Braided Tuflux® SIL (Sartorius) vs Sani-Tech® STHT®-R (Saint-Gobain)

Comparability Guide

SARTORIUS

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1. Introduction

Sartorius bags and systems are widely used in biopharmaceutical processes in a variety of unit operations for 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 FMS (Fluid Management Systems).

Product intermediates are also filtered and stored between UF | DF and chromatography purification steps in gamma sterile fluid management systems. FMS 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, reinforced silicone tubing such as Braided Tuflux® SIL is a key element for the successful implementation of disposable manufacturing processes.

Braided Tuflux® SIL, Sartorius reinforced silicone tube for pressurized applications is qualified, manufactured and released according to stringent product validation protocols and quality control testing to offer safe and robust single-use processes to end users for biopharmaceutical applications.

This guide demonstrates comparability and variances between reinforced silicone tubing from different suppliers, notably the Braided Tuflux® SIL tube from Raumedic | Sartorius and the Sani-Tech® STHT®-R tube from Saint-Gobain.

Braided Tuflux® SIL tube is the Sartorius standard silicone reinforced tube and replaces the Sani-Tech® STHT®-R silicone reinforced tube from Saint-Gobain in all new standard FMS.

2. General Features

Physical properties

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

SIL Tubing Type	Color	Hardness Shore A	Operating Temperature Range	Tensile Strength at Break (ISO 527-3)	Elongation at Break (ISO 527)
Braided Tuflux® SIL (Sartorius)	Translucent	60 ± 5	-20 °C to + 135 °C (-4 °F to + 275 °F)	> 8 MPa	> 500 %
Sani-Tech® STHT®-R (Saint-Gobain)	Translucent	65	-62 °C to 260 °C (-80 °F to 500 °F)	> 13 MPa	> 600 %

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).

Tensile properties:

Purpose and test method

A tensile test consists of applying an elongation to a tubing 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 is calculated by dividing the load at break by the original cross-sectional area of the specimen. The tensile strength test is performed with a tensile machine in stretching or elongation 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. A high elongation at break often means high flexibility.

	Printing of ID and OD Dimensions onthe Tubing	Coils Wrapped in Double Packaging	Low-Tack	Post Curing	Sterilization Resistance
Braided Tuflux® SIL (Sartorius)	Yes	Yes	Yes	Yes	γ-irradiation Autoclave ETO
Sani-Tech® STHT®-R (Saint-Gobain)	Yes	Yes	No	Unknown	γ-irradiation Autoclave ETO

Tubing printing

"a | b + c | d" where a | b is the internal dimension and c | d the outer dimension of the tubing in inches.

The innocuity of the ink is proven on printed tubing by tests performed according to ISO 10993-5.

Low-Tack

The external tube surface is treated by plasma heat treatment which provides a less sticky surface of this silicone tube surface (low-tack) in comparison with common non treated silicone products.

3. Biocompatibility

Silicone tubing meets the requirements of the following biocompatibility tests:

	E.P. 3.1.9 (for silicone material in non-sterile condition)	USP <88> Class VI	USP <87> or ISO 10993-5	USP <85> (in non-sterile)
Braided Tuflux® SIL (Sartorius)	Yes	Yes	Yes	Yes
Sani-Tech® STHT®-R (Saint-Gobain)*	Yes	Yes	Yes	Yes

*The Sani-Tech® STHT®-R data are obtained on the basis of the compositional information we receive from Saint-Gobain supplier. Sartorius ensures that this supplier has the required skills, capacity and equipment to manufacture and supply the raw materials in a professional manner, using qualified and competent personnel.

Purpose and test method

Biocompatibility tests are performed to demonstrate that the tubing is biocompatible and meets or exceeds the current USP and ISO requirements.

Tests for Braided Tuflux® SIL are carried out on tubing samples before and after sterilization treatments (50 kGy gamma irradiation and autoclave treatment up to 134 °C) and up to 5 years ageing. The tubing samples were supplied to an independent testing facility to evaluate compliance to USP <88> class VI and USP <87>.

4. Physico-Chemical Properties

	RoHS Compliant	USP <661> Compliant	ADCF	REACH Compliant
Braided Tuflux® SIL (Sartorius)	Yes	Yes	Yes	Yes
Sani-Tech® STHT®-R (Saint-Gobain)*	Yes	Yes	TSE | BSE compliant	Yes

*The Sani-Tech® STHT®-R data are obtained on the basis of the compositional information we receive from Saint-Gobain supplier. Sartorius ensures that this supplier has the required skills, capacity and equipment to manufacture and supply the raw materials in a professional manner, using qualified and competent personnel.

USP <661> Containers, Physico-Chemical Tests – Plastic Purpose

Physico-chemical tests are designed to determine physical and chemical properties of Braided Tuflux® SIL tubing and their extracts.

Tests for Braided Tuflux® SIL are carried out on tubing samples before and after sterilization treatments (50 kGy gamma irradiation and autoclave treatment up to 134 °C) and up to 5 years ageing.

ADCF certified

Tubing material does not contain any animal derived components.

REACH

Tubing material is free from any substances defined as SVHC – Substances of Very High Concern – by the European REACH regulation, Annex XIV.

RoHS

Tubing material does not contain or exceed the limit values of any hazardous substances according to directive 2011/65/EC (RoHS) and amendment 2015/863.

5. Pressure Resistance

The aim of the water pressure resistance test is to assess the pressure resistance performances of the Braided Tuflux® SIL and ® STHR-R tube after either 50 kGy gamma-irradiation or autoclave treatment and 5 years ageing.

The water burst pressures have been measured and are summarized in the tables below:

Table 1: Burst pressures for tubes after 50 kGy gamma-irradiation and 5-year ageing

Tubing Sizes	Braided Tuflux® SIL Burst Pressure [bar | psi]	Sani-Tech® STHT®-R Burst Pressure [bar | psi]
⅛" × 0.355"	68.4 | 992.1	73.2 | 1061.7
¼" × ½"	48.4 | 702.0	55.7 | 807.9
⅜" × ⅝"	44.9 | 651.2	54.2 | 786.1
½" × ⅞"	38.6 | 559.8	62.0 | 899.2
¾" × 1⅛"	23.0 | 333.6	24.1 | 349.5
1" × 1⅜"	16.7 | 242.2	20.9 | 303.1

Table 2: Burst Pressures for tubes after autoclave treatment and 5-year ageing

Tubing Sizes	Braided Tuflux® SIL Burst Pressure [bar | psi]	Sani-Tech® STHT®-R Burst Pressure [bar | psi]
⅛" × 0.355"	61.1 | 886.2	65.7 | 952.9
¼" × ½"	47.3 | 686.0	50.2 | 728.1
⅜" × ⅝"	47.3 | 686.0	53.3 | 773.1
½" × ⅞"	31.6 | 458.3	55.0 | 797.7
¾" × 1⅛"	21.6 | 313.3	24.0 | 348.1
1" × 1⅜"	14.5 | 210.3	20.5 | 297.3

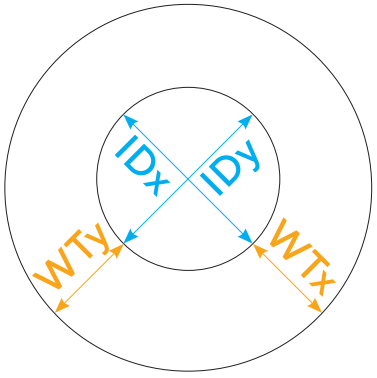
These burst pressure performances are at very high-pressure levels that will not be reached in real biopharmaceutical applications at customers. Therefore, both tubes are matching with real process requirements.

6. Dimensional Assessment

Dimensional measurements (Internal Diameter ID and Wall Thickness WT) have been performed to assess the variability of the tube after different treatments for Braided Tuflux® SIL and Sani-Tech® STHT®-R tubes.

These different treatments and ageing are:

- Non-Sterile (NS/t = 0)
- Non-Sterile and 5-year ageing (NS/t = 5 y)
- 50 kGy gamma-irradiation (50 kGy/t = 0)
- 50 kGy gamma-irradiation and 5-year ageing (50 kGy/t = 5 y)
- Autoclave treatment at 135 °C for 10 min (AC/t = 0)
- 100 cycles of autoclave treatment at 135 °C for 10 min (100x AC/t = 0)
- Autoclave treatment at 135 °C for 10min and 5-year ageing (AC/t = 5 y)



For all the conditions, the ID and WT have been measured and compared to the NS/t = 0 ID and WT to assess the variations after 50 kGy gamma-irradiation or Autoclave treatment and ageing.

Based on those test results, no impact of ageing or treatment has been observed on the dimensional properties.

7. Evaluation Extractable Profile

7.1 Information Extractables Testing

Extractables are compounds that are extracted from plastic materials using conditions that accelerate or exaggerate the normal conditions of use of the component or system. The extractables profiles of the Braided Tuflux® SIL tube from Sartorius and Sani-Tech® STHT®-R from Saint-Gobain are evaluated. An overview of the extractables is provided. It is recommended to use the Extractables Guide or BPOG reports of Tuflux® SIL tube provided by Sartorius for process qualification and risk assessment.

The extraction protocol for the comparison study is aligned with published industry guidelines and official standards (USP <665>).[1,2] Time for the extraction was 21 days at 40 °C with a surface area to extraction volume ratio recommended to 6 cm^2/mL. 50 % ethanol was selected as a worst-case extraction solution to encompass extractables that can be expected in aqueous and organic process streams. Test items after autoclaving or sterilization by irradiation were investigated. Irradiation (gamma dose ≥ 50 kGy) and autoclaving (135 °C for 10 min) were performed at equal conditions for the Braided Tuflux® SIL and Sani-Tech® STHT®-R tubing. The full set of analytical methods was applied aligned with USP <1663>. The extracts were evaluated using orthogonal analytical methods using screening methods, such as gas-chromatography mass spectrometry (GC-MS), liquid chromatography coupled with an ultraviolet (UV) and a MS detector, and ICP-MS for targeting elemental impurities listed in ICH Q3D (R2) and USP <232>.[3,4]

7.2 Expected Extractables

The polymeric material for both types of tubing is a platinum-cured silicone polydimethylsiloxane (PDMS). The material qualities for both types meet the highest standards and are classified as USP <88> class VI compliant. Compounds present and potentially released from different platinum-cured PDMS elastomers are considered comparable. The polymer backbone is identical and polymerization and curing techniques are similar for PDMS. Consequently, the extractables and leachables profiles of such elastomers are expected to be equivalent. See Jenke et al. “The chromatograms from all the silicone materials were similar (same peaks but different relative sizes)”.[5] Expected extractables include mostly cyclic oligomers and low molecular weight linear polydimethylsiloxanes.[6–8] The material of the braided mesh is polyethylene terephthalate (PET). PET is known to be one of the most inert polymers. Main extractables are typically oligomers of PET, such as the PET cyclic dimer (CAS 24388-68-9).[9] They are not expected to migrate through the silicone layer under application conditions used at customers because of their high molecular weight. In addition, the total polymer volume of the PET mesh compared to the polymer volume of the silicone is low. Therefore, the impact of the PET mesh on the extractables profile of the tubes is expected to be negligible. Nonetheless, most common PET oligomers were specifically targeted in the LC-HRMS screening analysis.

7.3 Results Extractables

Results for the gamma irradiated tested tube samples were selected for the evaluation since these extracts revealed the present extractables at a higher level and quantity compared to the autoclaved test items. The extractables profile for gamma irradiated Braided Tuflux® SIL and Sani-Tech® STHT®-R tubing of the 50 % ethanol extracts are equivalent. Typical extractables, such as cyclic siloxanes, smaller linear siloxanes, and traces of platinum were detected. The concentrations of the different extractables were mainly on the same order of magnitude between the two tested tube samples but generally lower for the Braided Tuflux® SIL tube. A detailed list of the extractables detected with GC-MS – the analytical method capable to detect most of the PDMS extractables – is shown in Table 1. The GC-MS chromatogram is provided in Figure 1.

Traces of the metal platinum used in the curing system as the only relevant element were detected at trace levels in the same order of magnitude in extracts of the two tubing (Table 2). No elements have been detected which are classified as class 1 or class 2 (a and b) according to ICH Q3D.

Table 3: Individual extractables in µg/cm² sorted according to retention time from GC-MS analysis of the 50 % ethanol extracts. The compounds represent typical extractables of PDMS elastomers.

Compound Name	CAS Number	Braided Tuflux® SIL irradiated	Sani-Tech® STHT®-R irradiated	Braided Tuflux® SIL autoclaved	Sani-Tech® STHT®-R autoclaved
Tetramethyldisiloxane-1,3-diol	1118-15-6	13	9.2	4.7	1.7
Octamethylcyclotetrasiloxane (D4)	556-67-2	0.31	0.73	0.054	0.051
2,2-Diethoxyacetophenone	6175-45-7	0.30	0.63	0.23	0.16
Hexamethyltrisiloxane-1,5-diol	3663-50-1	0.50	2.1	0.23	0.044
Diethoxy-tetramethyldisiloxane	18420-09-2	0.075	0.51	0.036	0.033
Decamethylcyclopentasiloxane (D5)	541-02-6	0.90	2.3	0.16	0.47
Dodecamethylcyclohexasiloxane (D6)	540-97-6	1.1	7.5	0.23	2.0
Tetradecamethylcycloheptasiloxane (D7)	107-50-6	0.70	10	0.13	3.1
2,4-Di-*tert*-butylphenol*	96-76-4	0.14	0.30	0.026	0.20
Hexadecamethylcyclooctasiloxane (D8)	556-68-3	0.60	10	0.11	2.5
Octadecamethylcyclononasiloxane (D9)	556-71-8	0.42	9.5	0.11	1.7
Eicosamethylcyclodecasiloxane (D10)	18772-36-6	0.31	8.7	0.10	0.96
Docosamethylcycloundecasiloxane (D11)	18766-38-6	0.29	7.8	**0.11**	0.58
Tetracosamethylcyclododecasiloxane (D12)	18919-94-3	0.35	8	0.14	0.45
Hexacosamethylcyclotridecasiloxane (D13)	23732-94-7	0.49	9.1	0.19	0.4
Octacosamethylcyclotetradecasiloxane (D14)	149050-40-8	0.66	10	0.26	0.37
Triacontamethylcyclopentadecasiloxane (D15)	23523-14-0	0.87	11	0.34	0.34
Dotriacontamethylcyclohexadecasiloxane (D16)	150026-95-2	1.0	9.9	0.39	0.29
Tetratriacontamethylcycloheptadecasiloxane (D17)	150026-96-3	1.2	8.6	0.43	0.26
Hexatriacontamethylcyclooctadecasiloxane (D18)	23523-12-8	1.1	6.4	0.38	0.20
Octatriacontamethylcyclononadecasiloxane (D19)	150026-97-4	0.95	4.8	0.34	0.16
Tetracontamethylcycloeicosasiloxane (D20)	150026-98-5	0.77	3.7	-	0.035
Dotetracontamethylcycloheneicosasiloxane (D21)	23523-13-9	0.13	2.7	0.018	-
Tetratetracontamethylcyclodocosasiloxane (D22)	1177831-23-0	-	0.67	-	-

Table 4: Results of the ICP-MS analysis

Element	CAS	Braided Tuflux® SIL irradiated	Sani-Tech® STHT®-R irradiated
Platinum (Pt)	7440-06-4	0.080	0.035

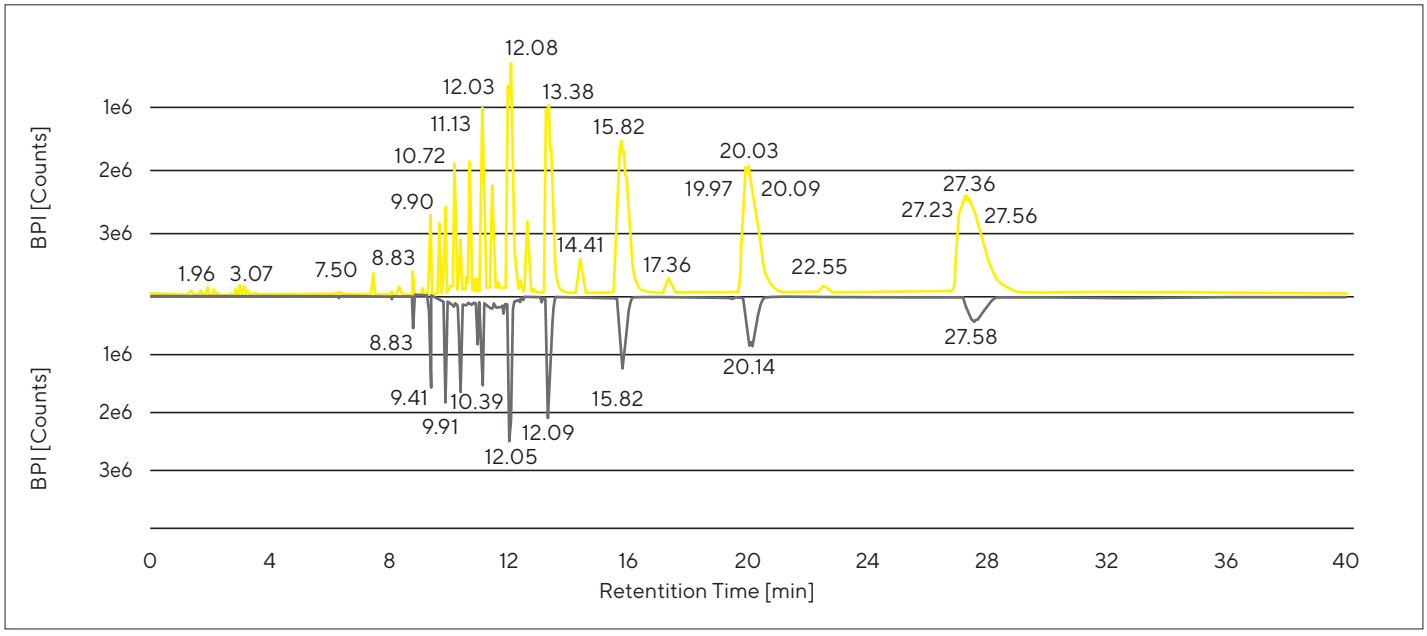


Figure 1: ESI pos LC-MS base peak ion (BPI) chromatograms of the 50 kGy irradiated Sani-Tech® STHT®-R 50 % EtOH extract (yellow) and the 50 kGy irradiated Braided Tuflux® SIL 50 % EtOH extract (black).

7.4 Risk Assessment Example

PDMS and oligomers of PDMS generally are of low toxicological concern. These compounds are used in the pharmaceutical industry as antifoams excipient, or can be found as auxiliary substances in container closure systems, e.g. as lubricant or for siliconization10,11 A threshold relevant to evaluate patient safety in the risk assessment is the Permitted Daily Exposure (PDE) value. The PDE values of several cyclic oligomers are reported in the literature. 12,13 Low-molecular weight cyclic siloxanes D3 and D4 are grouped and a parenteral PDE of 2,400 µg/day was established. The PDE of the higher-molecular D5 to D19 was derived to 12,000 µg/day.

The following application scenario is considered using extractables quantities provided in Table 1 for the calculation of the patient exposure. A total volume of 100 L of a process solution is pumped into a final storage container using an irradiated tube with a length of 2 meter and an inner diameter of ½" (inner surface area 800 cm^2). The daily patient dose is set to 1,000 mL.

The value of the 50 % ethanol is selected to describe a worst-case scenario, levels of silicones in aqueous process solutions are significantly lower and higher-molecular weight siloxanes are usually completely absent.

Calculated worst-case concentrations of Octamethylcyclotetrasiloxane (D4) in the process solution are:
Braided Tuflux® SIL 0.31 µg/cm^2 * 800 cm^2/100 L = 2.48 µg/L = **0.00248 µg/mL**
Sani-Tech® STHT®-R 0.73 µg/cm^2 * 800 cm^2/100 L = 5.84 µg/L = **0.00584 µg/mL**

The toxicological threshold PDE is compared with the maximum uptake of the compound (patient exposure) which results in a safety margin which should be > 1 to confirm patient safety.

$$\textit{Safety Margin} = \frac{\text{PDE}}{\text{Maximum uptake (volume dose} \times \text{D3 concentration)}}$$

Safety Margin for Braided Tuflux® SIL $\frac{2{,}400\ \mu g/day}{1{,}000\ mL/day \times 0.00248\ \mu g/mL)} = 600$

Safety Margin Sani-Tech® STHT®-R $\frac{2{,}400\ \mu g/day}{1{,}000\ mL/day*0.00584\ \mu g/mL)} = 411$

In the example, the outcome of the safety assessment is identical for both tubes: the safety margin for both tubing is **>> 1**, the daily patient exposure is **significantly** lower than the PDE.

7.5 Comparator Approach

Finally, acknowledging the comparator approach described in USP <665> equivalency between the two types of silicone tubing might be established in authorized pharmaceutical processes.1 Details are provided in USP <1665>.14 To establish that a SU component is suitable for use, equivalence between a comparator and a component needs to be shown. Further chemical characterization of the SU component is not required as the claim of equivalence is justified. The selection and qualification process is completed when justification is given.

According to USP <665>, equivalency is assessed for seven key parameters. Four of the seven aspects can be evaluated by the supplier. These are: 1) both components are manufactured from the same materials, 2) are designed the same way, 3) are equivalent in terms of the function they perform, and 4) are equivalent in terms of how they have been processed (e.g., sterilization). The remaining three aspects describe the conditions of use, how the component is prepared for use (flushing), and the type of process output (drug substance or product). They are process-related and need to be evaluated by our customers. Considering that the silicone tubes perform the same functions, equivalence of these aspects should be established as well.

7.6 Comparator Approach

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(14) United State Pharmacopoeia <1665> Plastic Components and Systems Used to Manufacture Pharmaceutical Drug Products. **2021**.

8. Document History

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