass transition phase) can be set from -55 °C to 135 °C for the TuFlux® TPE tube whatever the treatments (NS, 50 kGy or AC).

Moreover, the operational temperature range can be set for the TuFlux® TPE tube from -55 °C to 135 °C.

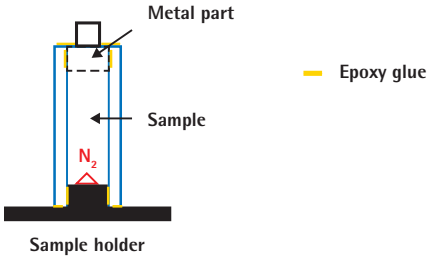
The following storage conditions shall apply:

- Temperature: 15 °C (59 °F) to 25 °C (77 °F)
- Relative humidity 30–60 %
- No exposure of the tubing material to direct sun-light or UV-irradiation sources

2.5.5 Oxygen Permeability

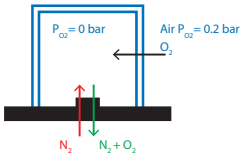
Purpose

This property is important when the product inside the TuFlux® TPE is sensible to oxidation and will be stored. The permeation phenomenon being driven by the partial pressure equilibrium on both sides of the tubing wall, no oxygen will enter the container if it is not consumed by the solution. The values displayed in this table are the maximum.



Method

The test has been conducted on TuFlux® TPE ½" × ¾" with a wall thickness of 3.2.



Test Results

Sample	OTR [cm^3/pkg/24 h]	Permeability [cm^3.mm/m^2/24 h/bar]
TuFlux® TPE 50 kGy	1.23	2440
TuFlux® TPE NS	1.35	3260
TuFlux® TPE AC	1.35	3132

2.6 Compression Set Data According to ISO 815.

To assess the ability of the TuFlux® TPE material to recover and resist permanent deformation after being compressed, the compression set (in %) is measured according to ISO 815 (Rubber, vulcanized or thermoplastic – Determination of compression set – Part 1: at ambient or elevated temperatures).

Method:

In order to perform these measurements, TPE cylinder sample specimens are prepared from a TPE plate produced from TuFlux® TPE granules:

Three cylinder specimens are produced and for each of them, the compression set under constant deflection (CB in %, compression for 24 h at 40 °C) is measured. The average and standard deviation of these 3 values are also reported.

Results

	Condition	Data	Compression Set C_B [%]
TuFlux® TPE material	INS/t = 0	Sample 1	39.7
		Sample 2	38.6
		Sample 3	39.0
		Average	39.1
		SD	0.6

2.7 Tensile Properties

The following values are determined on standard test specimens punched from a press plate.

Purpose and Test Method

A tensile test consists in applying an elongation to a normalized test specimen and measuring the resulting strength. Mechanical properties can then be defined from the stress-strain curve.

Tensile Strength at Break (TS)

The stress a material can withstand before breaking is calculated by dividing the load at break by the cross section area of the specimen. The tensile strength test is performed with a tensile machine in traction mode.

Elongation at Break

The elongation is recorded at the moment of specimen rupture and often expressed as a percentage of the original length. Materials with high elongation at break withstand a high deformation before rupture.

Test Results

	Condition	Min Tensile Strength (MPa)	Specifications
TuFlux® TPE	NS/t = 0	11.9	Tensile Strength ≥ 5.0 Mpa
	NS/t = 2 y	12.5	
	NS/t = 3 y	11.5	
	NS/t = 5 y	12.0	
	50 kGy/t = 0	7.7	
	NS/t = 1 y > 50 kGy > 50 kGy/t = 2 y	7.3	
	NS/t = 2 y > 50 kGy > 50 kGy/t = 3 y	6.1	
	AC/t = 0	12.0	
	NS/t = 1 y > AC > AC/t = 1 y	10.2	
	NS/t = 2 y > AC > AC/t = 3 y	10.8	

	Condition	Min Elongation at Break [%]	Specifications
TuFlux® TPE	NS/t = 0	827	Elongation at Break ≥ 450 %
	NS/t = 2 y	826	
	NS/t = 3 y	815	
	NS/t = 5 y	820	
	50 kGy/t = 0	826	
	NS/t = 1 y > 50 kGy > 50 kGy/t = 2 y	764	
	NS/t = 2 y > 50 kGy > 50 kGy/t = 3 y	758	
	AC/t = 0	879	
	NS/t = 1 y > AC > AC/t = 1 y	824	
	NS/t = 2 y > AC > AC/t = 3 y	846	

Specification

Properties	Standards	Units	Value
Tensile Strength	ISO 527-3	MPa	≥ 5.0
Elongation at Break	ISO 527-3	%	≥ 450

2.8 Chemical Compatibility

Purpose
A chemical resistance study is conducted to assess the resistance of TuFlux® TPE to a variety of chemical solutions.

Test Method
The tubes are tested according to the ASTM D543-14 (Standard Practices for Evaluating the Resistance of Plastics to chemical reagents for 7 days at RT) (or 1 day at RT for 3 chemical reagents) with the following 24 chemical reagents for worst case or for their representativeness in customer applications:

Test Results

Chemical Reagents	Test Conditions	Compatibility with 50 kGy TuFlux® TPE	Compatibility with AC TuFlux® TPE
95 % Ethanol	7 d at RT	Compatible	Compatible
70 % Ethanol		Compatible	Compatible
100 % Ethyl acetate		Not compatible	Not compatible
100 % Glycerol		Compatible	Compatible
3 % (1M) Hydrochlorid acid		Compatible	Compatible
1 % Citric acid		Compatible	Compatible
10 % (3,3M) Hydrochlorid acid		Compatible	Compatible
25 % (4,3M) Phosphoric acid		Compatible	Compatible
5M Ammonium hydroxide (pH14)		Compatible	Compatible
1 % (0,4M) Sodium hydroxide		Compatible	Compatible
50 % (19M) Sodium hydroxide		Compatible	Compatible
Buffer pH 4,6: Acetate buffer solution		Compatible	Compatible
Buffer pH 10: Borax sodium hydroxide		Compatible	Compatible
Buffer pH 7,2: Phosphate buffer solution		Compatible	Compatible
27 % (50 mM) Sodium acetate		Compatible	Compatible
100 % Triton X-100		Compatible	Compatible
100 % Tween 80		Compatible	Compatible
100 % Olive oil		Not recommended	Not recommended
100 % N,N-dimethylacetamide (DMA/DMAc)	7 d at RT	Not recommended	Not recommended
20 % N,N-dimethylacetamide (DMA/DMAc)	1 d at RT	Compatible	Compatible
100 % Dimethyl sulfoxide (DMSO)	7 d at RT	Compatible	Compatible
100 % N,N-dimethylformamide (DMF)	7 d at RT	Compatible	Compatible
20 % N,N-dimethylformamide (DMF)	1 d at RT	Compatible	Compatible
100 % 1,2-Propanediol (Propylene glycol PG)	7 d at RT	Compatible	Compatible
100 % Acetonitrile (ACN)	7 d at RT	Compatible	Compatible
100 % N-methylpyrrolidone (NMP)	7 d at RT	Not recommended	Not recommended
20 % N-methylpyrrolidone (NMP)	1 d at RT	Compatible	Compatible

2.9 Biocompatibility

Purpose and Test Method
Biocompatibility tests are performed to demonstrate that TuFlux® TPE is biocompatible and meets or exceeds the current USP and ISO requirements. Tests are carried out on TuFlux® TPE samples before and after gamma irradiation (50 kGy) or autoclave treatment (30 minutes at 123 °C).

TuFlux® TPE tubing samples were supplied to an independent testing facility for evaluation under the current USP <88> Class VI, USP <87> and ISO 10993-5 Biocompatibility standards.

USP <87> and ISO 10993-5: Biological Reactivity Tests, In Vitro
Within the context of a cytotoxicity test according to USP <87> (equivalent to ISO 10993-5) no substances with cytotoxicity effects were detected. The test has been performed on non-sterile, gamma irradiated (50 kGy) and autoclaved samples (30 min at 123 °C).

USP <88> Class VI: Biological Reactivity Tests, In Vivo
TPE material meets the requirements of the USP <88> Class VI tests, meaning that biological neutrality has been proven via these experiment tests on non-sterile, gamma irradiated (50 kGy) or autoclaved sterilized (30 minutes at 123 °C) tube samples.

- Intracutaneous test
- Systemic injection test
- Implantation test (5 days)

Test Results

Condition	Norm	Conclusion
NS/t = 0	USP <87> ISO1993-5	Compliant
	USP <88> Class VI	Compliant
50 kGy/t = 0	USP <87> ISO1993-5	Compliant
	USP <88> Class VI	Compliant
AC/t = 0	USP <87> ISO1993-5	Compliant
	USP <88> Class VI	Compliant
50 kGy/t = 3 y	USP <87> ISO1993-5	Compliant
	USP <88> Class VI	Compliant
AC/t = 3 y	USP <87> ISO1993-5	Compliant
	USP <88> Class VI	Compliant
NS/t = 5 y	USP <87> ISO1993-5	Compliant
	USP <88> Class VI	Compliant

2.10 Other USP Compliances

USP <85>: LAL Endotoxin Test
TuFlux® TPE (non-sterile, t = 0) passed LAL Endotoxin Test according to USP <85> (equivalent to EP 2.6.14).

2.11 USP<788>: Particulate Matter

TuFlux® TPE tubing after pumping releases particulate matter in quantities below the specifications for large volume parenteral containers > 100 mL given in the current USP<788>.

2.12 ADCF Certified

TuFlux® TPE raw material does not contain any animal derived components and Raumedic does not add any animal derived components during the TuFlux® TPE tube extrusion process.

2.13 Tubing Printing

TuFlux® TPE is delivered printed with the following printing: "Sartorius Stedim Biotech – TuFlux® TPE a/b" × c/d" – made by Raumedic", where a/b is the internal dimension and c/d the outer dimension of the tubing in inch.

A strong exposure of the TuFlux® TPE printing on the outer surface with ethanol might result in partial ink removal.

The inocuity of the ink is proven by the tests performed according to ISO 10993-5.

2.14 Sterilization Compatibility

The TuFlux® TPE may be unsterile when sold as a stand-alone product or sterile when sold pre-assembled on Sartorius Stedim Biotech bags. The tubing TuFlux® TPE is coiled in the relevant specified supply length and are supplied welded in double PE-bags, however non-sterile. TuFlux® TPE tubing can be sterilized according the well-known methods of sterilization technique, while we especially recommend sterilization via gamma rays (up to 50 kGy), water vapour (up to 123 °C for 30 minutes).

It is the responsibility of the user to validate a sterilization process with autoclave for TuFlux® TPE.

2.15 Shelf Life and Recommended Storage Conditions

The shelf life of TuFlux® TPE is 5 years in non-sterile and 3 years in sterile conditions described in chapter 2.12.

There is no substantial change of the specified physical, chemical and physiological parameters of the tubing material after that period of time.

3. Functional Tests

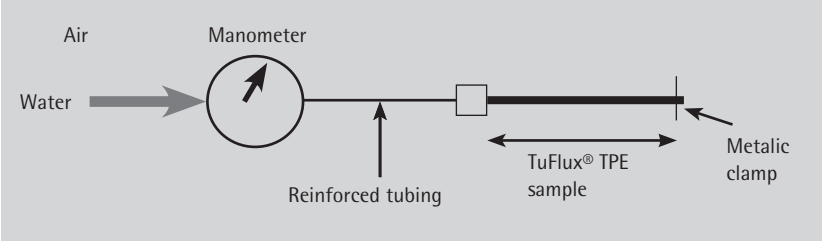
The tests of the TuFlux® TPE have been performed according to Sartorius Stedim Biotech or Raumedic internal standard methods. The qualification tests were performed at ambiant temperature.

3.1 Burst Pressure Test

Purpose
The goal of the burst pressure test is to assess the pressure resistance of the tubing in non-sterile and after either 50 kGy or AC treatments and ageings, depending on the tubing dimensions (inside diameter and wall thickness).

Test Method
The pressure is increased with a constant rate (0.1 bar/s) until the failure of the tubing.

The test method is described in the scheme below:



The Water Burst Pressure (BP in bar) and the pressure at 10 % OD elongation (PEI in bar) have been measured with the following dimensions & conditions described in the table below

- 1/8" × 1/4" TuFlux® TPE tube
- 1/4" × 3/8" TuFlux® TPE tube
- 1/4" × 7/16" TuFlux® TPE tube
- 3/8" × 5/8" TuFlux® TPE tube
- 1/2" × 3/4" TuFlux® TPE tube
- 3/4" × 1" TuFlux® TPE tube
- 3/4" × 1 1/8" TuFlux® TPE tube

For each condition, 3 × 1 m tubes have been prepared for Burst Pressure (BP) and 10 % OD elongation (PEI) measurements.

Dimensions ID × OD ["]	Condition	Mean Pressure at 10 % OD Elongation (PEI) [bar]	Mean Burst Pressure [bar]
1/8 × 1/4	NS/t = 0	5.1	5.8
	50 kGy/t = 0	5.0	5.7
	AC/t = 0	5.1	5.9
	NS/t = 5 y	4.9	6.2
	50 kGy/t = 5 y	4.6	5.0
	AC/t = 5 y	5.1	5.4
1/4 × 3/8	NS/t = 0	2.5	3.7
	50 kGy/t = 0	2.3	3.7
	AC/t = 0	2.1	3.8
	NS/t = 5 y	2.8	4.0
	50 kGy/t = 5 y	2.4	3.6
	AC/t = 5 y	2.4	3.9
1/4 × 7/16	NS/t = 0	3.3	4.9
	50 kGy/t = 0	3.3	4.6
	AC/t = 0	3.4	4.7
	NS/t = 5 y	3.2	5.1
	50 kGy/t = 5 y	3.0	4.5
	AC/t = 5 y	3.2	4.9
3/8 × 5/8	NS/t = 0	3.3	4.8
	50 kGy/t = 0	3.5	4.5
	AC/t = 0	3.3	4.8
	NS/t = 5 y	3.1	4.8
	50 kGy/t = 5 y	3.2	4.4
	AC/t = 5 y	3.3	4.8
1/2 × 3/4	NS/t = 0	2.5	3.6
	50 kGy/t = 0	2.3	3.0
	AC/t = 0	2.1	3.2
	NS/t = 3 y	2.9	3.8
	NS/t = 2 y > 50 kGy > 50 kGy/t = 3 y	2.9	3.6
	NS/t = 2 y > AC > AC/t = 3 y	3.0	3.9
3/4 × 1	NS/t = 0	1.5	2.5
	50 kGy/t = 0	1.5	2.5
	AC/t = 0	1.7	2.8
	NS/t = 5 y	1.6	2.8
	50 kGy/t = 5 y	1.6	2.5
	AC/t = 5 y	1.8	3.0
3/4 × 1 1/8	NS/t = 0	2.6	3.7
	50 kGy/t = 0	2.6	3.6
	AC/t = 0	2.7	3.6
	NS/t = 5 y	2.6	3.8
	50 kGy/t = 5 y	2.5	3.5
	AC/t = 5 y	2.6	3.6

3.2 Pumping Life Time

Purpose
The goal of the pumping life time test is to assess the mechanical resistance of the tubing under pumping conditions.

Test Method
The aim of the Pumping Life Time (PLT) trial is to assess the durability in hour or in volume of the tube pumped at the maximum speed of the pump (320 rpm for biggest pumps and 220 rpm for smallest pumps) until the tube breaks and leaks.

The Pumping Life Time (PLT) is measured at SSB

- for the ½" × ¾" TuFlux® TPE tube (the most common and used tube size)
- for the ¼" × 7/16" TuFlux® TPE tube (the smallest most common and used tube)
- for the ¾" × 1⅛" TuFlux® TPE tube (the largest tube)

at

- NS/t = 0
- NS/t = 3 y
- 50 kGy/t = 0
- 50 kGy/t = 3 y
- AC/t = 0
- AC/t = 3 y

For each condition, 3 × 2 m tubes are prepared and placed in a closed system where tap water is pumped in recirculation in the tube at the maximum pump speed of 320 rpm (½ and ¾ ID) or 220 rpm (for ¼ ID) with Watson Marlow pumps (520 or 720 series dependent on the tube diameter).

Mean pumping life time in hours

PLT [h]	NS		50 kGy		AC	
	t = 0	t = 3 y	t = 0	t = 3 y	t = 0	t = 3 y
¼ × 7/16	289	332	111	168	201	344
½ × ¾	165	77	57	48	149	101
¾ × 1⅛	100	76	91	48	55	106

Mean pumping volume in liter

Volume [kL]	Pump Flow Rate [L/min]	NS		50 kGy		AC	
		t = 0	t = 3 y	t = 0	t = 3 y	t = 0	t = 3 y
¼ × 7/16	1.5	26	29,880	10	15	18	31
½ × ¾	12	119	55,440	41	35	107	73
¾ × 1⅛	21	126	95,760	115	60	69	134

4. Welding, Co-Welding & Sealing

4.1 Welding

The Thermoplastic Elastomer tubing TuFlux® TPE can be sterile connected to other TPE tubing with heat welding.

Using Sartorius Stedim Biotech´s BioWelder® TC, TuFlux® TPE can be used in wide range of applications.

TuFlux® TPE parameters have to be installed on BioWelder® TC.

Please contact Sartorius Stedim Biotech local Service team in case a parameter installation is needed.

For ease of use and to avoid mishandling, the color stripe for each dimension of TuFlux® TPE is corresponding to the correct BioWelder® tube holders (see chapter 2.2 for TuFlux® TPE color coding).

TuFlux® TPE can be welded to other TuFlux® TPE tubes within the same dimensions. The sterilization modes (gamma irradiation & autoclaving) can be used in all combinations.

TuFlux® TPE parameter development and qualification for BioWelder® TC include the following testing:

- Visual inspection
- Pressure test
- Tensile strength test
- Bacterial challenge test

For more details please refer to the BioWelder® TC Validation Guide.

Welding capabilities for TuFlux® TPE with BioWelder® TC.

System	BioWelder® TC
Tube	**TuFlux® TPE**
TuFlux® TPE 1/8" × 1/4"	✓
TuFlux® TPE 1/4" × 7/16"	✓
TuFlux® TPE 1/4" × 3/8"	✓
TuFlux® TPE 3/8" × 5/8"	✓
TuFlux® TPE 1/2" × 3/4"	✓
TuFlux® TPE 3/4" × 1"	✓

✓ = validated welding parameters on BioWelder® TC

4.2 Co-Welding

The development and validation of TuFlux® TPE welding parameters allow connections of TuFlux® TPE to C-Flex® 374 and of TuFlux® TPE to AdvantaFlex® within the same diameters. The sterilization modes (gamma irradiation & autoclaving) can be used in all combinations. TuFlux® TPE parameters have to be installed on BioWelder® TC.

Please contact Sartorius Stedim Biotech local Service team in case a parameter installation is needed.

TuFlux® TPE parameter development and qualification for BioWelder® TC include the following testing:

- Visual inspection
- Pressure test
- Tensile strength test
- Bacterial challenge test

For more details please refer to the BioWelder® TC Validation Guide.

Co-welding capabilities with TuFlux® TPE welding parameters

System	BioWelder® TC	BioWelder® TC
Tube	**C-Flex® 374**	**AdvantaFlex®**
TuFlux® TPE 1/8" × 1/4"	✓	✓
TuFlux® TPE 1/4" × 7/16"	✓	✓
TuFlux® TPE 1/4" × 3/8"	✓	✓
TuFlux® TPE 3/8" × 5/8"	✓	✓
TuFlux® TPE 1/2" × 3/4"	✓	✓
TuFlux® TPE 3/4" × 1"	✓	✓

✓ = validated co-welding parameters on BioWelder® TC

4.3 Sealing

The TuFlux® TPE tubing can be sealed (sterile disconnection) with BioSealer® from Sartorius Stedim Biotech.

BioSealer parameters for TuFlux® TPE are validated for gamma irradiated (25–40 kGy) and autoclaved (121 °C, 20 min) conditions. Parameter development for BioWelder® TC include the following testings:

- Visual inspection
- Pressure test

For more details please refer to the BioSealer® technical report on TuFlux® TPE.

System	BioSealer®	BioSealer® Parameters
Tube		
TuFlux® TPE 1/8" × 1/4"	✓	P3
TuFlux® TPE 1/4" × 3/8"	✓	P3
TuFlux® TPE 1/4" × 7/16"	✓	P3
TuFlux® TPE 3/8" × 5/8"	✓	P8
TuFlux® TPE 1/2" × 3/4"	✓	P8

✓ = validated sealing parameters for BioSealer®

5. Cell-culture Trials

The aim is to assess whether the TuFlux® TPE tube is compatible with cell-growth (not inhibiting it) and then suitable to be used in bag systems or bioreactors for cell culture.

The cell-culture trials are performed according to the scheme on Figure 1 with the following conditions:

- Cell line: CHO-DG44 cells expressing human IgG1
- Medium: ActiCHO-SM
- Extraction ratio of R1 = 0.88 cm²/mL in the 500 mL Medium during 3 days incubation at 37 °C
- then, obtention of the ratios R2 = 0.29 cm²/mL and R3 = 0.088 cm²/mL by respective 3× and 10× dilution of the extract
- Agitation of the shaking platform: 160 rpm
- Temperature: 36.8 °C
- CO_2 concentration: 7.5 %
- Humidity: 80 %
- Initial cell density: 0.2×10^6 cells/mL
- Working volume: 10 mL/well
- Cultivation time: 3 days

The tube treatments (50 kGy and AC) and cell-culture trials are handled and performed for the ½" × ¾" TuFlux® TPE tube at the following conditions:

- 50 kGy/t = 0
- 50 kGy/t = 5 y
- AC/t = 0
- AC/t = 5 y

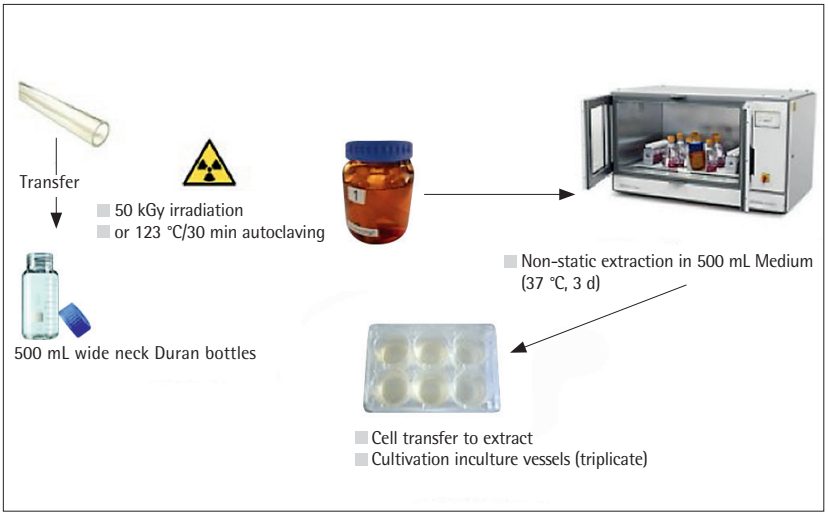


Figure 1: Cell-culture trial scheme

Table 1: Cell-growth results for 50 kGy TuFlux® TPE Tube at t = 0 and t = 5 y

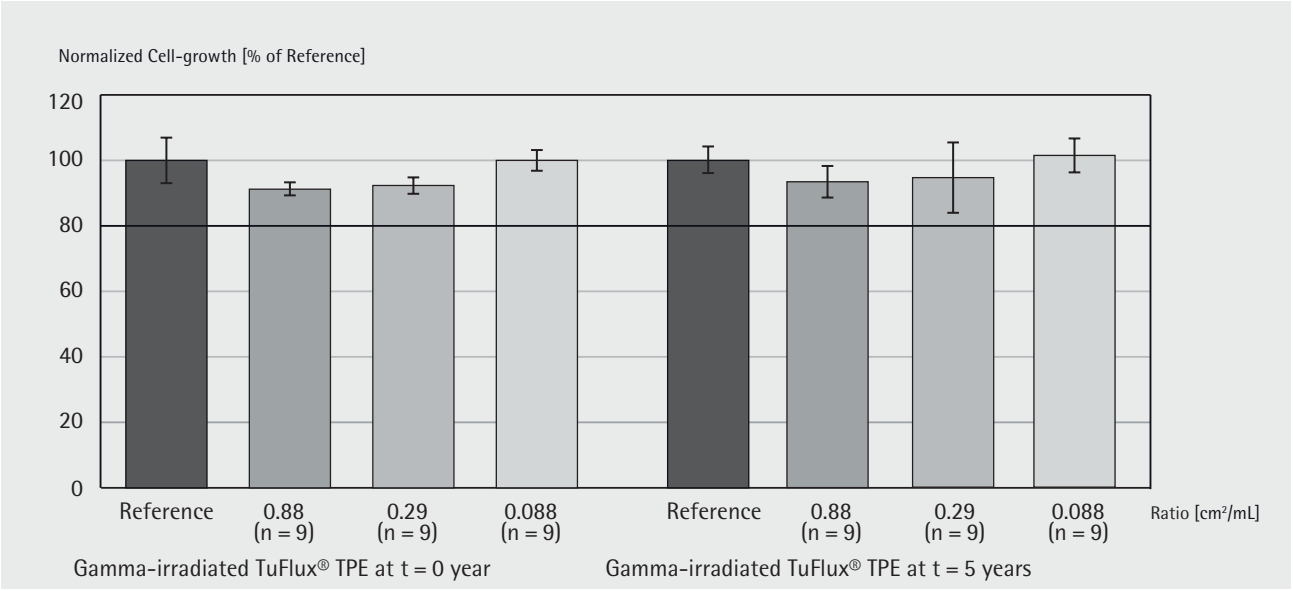
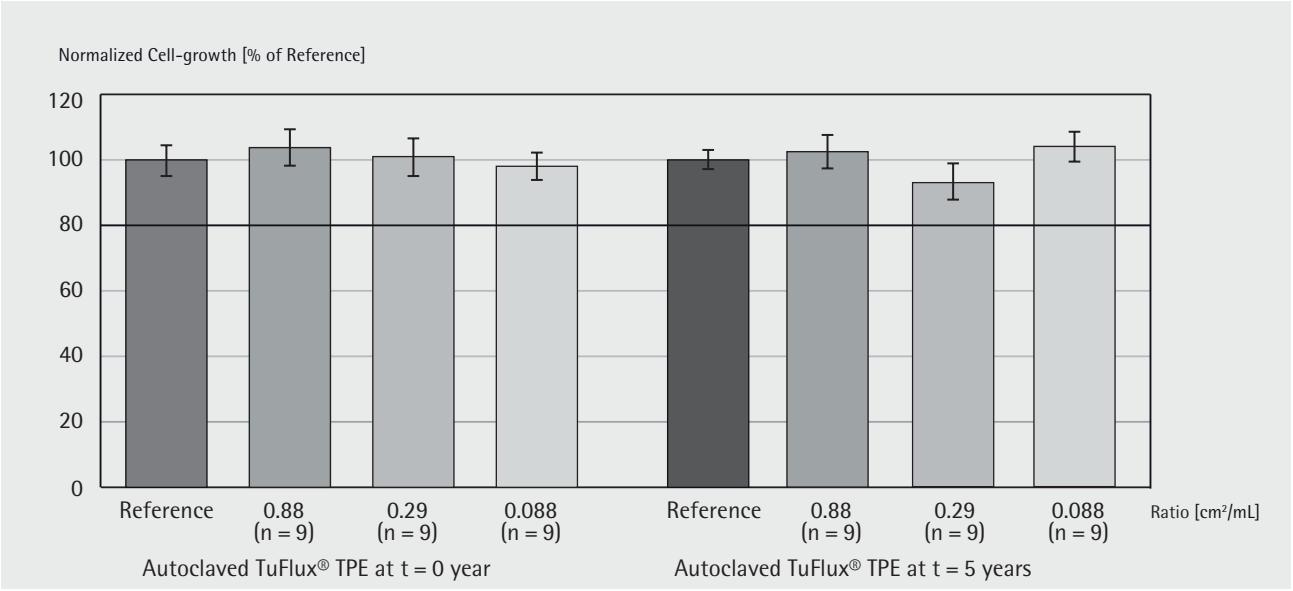


Table 2: Cell-growth results for autoclaved TuFlux® TPE Tubes at t = 0 and t = 5 y



Both 50 kGy and AC TuFlux® TPE tubes can be used for cell-growth applications after 5 y ageing and even at worse case extraction ratios.

6. Example Certificate of Release for Stand Alone Coils

6.1 Example of Certificate of Release for Stand Alone Coils

RAUMEDIC Lifeline to Health

sartorius stedim biotech

CERTIFICATE OF RELEASE

Product Description:

Product Description:	**DESCRIPTION**
Reference:	**FSA XXXXXX**
Batch number:	**xxxxxxxx**
Expiry date:	**YYYY-MM**
Batch Quantity:	**999999 m**
Revision level:	**xx**

Specifications:

NON STERILE PRODUCT

STATEMENTS

Biological Reactivity Tests in vitro and in vivo:	SARTORIUS STEDIM Biotech components have passed USP <87> and USP <88> testing and are classified USP Class VI. SARTORIUS STEDIM Biotech components have passed Cytotoxicity Test according to ISO 10993-5
Physicochemical Test:	SARTORIUS STEDIM Biotech components have passed USP <661> tests for plastic Components
Animal Derived Component Free (ADCF) status:	Conform to the European Guidance EMA/410/01 rev 03 and the European Pharmacopeia (EP) 5.2.8

BATCH TESTING

Product conformity: Product conforms to Technical Delivery Specifications

- Hardness Shore A (DIN EN ISO 868): 60 ± 5
- Tensile strength break (MPa) (DIN EN ISO 527): ≥ 5.0
- Elongation at break (%) (DIN EN ISO 527): ≥ 450

We certify that this batch has been manufactured, controlled and released by Raumedic following applicable current Good Manufacturing Practice (cGMP).

Date of Release: YYYY/MM/DD

RAUMEDIC AG
Last name First name
Head of Quality Management
This certificate has been issued by computer and therefore does not bear a signature

Manufactured by Raumedic
RAUMEDIC AG
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