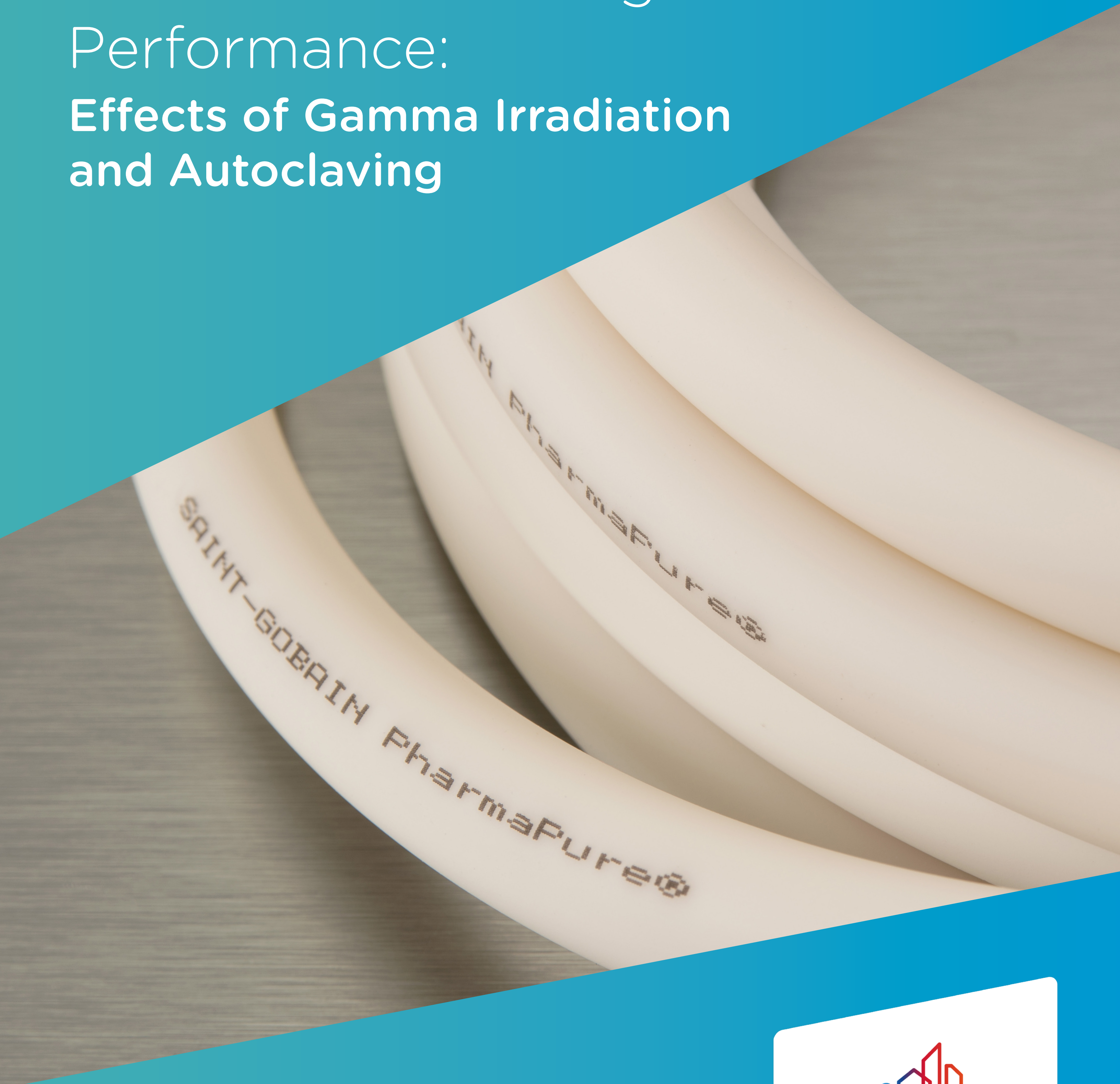
WHITE PAPER 0132

PharmaPure® Tubing Performance:

Effects of Gamma Irradiation and Autoclaving



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SAINT-GOBAIN

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ABSTRACT

This paper evaluates the effects of gamma irradiation and autoclaving on the key performance attributes of Saint-Gobain Life Sciences' PharmaPure® tubing. Sterilization methods, such as gamma irradiation or autoclaving (steam), can affect polymers by causing polymer chain scission and cross-linking, altering their physical properties. The extent of these changes varies depending on the specific polymer. The impact on the polymer increases with increased dosage or with autoclaving, time, and temperature. Prior documentation for Saint-Gobain Life Sciences' PharmaPure® tubing recommended autoclaving, EtO, and gamma irradiation level of no more than 25 kGy. Recent work has shown that PharmaPure® tubing can withstand gamma irradiation up to 50 kGy and still outlast silicone tubing in peristaltic pumps by up to 10x while maintaining other key performance attributes, such as burst, minimum bend radius, durometer, and low spallation.

INTRODUCTION

Saint-Gobain Life Sciences' PharmaPure® tubing is a premium, biologically compatible peristaltic pump tube developed especially for pharmaceutical, biotechnology, and laboratory applications. This tubing is designed to deliver exceptional pump life, minimal particulate spallation, and very low permeability. The superior flex life characteristics of PharmaPure® tubing can reduce production downtime due to pump tubing failures. In addition, PharmaPure® tubing's low permeability is ideal for protecting sensitive cell cultures, fermentation, separation, purification, process monitoring, and sterile filling. These applications all require sterilization. This white paper presents data on PharmaPure® tubing exposed to 35-40 kGy and 50 kGy of gamma irradiation, along with autoclave cycle of 121°C and 30 minutes.

KEY PERFORMANCE ATTRIBUTES:

Burst Pressure

Burst pressure is the resistance of PharmaPure® tubing to hydraulic pressure. Burst pressure is performed at room temperature following ASTM D1599. PharmaPure® shows a small drop in burst pressure following gamma irradiation but still maintains 73 psi burst pressure for 1/2” ID x 3/4” OD size tubing and 68 psi for 1/4” ID x 3/8” OD size tubing. After 35-40 kGy of gamma irradiation, burst pressure drops by only 0.2% to 74.8 psi. After autoclaving, burst pressure increases slightly or stays the same depending on the size of the tube.

If a safety rating of 5:1 is used, the drop in working pressure after 50 kGy goes from 15.6 psi to 14.6 psi for 1/2” ID and 15 psi down to 14.96 psi for 35-40 kGy and drops to 13.6 psi for 50 kGy for 1/4” ID (See Figure 1 for working pressure).

Figure 1: Burst pressure and the working pressure with a 5:1 safety rating

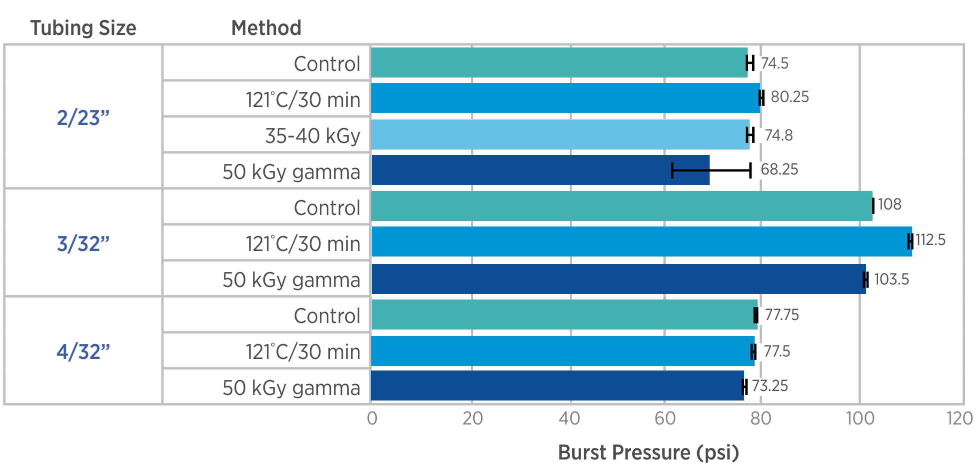
Tube (ID x OD)	Control	35-40 kGy Gamma	50 kGy Gamma	Autoclave 121°C/30min
1/4” x 3/8”	15.0	15.0	13.6	16.1
1/4” x 7/16”	21.6	-	20.7	22.5
1/2” x 3/4”	15.6	-	14.6	15.5

The average burst pressure is presented below in Figure 2 on three different sizes of PharmaPure® tubing, looking at the effect of both irradiation and autoclave:

- 2/32” wall thickness: 1/4” ID x 3/8” OD
- 3/32” wall thickness: 1/4” ID x 7/16” OD
- 4/32” wall thickness: 1/2” ID x 3/4” OD

The data shows an increase in performance after autoclave cycle of 121°C and 30 min and a small decrease in performance with 50 kGy gamma and no change at 35-40 kGy.

Figure 2: Average burst pressure by wall thickness after autoclave and gamma irradiation



MINIMUM BEND RADIUS

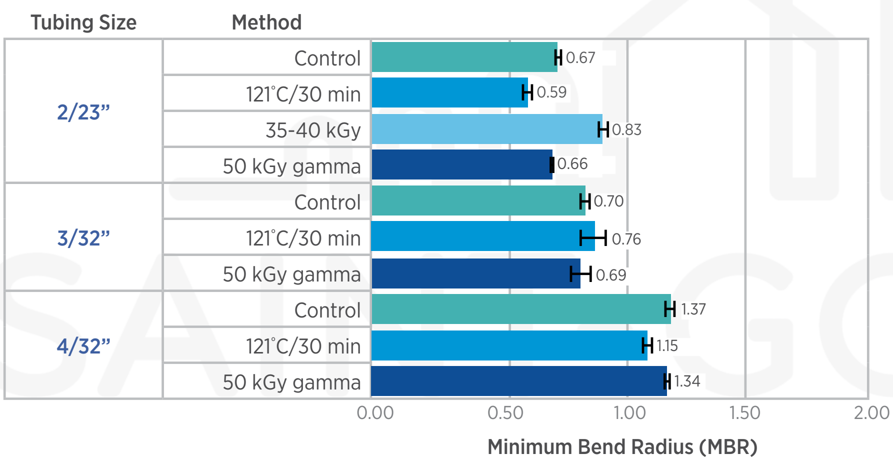
The minimum bend radius (MBR) is the smallest radius the tubing can bend before kinking. This is the point at which liquid would theoretically no longer be able to flow through the tube.

The average minimum bend radius Is presented below in Figure 3 on three different sizes of PharmaPure® tubing looking at the effect of both irradiation and autoclave:

- 2/32" wall thickness: 1/4" ID x 3/8" OD
- 3/32" wall thickness: 1/4" ID x 7/16" OD
- 4/32" wall thickness: 1/2" ID x 3/4" OD

The minimum bend radius is not significantly affected by gamma or autoclaving, assuring normal liquid flow.

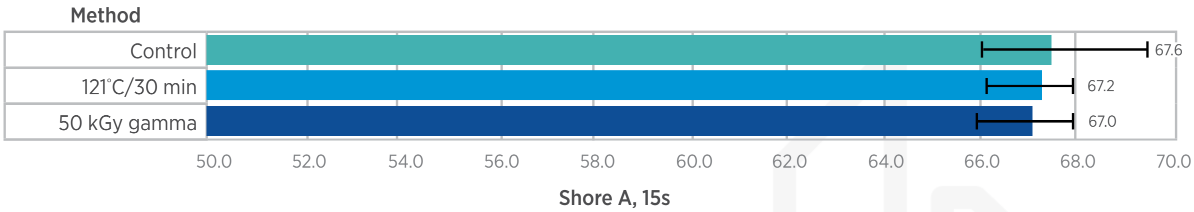
Figure 3: Bend radius testing of PharmaPure® tubing



DUROMETER

Durometer is a measurement of the hardness of a material. Testing was done following ASTM D2240. After gamma irradiation or autoclaving, durometer dropped by less than one point.

Figure 4: Durometer testing of PharmaPure® tubing

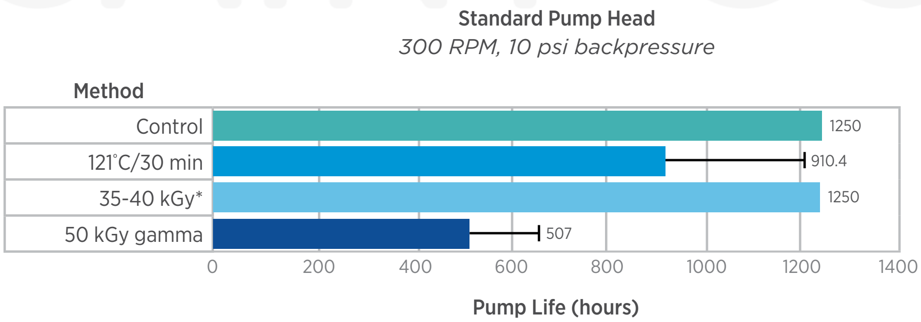


PUMP LIFE

A Masterflex® L/S® 3-roller standard pump head #7017-21 is operated at 300 RPM with 10 psi of backpressure on 1/4” ID x 3/8” OD tubing. Backpressure is formed by flow-restriction of the tube with an inline pressure gauge. The tubing is tested until failure. Failure is determined by a leak sensor that automatically stops the pump when moisture is detected and records the number of hours. Pump life is studied as tube failure/rupture. The test is performed at room temperature (73°F). Pump life was tested until 1,250 hours when the test is stopped.

PharmaPure® tubing shows a drop in pump life of 59%, but still maintains an average pump life of over 500 hours for 50 kGy. A pump life of over 500 hours for most customers is longer than required. When PharmaPure® was gamma irradiated and pumped without backpressure, the tube lasts until the end of the test with no failures at 1,250 hours.

Figure 5: Pump life testing for PharmaPure® tubing



At 1,250 hours, the control and 35-40 kGy with no back pressure were shut off with no failures.

**No backpressure*

SPALLATION

Spallation (or particle shedding) results from the shear-compression force in a peristaltic pump, which causes particles to be released from the tubing in the flow path.

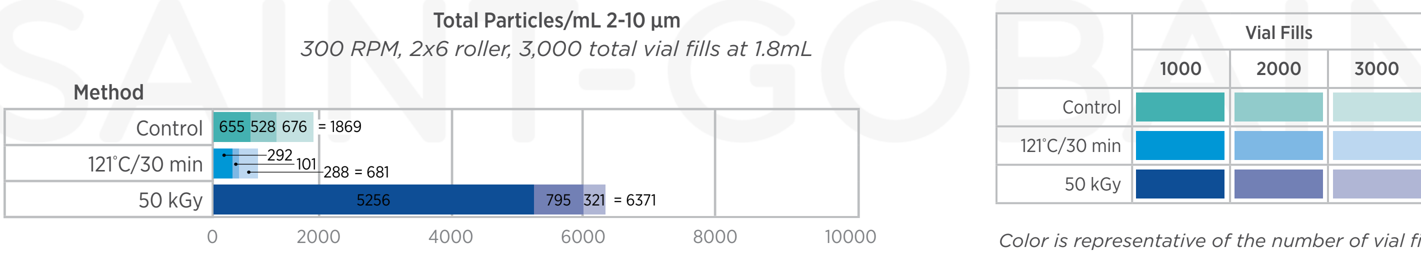
Spallation was analyzed here with imaging flow cytometry (IFC) paired with image analysis software to analyze the particles quantitatively and qualitatively released in the fluid path for more precise measurement.

1/16" x 3/16" tubing was loaded onto a 2x6 roller peristaltic pump at 300 RPM head, and 100mL of water was recirculated for 1,000 vial fills of 1.8mL. The 100mL of water was imaged through a flow cytometer, which can obtain a particle count and size for all particles in the fluid path. This was repeated for 3,000 vial fills total with the same tube.

RESULTS

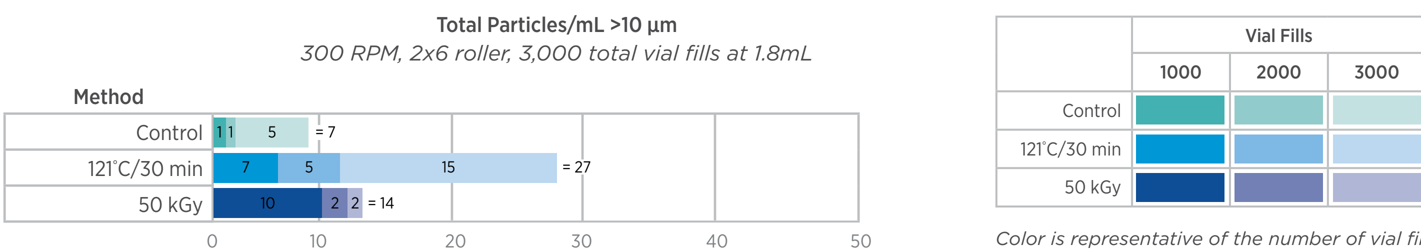
Spallation is represented by particles/mL from 2-10 µm and >10 µm. These two graphs illustrate total subvisible and visible particles produced in the fluid path by tubing for different sterilization methods compared to as-manufactured tubing for the same test. Gamma irradiation increases spallation for PharmaPure® tubing due to the breakdown of the polymer, but it is mainly for subvisible particles less than 10 µm. This spallation is minimal compared to other TPE tubing and decreases with time for gamma irradiation. After autoclaving, there is a decrease in subvisible particles but a small increase in visible particles greater than 10 µm. Flow imaging cytometry, an orthogonal method for USP <788>, has a higher amount of particles/mL allowed due to counting any oil particles as spallation. For subvisible particles with flow imaging cytometry, there is the possibility that the counts could be coming from an oil that is released. Most particles came off in the first 1,000 vial fills following gamma, significantly decreasing in 2,000 and 3,000 vial fills, further indicating that it could be small oil particles and not spallation. Gamma irradiation released fewer particles than autoclave for large particles >10 µm.

Figure 6: Spallation data for 2-10 µm (particles/mL) for PharmaPure® tubing



Color is representative of the number of vial fills performed in the graph on the left, which shows the amount of spallation after each 1,000 vial fills and the total amount of spallation.

Figure 7: Spallation data >10 µm (particles/mL) for PharmaPure® tubing



Color is representative of the number of vial fills performed in the graph on the left, which shows the amount of spallation after each 1,000 vial fills and the total amount of spallation.

BRITTLE POINT TEMPERATURE

Brittle point temperatures were measured using ASTM D 746 “Standard Test Method for Brittleness Temperature of Plastics and Elastomers by Impact.” There was no change observed after gamma irradiation.

Figure 8: Brittle point temperature ASTM D746

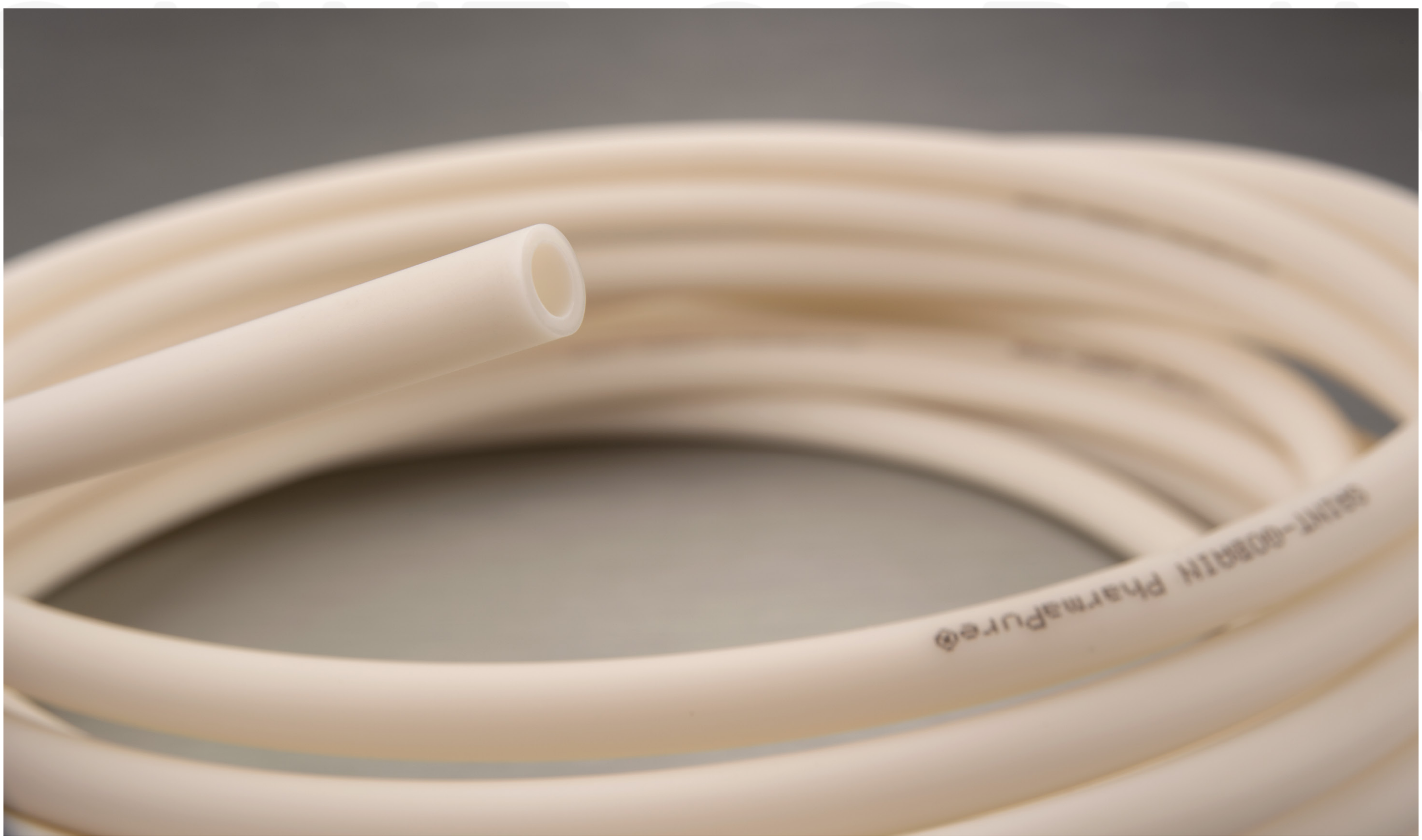
Tubing	Control	50 kGy Gamma
PharmaPure®	-66.8°C	-66.8°C

EXTRACTABLES

The Saint-Gobain Life Sciences Extractables Protocol is always performed in the worst-case scenario. Log in to the Saint-Gobain Biopharm website to request the extractable data after 50 kGy for PharmaPure® tubing:
www.biopharm.saint-gobain.com/validation-technical

CONCLUSION

Saint-Gobain Life Sciences has determined, based on performance data following irradiation, that PharmaPure® Low Spallation Peristaltic Pump Tubing is compatible with irradiation of up to 50 kGy and autoclave cycle of 121°C and 30 minutes. There is a drop in the physical properties of PharmaPure® tubing following irradiation, as expected with most TPEs, including other Saint-Gobain Life Sciences tubing. The drop in properties is minimal and not expected to impact the functionality of the tubing following irradiation of up to 50 kGy.



About

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Heidi has an MS in Materials Process Engineering from Worcester Polytechnic Institute and a BSE in Chemical Engineering from the University of Massachusetts in Amherst. She has spent 20 years specializing in silicone formulations and application specific testing. Her current research is focused on tubing used in final fill drug manufacturing.

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Tony Perovsek is the Validation Manager for the Bioprocess Solutions division of Saint-Gobain Life Sciences. His background includes 20 years in pharmaceutical and medical device validation for companies such as Boehringer Ingelheim and VWR.

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Maureen manages multiple product lines at Saint-Gobain Life Sciences' Bioprocess Solutions division. She holds an MS in Materials Science Engineering and brings a decade of experience in marketing, strategy, and innovation.

Saint-Gobain Life Sciences

The Bioprocess Solutions business of Saint-Gobain Life Sciences is an industry-leading provider of materials science-based solutions for single-use fluid management, including TPE and silicone tubing, connection and flow control components, bioprocess and cell culture bags, filtration products, sensors, and over-molded technology, all available in customized assemblies that are produced in 20 manufacturing facilities located around the world. To find out more about Saint-Gobain Life Sciences and to learn how we can assist you with your application needs, visit our website.