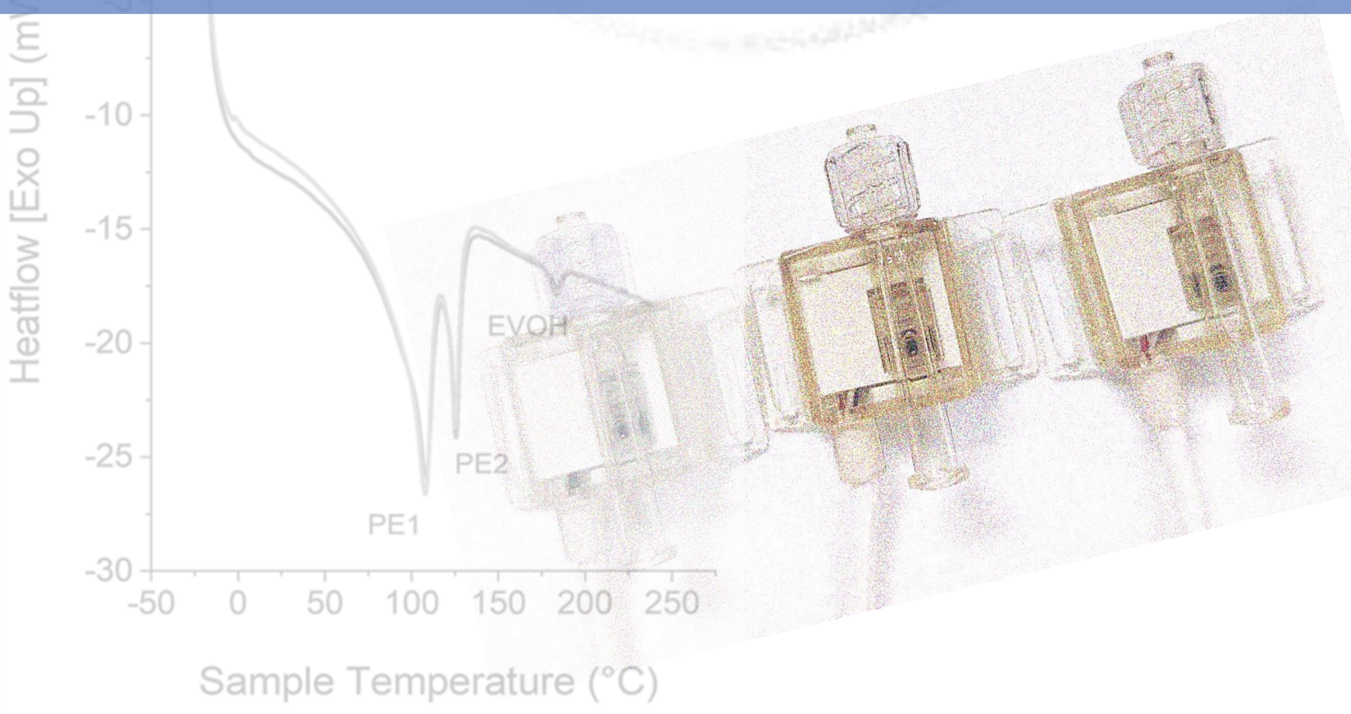
2023

X-RAY STERILIZATION OF SINGLE-USE BIOPROCESS EQUIPMENT

PART II – REPRESENTATIVE QUALIFICATION DATA



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1 Executive Summary

Since the publication of Part I of this series on qualification of X-ray sterilization of single-use bioprocess equipment in May 2021, security of supply challenges with availability of irradiation sterilization have continued to increase, leading a number of single-use component and system suppliers to issue change notifications with plans to implement X-ray irradiation between late 2022 and mid-2023. To support the risk assessments needed for implementation, multiple BPSA member companies have been working to generate and share supporting data aligned to the science-based protocol outlined in Part I. This white paper includes representative examples of data comparing X-ray and gamma irradiated components, generated by multiple component manufacturers for different types of single-use components and materials.

Specifically, representative single-use biocontainers, filters, connectors and sensors have been evaluated for X-ray compatibility by their manufacturers in accordance with BPSA recommendations as outlined in the table below. The resulting data, described and summarized in this paper, demonstrate equivalent impact of X-ray irradiation of single-use materials as gamma. The types of component-specific physical and functional testing performed on various components are detailed in SECTION 3, whereas examples of materials, chemical and biological testing common to most components are shown in SECTIONS 4, 5 and 6. These examples not only help verify the science-based understanding that X-ray and gamma are equivalent, but show how data from different labs, components, and suppliers are summarized and interpreted.

Table 1: Components and types of testing evaluated. (●) Testing completed with equivalent results for X-ray and gamma and example data included, (▪) Testing completed with supplier statement of equivalent results, (◔) Testing in progress, (○) Testing not available at the time of this publication

	Primary MOC	Materials	Physical	Functional	Chemical	Biological
Biocontainer						
Flexsafe® bag (S80 film)	PE's/EVOH	●	●	●	●	●
Connector						
Lynx® S2S	PSU, Sil	●	●	●	●	●
AseptiQuik® AQG	PC, PPSU, PE, PES, Sil	●	●	●	○	○
Filter						
Kleenpak™ EKV Capsule	PP, PES, EPDM	●	●	●	●	●
Sensor						
PendoTECH Single Use Pressure Sensor™	PSU	●	●	●	▪	▪
BroadleyJames pH Sensor	Glass, PEEK, EPDM, Si(Pt)	○	○	●	○	○
Tubing						
Pumpsil®- Bioprene®-Pureweld®	Si(Pt)-TPV-TPE(SEBS)	●	●	●	◔	◔
AdvantaFlex™ APAF	TPE	●	●	●	●	○
Liveo™ Pharma Tubing	Si(Pt)	●	●	●	▪	●
C-Flex® 374 Tubing	TPE	●	●	●	◔	●
SaniTech® Ultra-C Tubing	Si(Pt)	●	●	●	◔	●

2 Temperature and Activation Associated with Radiation Processing

Activation or inducement of radioactivity in X-ray treated materials is generally considered to be low risk for single-use materials but is cited as a requirement to be evaluated per ISO 11137. Multiple suppliers have confirmed successful activation testing on numerous single-use materials following X-ray irradiation using a 7.5 MeV source (maximum energy for X-ray sterilization purposes), including polymers, stainless steel clamps, and magnets, with no reports of significant activation. Tested materials following irradiation at 55 to 65 kGy are listed in Table 2. In parallel, products manufactured with materials listed in Table 2 and representative of their product families, which have been irradiated at 80±10 kGy to exaggerate the potential effect of activation also show no reports of significant activation. The results are summarized in Table 3.

Table 2: Quantity and type of uniquely sourced single-use materials evaluated and shown to exhibit no meaningful[1] activation.

Materials	Qty	Materials	Qty
Ethylene propylene diene monomer (EPDM)	1	Polyethylene terephthalate glycol (PETG)	1
Polyamide (PA)	5	Polyolefin (POE)	2
Polybutylene terephthalate (PBT)	4	Polypropylene (PP)	8
Polycarbonate (PC)	1	Polysulfone (PSU)	1
High-density polyethylene (HDPE)	1	Polyvinyl chloride (PVC)	1
Low-density polyethylene (LDPE)	1	Polyvinylidene fluoride (PVDF)	2
Neodymium-containing magnet alloy	1	Stainless steel (clamp)	1
Polyether ether ketone (PEEK)	1	Styrene-butadiene copolymer (SBC)	1
Polyethylene (PE)	1	Silicone (Si)	8
Polyethylene terephthalate (PET)	1	Thermoplastic elastomer (TPE)	3

Table 3: Products evaluated and show to exhibit no meaningful activation[1].
The maximal temperatures recorded during activation assay at 80±10 kGy are listed.

Product Name	Quantity	Maximal Temperature Recorded
Flexsafe® STR	Several	37.5-42.5°C
Flexsafe® Pro Mixer	Several	35-37.5°C
Flexel® Magnetic Mixer	Several	35-37.5°C
Flexboy®	Several	35-37.5°C

Temperature levels during irradiation are generally expected to be lower during X-ray, as only the material in front of the beam is adsorbing radiation and generating heat, as compared to the entire vault in the case of gamma. However, as the concept[2] of dose rate is higher with X-ray, an assessment to demonstrate showing the shorter dosing time does not lead to transiently higher heat levels in the material may be helpful. In this assessment, it may help to consider that dose rate is not constant for X-ray or gamma, and that during X-ray irradiation, the SUS typically receives many abbreviated X-ray doses as it circulates on a conveyor, with the vast amount of time spent on the conveyor exposed to ambient temperature and not in front of the beam. In some cases, suppliers have communicated using temperature-sensitive stickers that record the maximum heat experienced during irradiation in increments of 2.5 °C. In one summary

[1] Significant or meaningful activation refers to levels of radionuclides exceeding natural background or accepted levels as described in recognized guidances, such as IAEA-TECDOC-1287 for Natural and induced radioactivity in food.

[2] "Concept" is used when describing dose rate to emphasize that dose rates, as more fully described in the first BPSA X-ray paper, are not constant for X-ray or gamma

evaluation the average maximum temperatures experienced during gamma irradiation was 40.0 ± 3.7 °C, whereas for X-ray irradiated samples at 50±5kGy, the average maximum temperature was 35.3 ± 4.7 °C. In all cases, the experiences with the team have been that maximum temperatures are generally the same or slightly lower with X-ray as compared to gamma.

3 Physical and Functional Component-Specific Testing

An overview of the component-specific functional and physical testing is summarized in Table 4. Examples of material, chemical, and biological testing common to all components are available in SECTIONS 3, 4 and 5.

Table 4: X-ray assessment summary

Primary Components		Physical & Functional Evaluation
Lynx® S2S connector 	☑	Bacterial Challenge / Soiling Test. Lynx® S2S connectors were tested utilizing a bacterial challenge method with 10^7 *B. diminuta* assuring a sterile fluid path.
	☑	Lynx® S2S connectors horse barbs, Oetiker clamps and tubing integrity testing
	☑	Pressure burst testing and actuation force testing
	☑	USP <788> for particulates *(supplemental[a])*
AseptiQuik® connector 	☐	Bacterial challenge test *(pending)*
	☑	Pressurized Leak Testing (Bubble Leak, Water Burst), Membrane Air Burst testing
Film S80 for Flexsafe® bag range 	☑	Sterility is claimed freshly after Gamma/X-ray sterilization and at the end of the shelf life (3 years)
	☑	Representative junctions between components tested and show equivalent strength and integrity results
	☑	packaging covered by the sterility testing
	☑	Gelbo flex testing
	☑	Permeability testing (OTR, CO2TR, WVTR)
PendoTECH Single Use Pressure Sensors™ 	☑	Performance and accuracy
	☑	Burst and leak testing

BPC pH Sensor	☑	Sensor Accuracy
	☑	Sensor Drift
Kleenpak™ EKV Filter 	☑	Bacteria retention (ASTM F838)
	☑	Filter integrity (water, alcohol)
	☑	Pressure versus flow rate
	☑	Particulates *(supplemental[a])*
	☑	Pressure burst
C-Flex® 374 Tubing	☑	Pressure burst
	☑	Bend Radius
	☑	Compression Set
SaniTech® Ultra-C Tubing	☑	Pressure burst
	☑	Bend Radius
AdvantaFlex™ Tubing	☑	Bend radius
	☑	Burst testing
Liveo™ Tubing	☑	Hydraulic Burst Pressure Resistance
	☑	Kink resistance
	☑	Compression Set
Pumpsil®, Bioprene®,Pureweld® Tubing	☑	Hardness
	☑	Endurance

[a]"Supplemental" indicates data not recommended in the original BPSA X-ray paper as high value to the assessment of X-ray, but may provide additional insight or confidence in the overall risk assessment approach.

3.1 Connectors

Connectors have a broad range of applications throughout single use, including sterile liquid transfer and microbiological sampling. Connectors are essential to guarantee a safe connection between two sterilized single-use disposable assemblies. In the pharmaceutical industry connectors are used in both the bulk production and final fill processes, ensuring the secure transfer of valuable product.

3.1.1 Lynx® S2S Connector

Lynx® S2S connectors are a single-use, single actuation, gamma- and autoclave-compatible disposable device for connecting sterilized fluid paths in biopharmaceutical processes. To demonstrate X-ray compatibility of the Lynx® S2S product family the testing below was performed following irradiation in the 45 to 60 kGy dose range. The materials of construction for Lynx S2S connectors are polysulfone and silicone.

(1) Pressure Burst Testing

The purpose of the burst test is to verify that, when connected and fully actuated, the male and female Lynx® S2S couplings will maintain a hydraulically tight seal under anticipated use pressures. The maximum operation pressure rating for Lynx® S2S connectors is 60 psi (4.14 bar). The Lynx® S2S unit being tested was subjected to hydraulic pressure until 200 psi (13.8 bars) was reached, a leak in an internal seal developed, or rupture of the device was observed. The acceptance criteria defined for this device was to reach at least 100 psi (6.9 bars) before observing any leaks. In total two lots of male/female connectors post X-ray irradiation were tested. The Pressure Burst testing studies show that X-ray irradiated Lynx® S2S connectors meet the specification and do not show evidence of degradation in terms of burst pressure.

Table 5: Pressure burst testing results for Lynx® S2S

Batch	Irradiation	Acceptance Criteria	PASS / FAIL
Lot 1 Male – 2020120007 Lot 1 Female – 2021020029	X-ray	>6.9 bar (> 100 psi)	PASS
Lot 2 Male – 2021020020 Lot 2 Female – 2021020031	X-ray		PASS

(2) Actuation Force Testing

The purpose of the actuation force test is to measure the force necessary to actuate male and female connectors. Lynx® S2S connectors did not show evidence of degradation in terms of actuation force.

Table 6: Actuation force results

Batch	Irradiation	Acceptance Criteria	PASS / FAIL
Lot 1 Male – 2020120007 Lot 1 Female – 2021020029	X-ray	≤ 31.3 kg (≤ 69 LBS) *Information only*	PASS *Information only*
Lot 2 Male – 2021020020 Lot 2 Female – 2021020031	X-ray		PASS *Information only*

(3) Bacterial Challenge / Soiling Test

As bacterial challenge test, a plug soiling test was selected for Lynx® S2S connectors post X-ray irradiation. Plugs were soiled with a minimum *B. diminuta* concentration of 10^7 colony forming units. Post actuation sterile Tryptic Soy Broth was passed through each connector and incubated for 7 days. Samples were examined for microbiological growth. Connectors were tested utilizing a bacterial challenge method (soiling test) with 10^7 *B. diminuta* assuring a sterile fluid path. No contamination was found in the Tryptic Soy Stream.

Table 7: Soiling test results

Batch	Irradiation	Acceptance Criteria	PASS / FAIL
Lot 1 Male – 2020120007 Lot 1 Female – 2021020029	X-ray	Absence of microbial growth in the fluid path	PASS
Lot 2 Male – 2021020020 Lot 2 Female – 2021020031	X-ray		PASS

(4) Fastener Testing (supplemental, supports junction integrity assessment)

The fastener product validation test procedure is a test procedure for single use assemblies testing tubing, Oetiker clamp, and hose barb connections. The connections were tested for leaks (bubble emission test) under dedicated pressures for five minutes. The X-ray fastener testing comparison study evaluated performance of the post X-ray and post gamma irradiated materials below.

- Lynx® connector horse barbs
- Pharma 50 tubing, Pharma 65 tubing, Pharma 80 tubing, Braided tubing, C-flex tubing,
- Appropriate size Oetikers

Table 8: Fastener Acceptance Criteria

Irradiation	Acceptance Criteria				
	Pharma 50	**Pharma 65**	**Pharma 80**	**Braided**	**C-flex 374**
Gamma	15 PSI[1]	15 PSI	65 PSI[2]	65 PSI	15 PSI
X-ray	15 PSI	15 PSI	65 PSI	65 PSI	15 PSI

[1] 15 psi = 1 bar; [2] 65 psi = 4.5 bars

The acceptance criteria are tubing dependent. For any connection that uses Pharma 80 or Braided tubing, the recommended test method is high pressure (65psi). For any other tubing type, the recommended test method is low pressure (15psi)

Table 9: Fastener Testing results

Irradiation	Results according to fastener product validation test method				
	Pharma 50	**Pharma 65**	**Pharma 80**	**Braided**	**C-flex 374**
Gamma	Conform	Conform	Conform	Conform	Conform
X-ray	Conform	Conform	Conform	Conform	Conform

The Fastener Testing shows equivalent integrity results between X-ray and gamma irradiated Lynx® and tubing horse barb connections.

3.1.2 AseptiQuik® (AQG) Connectors

The AseptiQuik® AQG product and materials were X-ray irradiated within the 50 to 60 kGy dose range as aligned to BPSA recommendations, and testing completed under Test Request #s 2022-086 and 2022-087. Representative part numbers (AQG17008, AQG17008HT, AQG17108) were selected to represent each of the AQG product lines (see Appendix Table 31).

(1) Bubble Leak Testing

Connected sets of AQG, AQG HT, and AQG PPSU were bubble leaked at 5 and 75 psi (0.34-5.2 bars). The connected set was submerged, pressurized, and observed for leaks for a minimum of 2 minutes. The bubble leak test was conducted following ASTM E515-11, Standard Practice for Leaks Using Bubble Emission Techniques. A pass would entail no bubbles forming or coming off the parts.

Table 10: Results of bubble leak testing on X-ray irradiated connectors

Connector	Treatment	Qty	Acceptance Criteria (with units)	Results
AQG	Post X-ray	30 Connected Sets	5 and 75 psi[1] No leaks for a minimum of 2 minutes	PASS
AQG HT	Post X-ray	30 Connected Sets	5 and 75 psi[1] No leaks for a minimum of 2 minutes	PASS
AQG PPSU	Post X-ray	30 Connected Sets	5 and 75 psi[1] No leaks for a minimum of 2 minutes	PASS

Note: [1]0.34 and 5.2 bars

(2) Water Burst Testing

The connected sets of AQG, AQG HT and AQG PPSU were water burst tested. Each connected set was placed on a test equipment fixture and pressurized with a water/air mixture at a predefined ramp rate until a failure occurred or reached 3000 psi (equipment limits).

Table 11: Results of water-burst testing on X-ray irradiated connectors

Connector	Treatment	Quantity	Acceptance Criteria	Results
AQG	Post X-ray	30 Connected Sets	Product bursts at a factor great than max operating pressure	PASS[1]
AQG HT	Post X-ray	30 Connected Sets	Product bursts at a factor great than max operating pressure	PASS[1]
AQG PPSU	Post X-ray	30 Connected Sets	Product bursts at a factor great than max operating pressure	PASS[1]

Note: [1]PASS indicates samples met the same internal burst test threshold as historical gamma samples.

(3) Membrane Air Burst

The unconnected product (AQG, AQG HT, and AQG PPSU) was placed on a fixture on the test equipment and pressurized with air at a predefined ramp rate until the membrane releases or reached 80 psi (equipment limits).

Table 12: Results of membrane air-burst testing on X-ray irradiated connectors

Connector	Treatment	Quantity	Acceptance Criteria	Results
AQG	Post X-ray	30	No published spec[1]	PASS[2]
AQG HT	Post X-ray	30	No published spec[1]	PASS[2]
AQG PPSU	Post X-ray	30	No published spec[1]	PASS[2]

Note: [1]No maximum operating pressure specified for these connectors in an unconnected state.
[2]PASS indicates samples met the same internal burst test threshold as historical gamma samples.

3.2 Biocontainer (Flexsafe®)

Scalable single-use products, such as bioreactors, filters, and bags, can be used for the actual manufacture and purification of pharmaceuticals. Single use biocontainer (or single use bags) can be used for the fermentation, cell cultivation and purification, storage, shipping, buffer preparation and focus on production processes in the biopharmaceutical industry. Flexsafe® bags with S80 Film (composed of layers of PE/EVOH/PE) were assessed following irradiation in the 45 to 60 kGy dose range.

3.2.1 Permeability

Table 13 summarizes the average permeability results, including carbon dioxide transmission rate (CO_2TR), oxygen transmission rate (OTR), water vaper transmission rate (WVTR) of the S80 film. To assess equivalency , a ratio of the X-ray and gamma permeation rates for each gas was determined. The ratio between the average values of the of X-ray and gamma sample measurements are within the equivalence interval for the CO_2TR, WVTR and O_2TR. The equivalence internal is defined for the OTR & CO_2TR with a ratio=$[OTR \& CO_2TR]_{X\text{-}ray}/[OTR \& CO_2TR]_{gamma} < 2.5$ and with a ratio <1.5 for the WVTR. The S80 film permeability properties between gamma and X-ray irradiation about the CO_2, water vapor and O_2 are equivalent.

Table 13: CO_2TR, OTR and WVTR permeability results for S80

Batch	Ageing	Irradiation modality	CO_2TR (cc/(m^2.24h))	OTR (cc/(m^2.24h))	WVTR (g/(m^2.24h))
1	t0[1]	Gamma	0.8±0.2	0.3±0.1	0.27±0.01
		X-rays	0.7±0.1	0.3±0.1	0.23±0.03
2	t0[1]	Gamma	0.8±0.1	0.3±0.1	0.24±0.01
		X-rays	0.8±0.1	0.3±0.2	0.25±0.01
	t3[2]	Gamma	0.6±0.1	0.3±0.1	0.20±0.01
		X-rays	0.7±0.1	0.2±0.1	0.21±0.03

[1]t0 = freshly after irradiation | [2]t3= 3 years after irradiation

3.2.2 Particulate, Mixing and Cell growth (supplemental to the initial BPSA protocol)

The particulate matter has been tested in representative Flexsafe® products (made of S80 film) according to the USP <788>. The results must be compliant to USP <788> and to the acceptance limits that are < 25 particles/mL for particles ≥10 µm and < 3 particles/mL for particles ≥25 µm. The tests performed on the Gamma and X-ray irradiated products show sub-visible particle test results compliant to USP <788>.

Cell growth assays have been performed on three gamma irradiated and three X-rays irradiated Flexsafe® representative bags according to ASTM E3231-19. No cell growth issue was observed with either irradiation sources.

The functionality of worst-case representative products was tested following gamma and X-ray exposure, with the conclusion that X-ray irradiated systems demonstrated the same level of performance as gamma irradiated systems. This included evaluation of packaging integrity, pH and conductivity measurements, and robustness assessment of the Flexsafe® Pro Mixer systems.

3.3 Sensors

3.3.1 Single Use Pressure Sensors™ (PREPS and PRESS)

PendoTECH single use pressure sensors (PREPS and PRESS) were evaluated for compatibility with X-ray irradiation following irradiation at >50 kGy and tested in accordance with previously published BPSA recommendations.

A risk analysis identified functionality and physical testing to be the most critical tests for X-ray qualification of single use sensors. Physical leak and burst testing were performed to validate sensor integrity post X-ray irradiation. These sensors were inspected for leaks at 60psi (4.14bar), and then exposed to 150 psi (10.34 bar) for burst testing. No leaks were visually identified, and all pressure decay tests were within the acceptable limit, confirming that X-ray irradiation does not impact the physical integrity of the sensor. Sensor performance and functionality were evaluated with a full range accuracy test. All sensors were within manufacturer's accuracy specification following X-ray irradiation, confirming sensor performance is not altered by X-ray irradiation.

(1) Physical Leak and Burst Testing

The integrity of pressure sensors from 3 different lots was challenged following exposure to an X-ray Irradiation dose >50kGy. All sensors were evaluated with a leak test that consisted of a 90 second pressure decay test at 60 psi (4.14 bar) as well as a visual inspection for leaks using soapy water. Additionally, a subset of these sensors were burst tested at 150 psi (10.34 bar) while also being inspected for leaks. The acceptance criteria were: Leak Test: Pressure Decay less than 0.03psi(2.07mbar)/second and no visual detection of leaks; Burst Test: No evidence of leaks or sensor damage after exposure to 150 psi (10.34 bar). Results are summarized in Table 14 with detail supplemental data available in the appendix.

Table 14: Leak and Burst Test Summary

Part Number	Lot Number	Number of repetitions (Serial Number testing)	Observations
PRESS-S-000	1210050	5x (29,27,28,30,32)	No leaks or bursts
PREPS-N-000	1203163	5x (35,36,37,38,39)	No leaks or bursts

No leaks were identified in any of the leak or burst testing and all pressure decay tests were within the acceptable limit, thus validating the sensor integrity of PendoTECH Single Use Pressure Sensors post X-ray Irradiation.

(2) Accuracy and Performance Testing

The functionality of pressure sensors from 3 different lots was challenged following exposure to an X-ray Irradiation dose >50kGy. All sensors were tested for accuracy across their full pressure range (0 to 60psi/4.14bar) by connecting them inline with a calibrated pressure gauge for reference (Table 15). The acceptance criteria were for all readings to be within PendoTECH's Pressure Sensor Accuracy Specification:

- 0 to 6psi/0.414bar: ±2% of reading
- 6 to 30psi/0.414 to 2.07bar: ±3% of reading
- 30 to 60psi/2.07 to 4.14bar: Typically, better than ±5% of reading

Table 15: Summary of sensor accuracy and performance testing results.

Part Number	Lot Number	Number of repetitions (Serial Number testing)	Gauge Pressure (Psi/Bar)					
			10/0.69	20/1.38	30/2.07	40/2.76	50/3.45	60/4.14
PRESS-S-000	1210050	8x (26,27,28,29,30,31,32,33)	Pass	Pass	Pass	Pass	Pass	Pass
PREPS-N-000	1203163	7x (35,36,37,38,39,40,41)	Pass	Pass	Pass	Pass	Pass	Pass
PREPS-N-025	1191570	7x (26,27,28,29,30,31,32)	Pass	Pass	Pass	Pass	Pass	Pass

All sensors were within PendoTECH's accuracy claim and did not significantly change after X-ray irradiation as expected, thus qualifying the performance of PendoTECH Single Use Pressure Sensors Post X-ray Irradiation.

3.3.2 Single-use pH Sensor (SU1800-16)

The Broadley-James SingleSense™ pH Sensor (SU800-16) is designed for installation into any Single-Use BPC. The design of the sensor incorporates a self-calibration function, which allows the end user to execute a calibration process of the sensor without the requirement for any extra equipment or chemical reagents such as buffers. This Single-Use sensor design aligns with the basic deliverables of single-use system/technology, allowing suppliers of the SUS to shoulder some of the responsibility of the system operation, freeing the end users to perform other tasks.

For example, one of the critical validations of the SU800 sensor design is this self-calibration feature, since this feature is a core sensor functionality for single-use applications. During the product development phase, this sensor feature together with other required chemical and biological analysis have been verified and validated post gamma irradiation treatment at 50kGy. For this X-Ray equivalency study, the task force at BPSA prioritized the validation of sensor functionality and the self-calibration feature. The results in this study conclude no impact of X-ray (47.7 to 51.3 kGy dose range) on sensor functionality of SU800 single-use pH sensor as compared to results found with gamma irradiation.

(1) Sensor Accuracy

With the self-calibration function designed into the sensor, the sensor accuracy is determined by two parameters of SU800 sensor: the sensitivity of the sensor (slope) and the pH value of the built-in storage/calibration solution. During the design phase of the SU800 sensor, the pH sensing component (sensing glass) has been verified to be highly resistant to irradiation and will not lose its sensitivity in five years after e-beam or gamma treatment. The storage/calibration solution is a formulated buffer system for providing a stable pH value of pH 6.7. The pH values of the storage/calibration solutions of five sensors were measured after X-ray exposure and compared with their values before X-ray (Table 16).

Table 16: Summary of sensor accuracy results

	Sensitivity, mV/pH			pH of Storage/calibration Solution		
SU800 SN	Before	After	Change, %	Before	After	Change, pH
113	58.3	57.7	-0.96	6.67	6.69	0.02
118	58.1	58.1	0.00	6.68	6.66	-0.02
120	58.0	58.0	0.03	6.67	6.68	0.01
121	58.0	58.2	0.33	6.68	6.68	0.00
122	57.9	58.1	0.33	6.68	6.70	0.02

The test data listed above passes supplier SU800 design/engineering specifications. No negative impact in performance due to the X-ray exposure was observed.

- A 1% change in sensitivity will result in < 0.01 pH change in pH measurement over the typical BPC operational range of pH 6 – 7.
- 0.02 pH unit is the maximum reproducibility of pH measurements in general lab environment with no specified temperature, pressure, and ionic strength of test media

(2) Sensor Drift

After the X-ray treatment, all sensors were tested for drift in our internal cell culture simulation system. The cell culture simulation system is designed with the same electrochemical environment of the cell culture process, without the cells. The media used in the system is formulated to represent cell culture media using similar electrolytic minerals and concentrations. The system operates at 37 ºC with CO_2 sparging to adjust and control the pH of the media during the simulation.

With the self-calibration function built in, the sensor drift behavior can be divided into two claims, one is the sensor signal drift without calibration, and the other is the sensor calibration buffer (the storage solution) pH value drift. By using the cell culture simulation system, both drift claims were checked. The pH of the media was from 6.93 – 7.13 during the run. The drift values of the sensor reading during the 16 days of a cell culture simulation run can be seen in appendix in Table 36. The Table 35 lists the drift values of the sensor reading during the 16 days of a cell culture simulation run.

The pH value of the sensor storage solution for self-calibration function are listed in Table 17.

Table 17: pH value of the sensor storage solution for self-calibration function

	pH of SU800 built-in Storage/Calibration Solution				
SU800 SN	**113**	**118**	**120**	**121**	**122**
4/6/2022	6.64	6.62	6.63	6.64	6.63
4/11/2022	-[1]	6.62	6.62	6.64	-[1]
4/15/2022	6.63	6.61	6.62	6.63	6.64

[1] "-": Sensor was not pulled back to its calibration position for the measurement.

As shown in the data, the pH value of the sensor built-in storage/calibration solution drifted about 0.01 pH unit through the 9-day's cell culture process. This indicates that if end-users do suspect the sensor signal drift beyond required pH range, the end user can always pull the sensor back into its storage/calibration chamber to check its accuracy and redo the sensor calibration if necessary.

3.4 Kleenpak™ Sterilizing-Grade Filter Capsule

Sterilizing-grade filter capsules may be used individually or integrated into single-use systems, where they help ensure the absence bacteria in the filter effluent. Representative Kleenpak™ capsules with Supor® EKV membrane were irradiated at 50 ± 5 kGy and evaluated as described by the physical and functional testing further below. All results supported the conclusion that X-ray and gamma irradiated filter capsules are equivalent.

3.4.1 Pressure Burst Testing

Representative untreated (n =3), gamma irradiated (n =3), and X-ray irradiated (n =3) filter capsules with Supor® EKV membrane (KA3EKVP1) were subjected to burst pressure testing at 40 °C (Figure 1). The burst pressures far exceeded those used during normal single-use operation. Both gamma irradiated and X-ray irradiated capsules showed slightly decreased burst pressures following irradiation, with both X-ray and gamma irradiated capsules showing equivalent results.

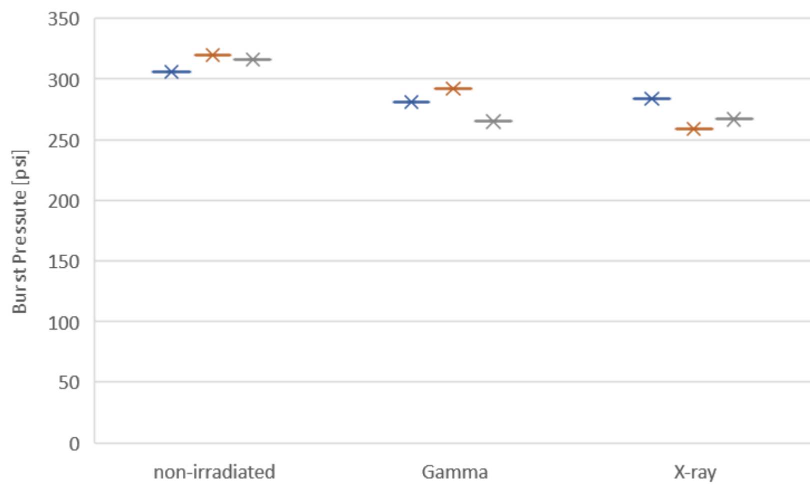


Figure 1: Pressure burst test results for untreated, gamma irradiated, and X-ray irradiated Kleenpak™ filter capsules

3.4.2 Pressure vs flow testing

Although retention characteristics are the primary function of bioprocess filters, the pressure vs. flow relationship can exhibit a significant impact on bioprocess operations. The water pressure vs. flow relationship was evaluated for two lots of untreated (n = 3), gamma irradiated (n = 3) and X-ray irradiated (n = 3) Kleenpak™ capsules with Supor® EKV membrane. The pressure versus flow trending data for X-ray irradiated capsules overlap those for untreated and gamma irradiated capsules (Figure 2) indicating no significant impact of irradiation and no differences between X-ray and gamma.

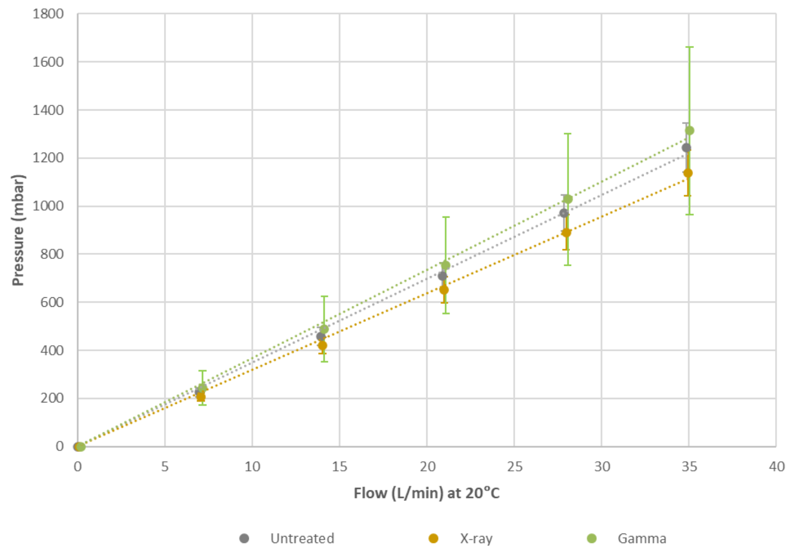


Figure 2: Water flow vs. differential pressure test results for untreated (black), gamma irradiated (green), and X-ray irradiated (gold) KA3EKVP1 filter capsules

3.4.3 Filter Integrity Testing

Filter integrity testing limits are correlated by filter manufacturers with successful bacteria retention test results, and represent the simplest, well-accepted method to assess the goodness and integrity of a sterilizing-grade filter. Untreated (number of samples (n) = 3), gamma irradiated (n = 3), and X-ray irradiated (n = 3) Kleenpak^{TM} capsules with Supor® EKV membrane from two lots were subjected to filter integrity testing using both water (Figure 3), and isopropyl alcohol/water (Appendix Figure 49) as the integrity test fluids. Whereas filters wet with alcohol mixtures readily wet uniformly, the water wet integrity testing may be more sensitive to any potential changes in surface tension of the membrane that would render the membrane more difficult to fully wet. All filters tested met the forward flow acceptance criteria, which is correlated to bacteria retention. In addition, there were no significant differences or trends observed with filters subjected to X-ray vs. gamma-irradiation. Hence the data indicate no impact of X-ray irradiation on filter integrity or wettability.

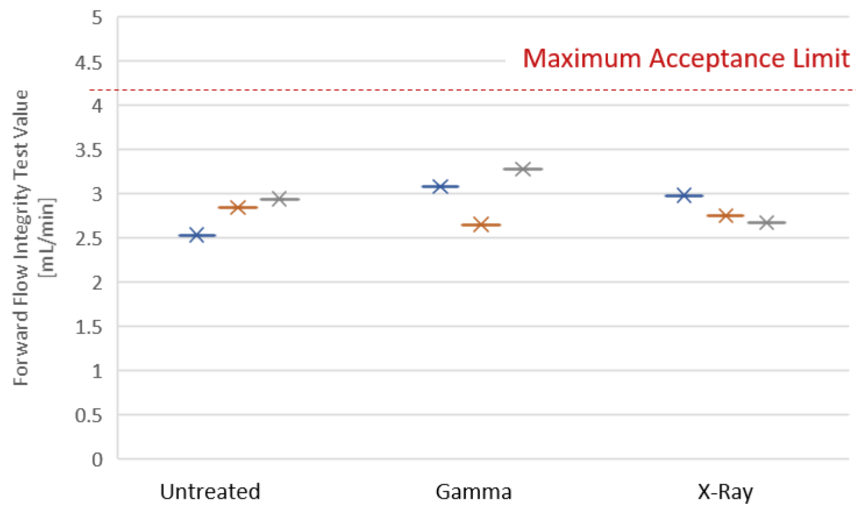


Figure 3: Forward flow filter integrity test results for untreated, gamma irradiated, and X-ray irradiated KA3EKVP1G filter capsules wetted with water.

3.4.4 Bacteria Challenge Testing

Representative Kleenpak™ capsules with Supor EKV membrane (KA3EKVP1) from two manufacturing lots were subjected to X-ray irradiation at 50 kGy demonstrated no downstream recovery of bacteria when challenged with *B. diminuta* at a concentration > 10^7 CFU/cm^2. This is a key requirement for sterilizing-grade filters and confirms X-ray-irradiated filters continue to meet this claim.

Table 18: Liquid microbial challenge test results for X-ray irradiated KA3EKVP1 filter capsules

Part Number	Serial Number	Total Challenge	Recovery	Titer Reduction	Challenge Level (CFU/cm²)	Pass / Fail
KA3EKVP1G	IE6401/0262 (x2)	4.3×10^{10}	0	$\geq 4.3 \times 10^{10}$	2.9×10^7	Pass
KA3EKVP1S	IE4976/0406 (x1)	5.2×10^{10}	0	$\geq 5.2 \times 10^{10}$	3.5×10^7	Pass
KA3EKVP1S	IE4976/0374 (x4)	2.6×10^{10}	0	$\geq 2.6 \times 10^{10}$	1.7×10^7	Pass

3.4.5 Particulates (supplemental)

Particulates are normally assessed by Cytiva for non-irradiated KA3EKVP1G filters on a lot release basis. Although particulates are not expected to be a significant risk associated with irradiation technology, the standard manufacturing lot release test was performed without any prior flushing on non-irradiated, gamma irradiated, and X-ray irradiated filters. All filters appeared demonstrated equivalent results, and all met Cytiva requirements aligned to USP <788> (See Appendix Figure 48).

3.5 Tubing

Physical and functional assessment of tubing may be accomplished through evaluation of bend radius, burst testing or other measure of durability. In addition, mechanical testing, such as tensile strength, elongation at break, tear resistance, durometer, and compression set may be evaluated as described in Section 5.5 Mechanical Evaluation of Materials.

3.5.1 Pumpsil®, Bioprene®, Pureweld® Tubing

Testing has been performed to assess the equivalence of the physical and functional properties of three Watson-Marlow tubing types following gamma and X-ray irradiation. The materials included platinum-cured silicone (Pumpsil®), TPV (Bioprene®) and SEBS (PureWeld®XL) and all tubing samples were 9.6 x 2.4mm LoadSure® elements, to minimize any variation due to tube loading. Samples of each tubing type were irradiated at 50±5 kGy and evaluated as described below. Physical properties assessed included discoloration/general appearance and hardness. Equivalence was determined visually for the discoloration and general appearance; for hardness, the mean and standard deviation of the data sets were compared *(See Mechanical Evaluation of Materials)*. A functional assessment was also carried out on the peristaltic durability of the tubing products; equivalence for this testing was established by comparing the mean and standard deviation of the data sets. In all tests the two irradiation modalities were shown to produce equivalent results.

(1) Endurance Tests

The pumping life of Pumpsil® is shorter than Bioprene® and PureWeld® XL so the duty points (speed and pressure) used for the test were half that of Bioprene® and PureWeld® XL. Test parameters were as follows:

- Pumpsil® – 110 rpm, 1 bar pressure
- Bioprene® and PureWeld® XL – 220 rpm, 2 bar pressure

Five replicates were tested for each tubing type for each irradiation and aging condition (60 samples in total for the data set). The data representing 5 years of aging is supplemental information. The results from the endurance test did not show any noticeable difference between gamma irradiation and x-ray irradiation for Pumpsil® and Bioprene®. There was an apparent difference for PureWeld®XL in the unaged samples where the X-ray irradiation appeared to give a longer lifespan that the gamma irradiation but there was minimal statistical difference in the overall data set so this not likely to be significant. The endurance test results are shown in Figure 4.

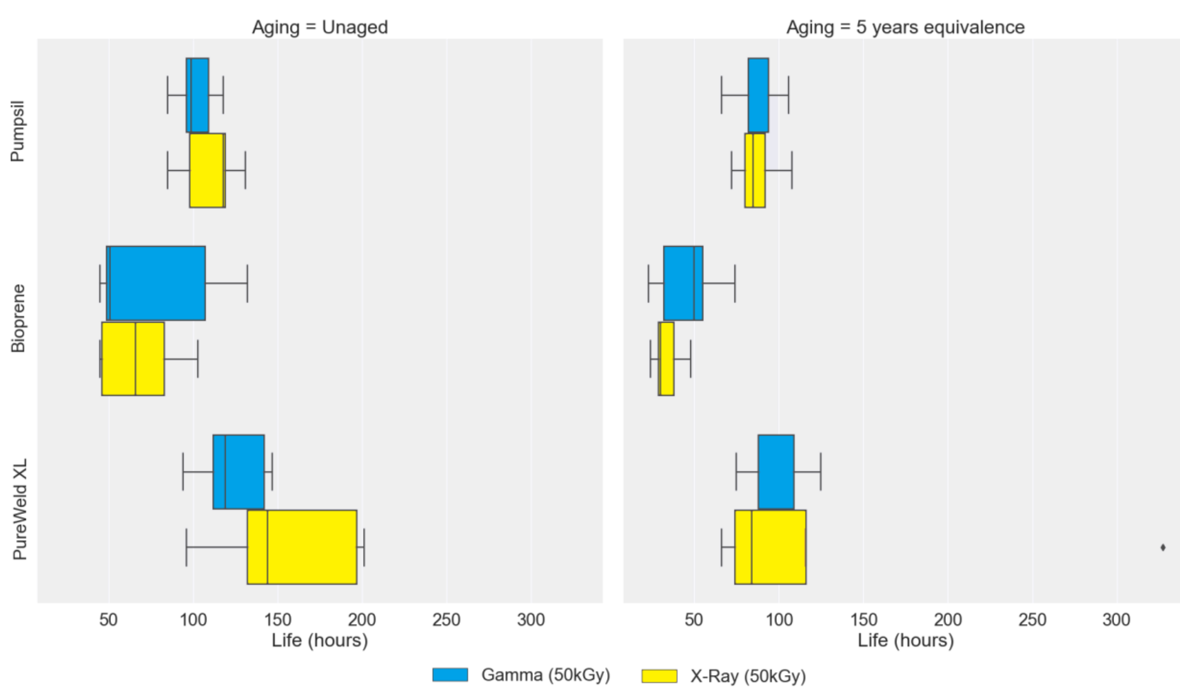


Figure 4: Box and whisker plots of the endurance tests. Aging data regarded as supplemental.

3.5.2 AdvantaFlex™ APAF TPE Tubing

(1) Bend Radius

Tubing bend radius characterizes the mechanical and flexural properties of TPE tubing. Tubing samples were cut into six 45 cm (18") samples for evaluation. Values for gamma and X-ray- irradiated tubing samples are shown in Appendix Table 37. Bend data indicate equivalent results between X-ray and gamma irradiated TPE tubing.

(2) Burst Testing

Burst testing characterizes the physical and functional characteristics of tubing and indicates the maximum pressure the tubing may withstand before rupture. These pressures typically far exceed those recommended by the manufacturer for use in single-use bioprocessing. Six tubing samples used for the bend radius evaluation were connected to stainless steel barbed TC fittings with a 17.0 mm Oetiker clamp and burst tested. Burst testing results demonstrate values of 78.3 ±0.6 psi (5.40±0.04 bar) for gamma irradiated tubing and 79.0 ± 0.6 psi (5.45±0.04 bar) for X-ray treated tubing. Detailed results of the burst testing are shown in appendix in Table 38. There was no discernable impact of X-ray as compared to gamma, and both X-ray and gamma tubing samples appeared equivalent.

3.5.3 Liveo™ Pharma Tubing

Four families of Liveo™ platinum-cured silicone tubing (Liveo™ Pharma-50, Liveo™ Pharma-65, Liveo™ Pharma-80, and Liveo™ Advanced Pump Tubing) were evaluated for X-ray compatibility. X-ray irradiated test samples received an irradiation dose of 51 to 56 kGy, whereas gamma irradiated test samples received a dose of 46 to 48 kGy.

(1) Hydraulic Burst Pressure Resistance and Kink Resistance

Tubing was tested according to the principles of ASTM D380 to determine the ultimate fluid pressure failure in a closed system. Tubing was prepared from the same batch for the test in three conditions: 1) without irradiation, 2) gamma irradiated 3) X-ray irradiated each tested in triplicate. Results are normalized to show relative performance when compared to the non-irradiated sample from each product (Figure 5). By these data, no discernable difference between gamma and X-ray exposed tubing was measured.

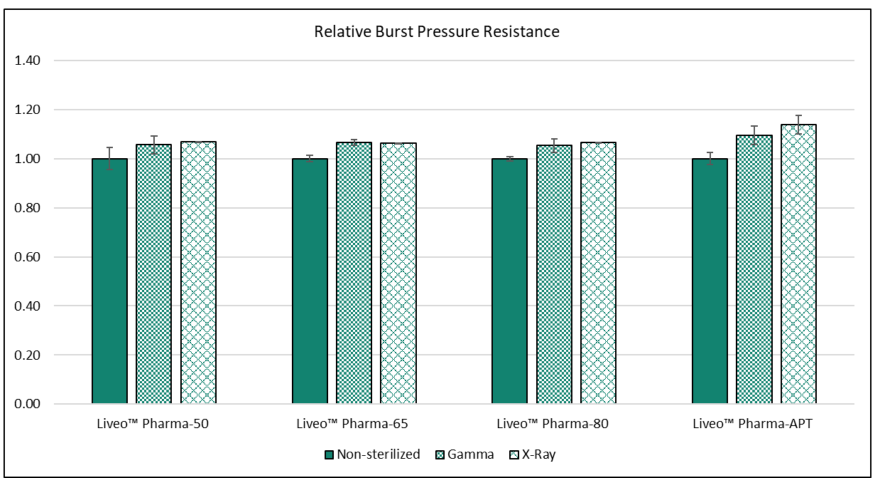


Figure 5: relative burst pressure resistance

The last of the physical and functional tests completed on Silicone tubing can be described as a kink resistance test (Figure 6). The kink resistance test is based on tubing fixtured in a stress/strain device which initiates with the crosshead lowering at a steady rate. During the test, water flow is established through the tubing and the test ends at the point water flow rate decreases by 50%. No differences in kink resistance between gamma and X-ray irradiated tubing were detected.

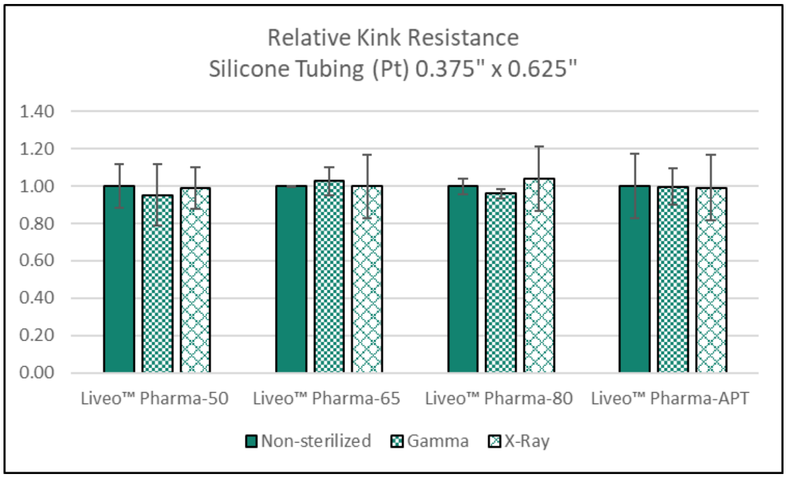


Figure 6: relative kink resistance of Liveo™ materials

3.5.4 Saint Gobain C-Flex® 374 Tubing

Functional and physical property testing were performed on C-Flex® 374 tubing and slab[3] material (all TPE) following gamma and X-ray irradiation in the 50±5 kGy dose range.

(1) Burst Pressure Testing

Burst pressure testing was performed on 10 tubing samples of C-Flex® 374 following gamma or X-ray irradiation (Figure 7). The maximum pressure reached at the point of failure was recorded for each sample. The results demonstrate equivalence between samples that were gamma and X-ray irradiated. It is typical for burst pressure to decrease follow irradiation of C-Flex® 374.

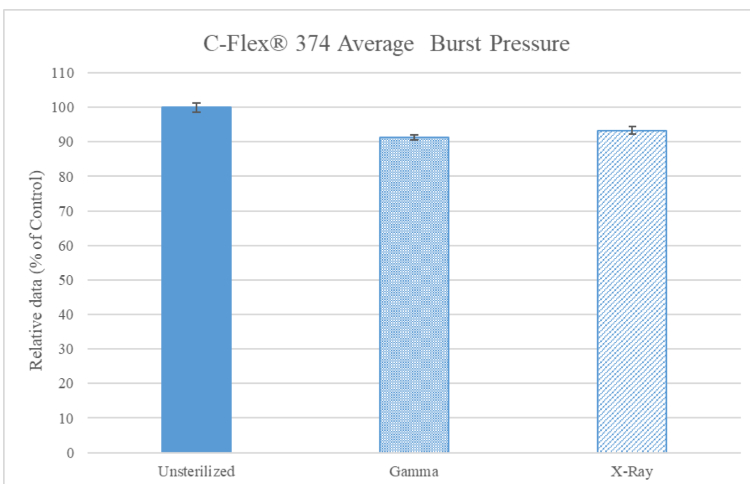


Figure 7: C-Flex® 374 relative average burst pressure results

[3] Slab refers to a thick, flat sheet of the same material that may be more appropriate for some types of testing

(2) Material Bend Radius

Bend radius or kink resistance testing determines how much a tube can be bent before kinking, the point at which liquid would theoretically no longer be able to flow through the tube. Material Bend Radius testing was performed on 10 tubing samples of C-Flex® 374 tubing after gamma and X-ray irradiation. The results demonstrate equivalence between samples that were gamma and X-ray irradiated. It is typical for C-Flex® 374 to increase in bend radius following irradiation. The Figure 8 displays the relative average of the ten samples from each testing group.

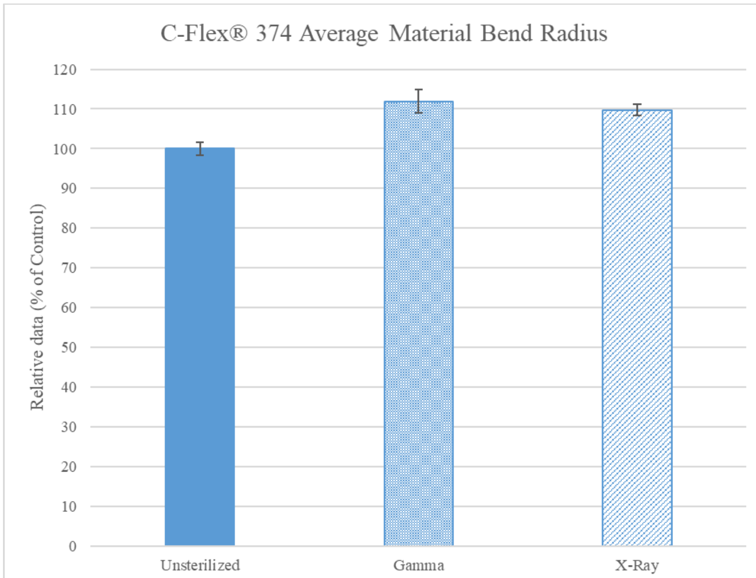


Figure 8: C-Flex® 374 relative average material bend radius results

3.5.5 Sani-Tech® Tubing

Functional and physical property testing has been performed on Sani-Tech® Ultra-C tubing and slab material (all pt-cured silicone) following gamma and X-ray irradiation in the 50±5 kGy dose range.

(1) Burst Pressure Testing

Burst Pressure testing was performed on 10 tubing samples of Sani-Tech® Ultra-C after gamma and X-ray irradiation. The maximum pressure reached at the point of failure was recorded for each sample. The results demonstrate equivalence between samples that were gamma and X-ray irradiated. It is typical for burst pressure to increase follow irradiation of Sani-Tech® Ultra-C due to cross-linking. The Figure 9 displays the relative average of the ten samples from each testing group.

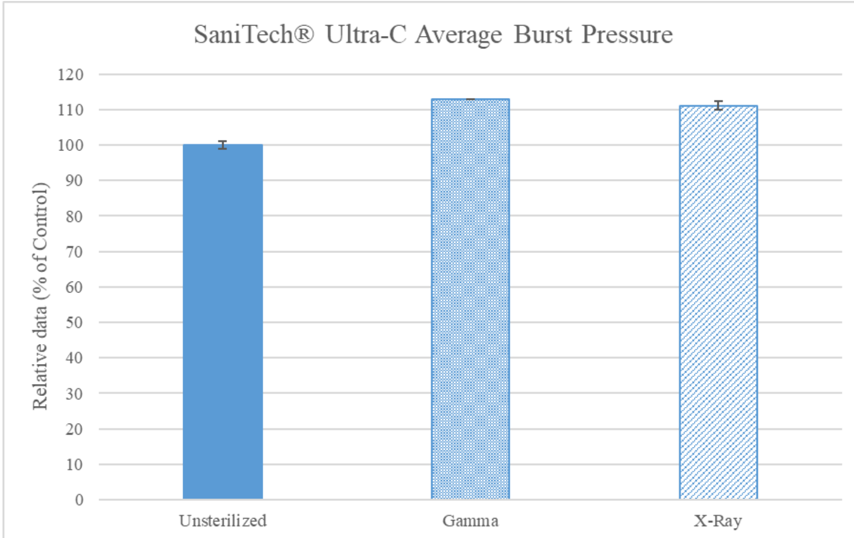


Figure 9: Sani-Tech® Ultra-C relative average burst pressure results

(2) Material Bend Radius

Material Bend Radius testing was performed on 10 tubing samples of Sani-Tech® Ultra-C tubing after gamma and X-ray irradiation. The results demonstrate equivalence between samples that were gamma and X-ray irradiated. It is typical for Sani-Tech® Ultra-C to increase in bend radius following irradiation. Figure 10 displays the relative average of the ten samples from each testing group.

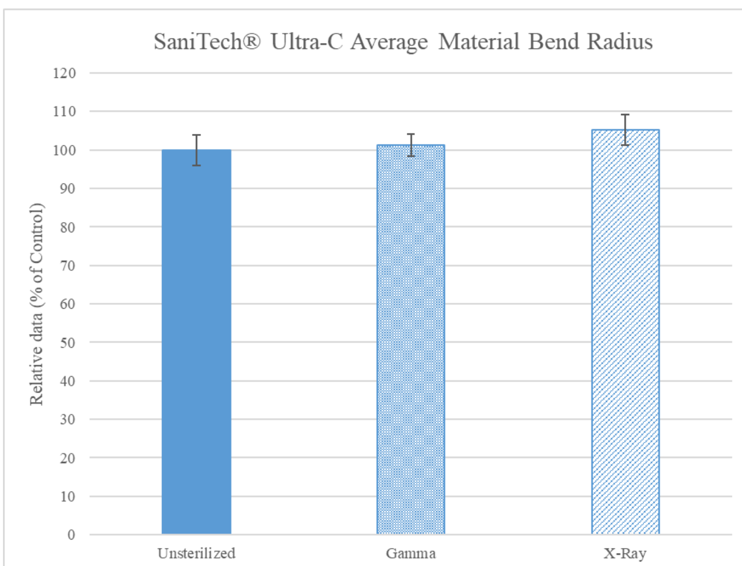


Figure 10: SaniTech® Ultra-C relative average bend radius results

4 Chemical Tests

4.1 Extractables

Whereas extractables and leachables are often performed to characterize materials or validate levels of chemical impurities that may migrate into or persist in the drug manufacturing process stream, the purpose of extractables testing for X-ray qualification is specific to verifying the materials are not adversely impacted in a meaningful way by the transition from gamma to X-ray. As the 50% ethanol/water mixture solvent, which is common to compendial requirements and industry recommendations, provides the largest distribution of unique extractables as compared to other industry (USP and BioPhorum) recommended single-use extraction solvents, this rich characterization profile is considered an ideal solvent for verifying the materials are not adversely impacted by X-ray as compared to gamma irradiation. Coupled with a fundamental understanding of irradiation and BPSA recommended materials testing, the extractables profiling is expected to verify that no new meaningful adverse effects manifest from X-ray as compared to gamma, and that any existing extractables and leachables validation studies are not impacted and thus remain valid after X-ray sterilization.

In risk assessment of the extractables profiles from a biomanufacturer perspective, the approach may be further simplified by focusing only on those compounds above the predetermined evaluation threshold for a particular drug manufacturing process.

4.1.1 Example (Lynx® S2S Connector)

Male and Female Lynx® S2S connectors, irradiated at 45 kGy to 60 kGy, were joined together and served as the extraction vessel. The connectors were extracted in 50% ethanol/water as further described in Appendix Table 29. 50% Ethanol was selected as the model solvent since it captures >95% of all the extractable compounds.

As shown in Figure 11, twenty-one compounds were identified in both the X-ray irradiated connectors and gamma irradiated Lynx® S2S connectors. The compounds consisted of siloxane compounds from O-rings and alkane compounds which are common irradiation breakdown products. The concentration in the extracts of the X-ray irradiated connectors were at comparable concentrations as found in the extracts of the gamma irradiated connectors.

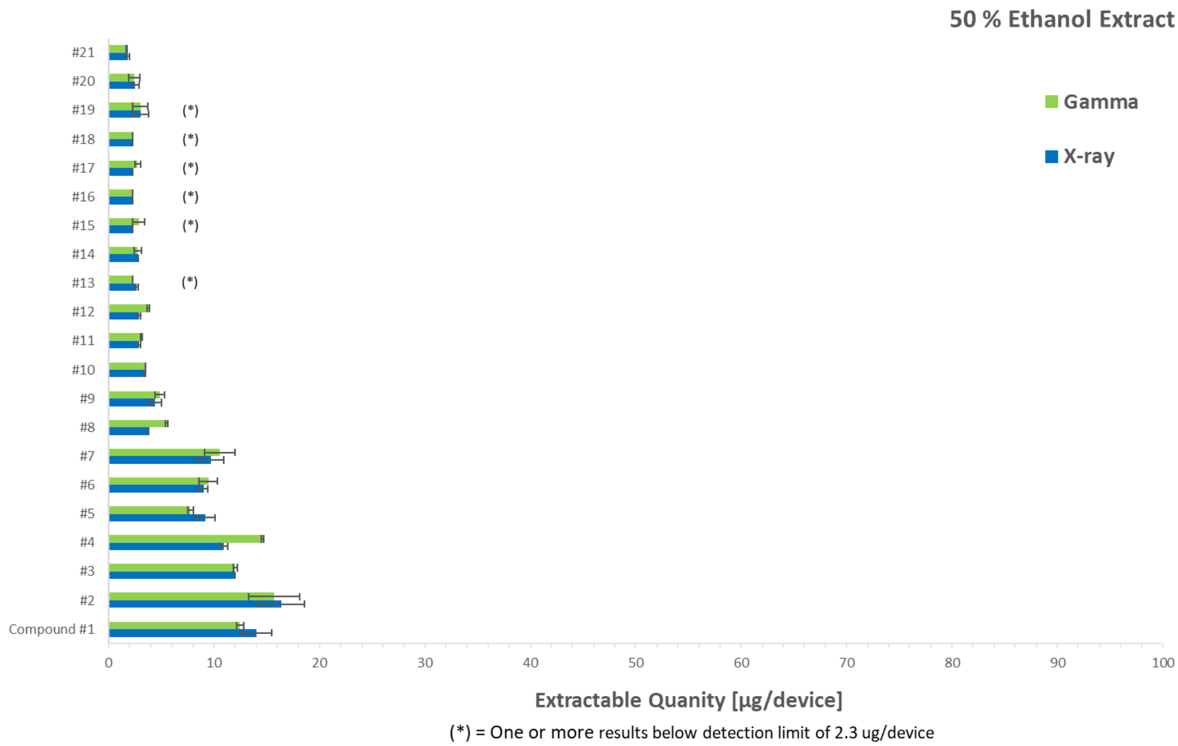


Figure 11: Main outputs of the extractables profile with ethanol extracts on Lynx® S2S Gamma and X-ray, by HPLC-UV, GC-MS-DI, GC-MS-HS

This model stream extractables study supports the conclusions that the level of extractables for the Lynx® S2S connectors subjected to X-ray irradiation are comparable to the Lynx® S2S connectors subjected to Gamma irradiation, and no new or higher concentrated compounds found are of concern.

Additional supplemental studies evaluating TOC of water extracts also demonstrated no increase in extractables associated with X-ray (See Table 30).

4.1.2 Example (Flexsafe® Biocontainer)

Representative Flexsafe® bags were irradiated at 50±5 kGy by X-ray or gamma, and then extracted in pure ethanol for 21 days at 40 °C. Ethanol (50% or pure) is an excellent solvent for material characterization since it provides signals at reasonable levels for reliable peak identification, and it generates comprehensive extractables profiles on a qualitative level[4]. The extraction solvent pure ethanol is compatible with almost all chromatographic screening methods and no sample preparation is required[5]. The data for the S80 film are published[5] (data freely downloadable in link given in the respective reference) and main outputs are summarized in Figure 12. As reported in review articles of radiolysis products, molecules generated from and released by the polymer during irradiation are equivalent for the different radiation sources[6]. Based on irradiation physics and previous literature, the extractable profile should be equivalent;

[4] Samuel Dorey, Ina Pahl, Isabelle Uettwiller, Paul Priebe and Armin Hauk, Theoretical and Practical Considerations When Selecting Solvents for Use in Extractables Studies of Polymeric Contact Materials in Single- Use Systems Applied in the Production of Biopharmaceuticals, Ind. Eng. Chem. Res. 2018, 57, 7077−7089

[5] Roberto Menzel, Samuel Dorey, Tanja Maier, Ina Pahl, Armin Hauk, X-ray sterilization of biopharmaceutical manufacturing equipment—Extractables profile of a film material and copolyester Tritan™ compared to gamma irradiation, BioTechnology Progress, 2021 https://aiche.onlinelibrary.wiley.com/doi/abs/10.1002/btpr.3214

[6] K. Paquette, Irradiation of Prepackaged Food Evolution of the U.S. Food and Drug Administration's Regulation of the Packaging Mater-annotated, chapter 12, 2004

present study is performed to assess and to confirm this equivalence. We take in account the qualitative information (number of extractables detected equivalent after gamma and X-ray irradiation) and the quantitative information (concentration in the same range for each extractable after gamma and X-ray, taking into account the uncertainties of the methodology). We could see that the decamethylcyclopentasiloxane (D5) and the dodecamethyl-cyclohexasiloxane (D6) are different as they originate from silicone tubing and their concentration greatly depends on the contact time with the extraction media during filling (not controlled during filling).

Extractables profiles are equivalent for the S80 films after irradiation with X-ray or gamma. The degradation of the additives for X-ray was identical to gamma. No difference was detected such as additional or completely new extractables within the methodology uncertainties.

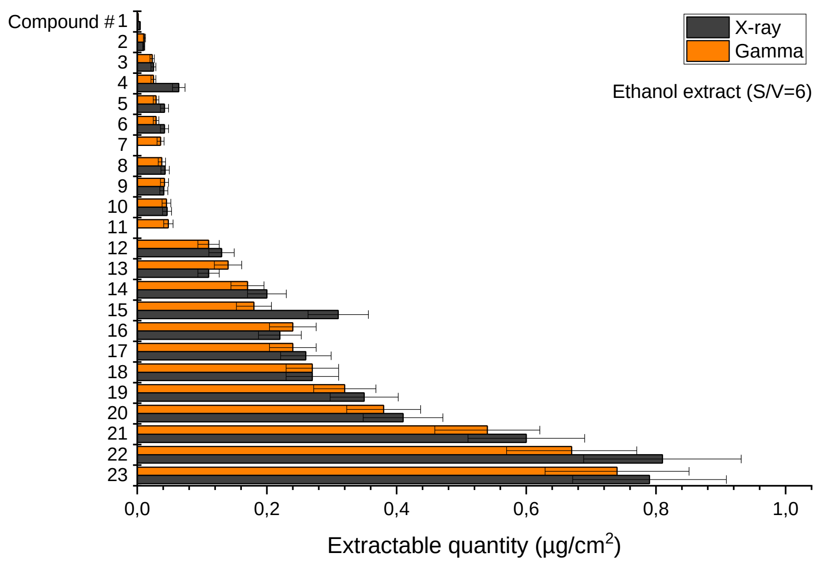


Figure 12: Main outputs of the extractables profile with ethanol extracts on S80 film after Gamma and X-ray, by IC, HPLC-UV, GC-MS and LC-MS

4.1.3 Example (Kleenpak™ capsules)

Two lots of representative Kleenpak™ capsules with Supor® EKV membrane were irradiated at 50 kGy by X-ray or gamma and then extracted in 50% ethanol/water for 24 hours at 40 °C, which is consistent with the USP <665> moderate-risk extractables testing. This 50% ethanol/water profile is common to both USP and BioPhorum standardized extraction profiles and is generally considered to provide the most abundant and most relevant extractables to facilitate risk assessment for pharmaceutical processing. The representative profiles showed 46 different compounds present in the X-ray treated filters, that were also present in the gamma irradiated filters. The compound concentrations were similar and overlapping for gamma and X-ray treated components (Figure 13).

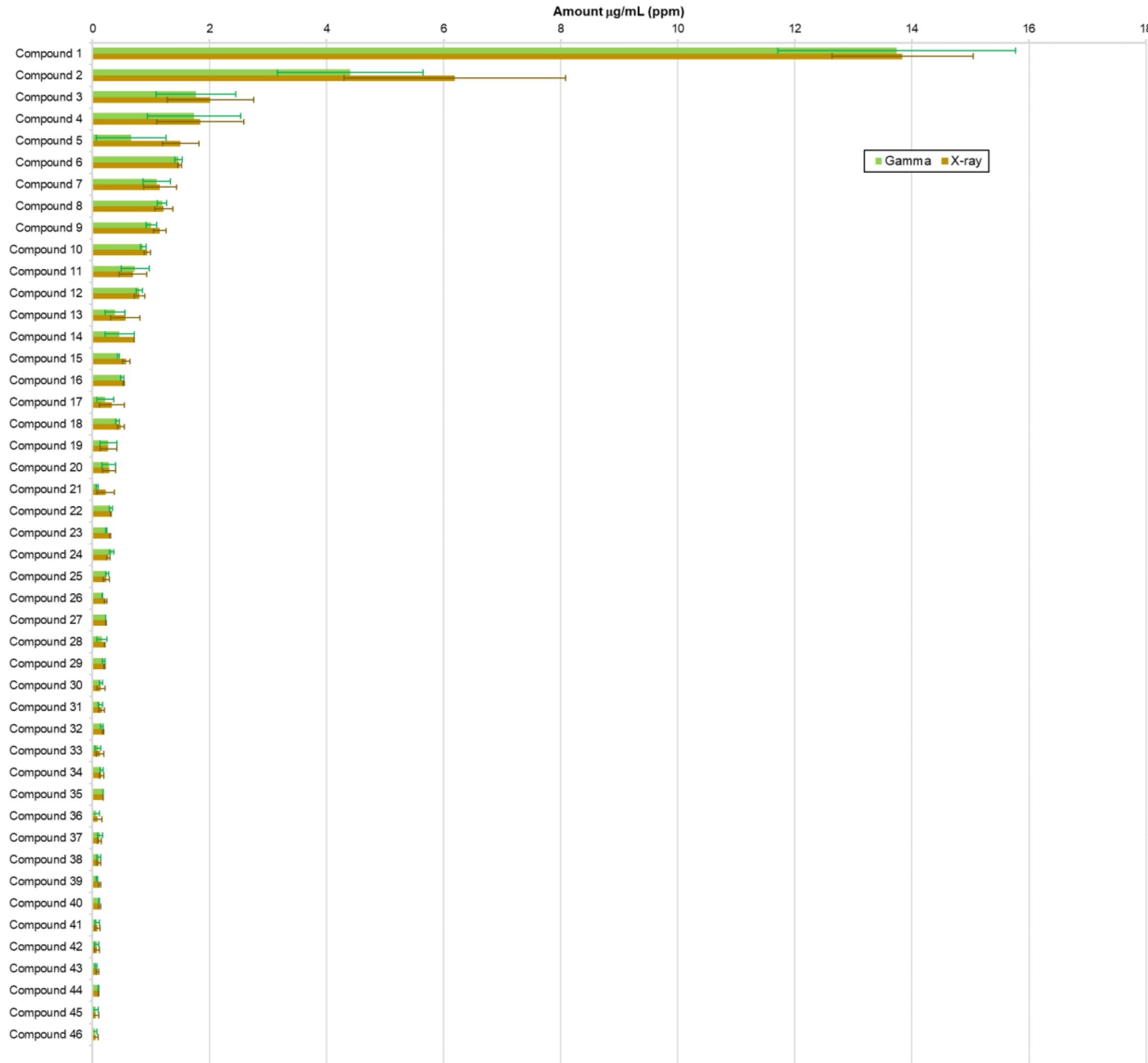


Figure 13: Grand summary of organic extractables (ppm) from gamma irradiated and X-ray irradiated KA3EKVP1 filter capsules. The gold bars show compounds detected following X-ray irradiation, whereas green bars indicate compounds following gamma. Error bars denote observed variation from tested lots.

The only compound(s) to show potentially higher levels in the X-ray treated components are as follows:

Compound #21: Irganox PS 800 oxidized was reported at levels 0.371 mcg/mL (micrograms/mL) and 0.077 mcg/mL in the X-ray treated components, and 0.097 mcg/mL and 0.067 mcg/mL in the gamma irradiated components. These levels are low and overlapping, and not indicative of any specific risk attributed to X-ray.

Based on ICP/MS results, no ICH Q3D elemental impurities were detected above the reporting limit (20 ng/mL). From an extractables standpoint, taking into account assay variation and the number of compounds reported in the extraction profiles, the X-ray sterilization technique appears equivalent to gamma irradiation.

4.1.4 Example (AdvantaFlex™ APAF TPE Tubing)

Representative samples of 0.375" I.D. x 0.625" O.D. APAF TPE tubing were irradiated at 50 kGy ± 5 kGy by X-ray or gamma, and then extracted in 50% ethanol/water for 21 days at 40 °C in accordance with USP <665> moderate risk extractables testing. Please note the samples were relatively short lengths, extracted by immersion in the solvent under agitation conditions. The representative profiles exhibited 52 total compounds showing strong congruence between both materials (See Figure 14). Compounds were ranked in order of abundance relative to levels detected in post-X-ray, with more ~75% of the compounds (n=38) being detected at relatively low levels less than 1 ppm. Any apparent differences in X-ray and gamma were identified and assessed as described further below. The overall conclusion of the assessment was there were no meaningful increases in compounds associated with X-ray or novel, unrelated compounds that could not be attributed to normal, expected variation.

Upon initial inspection, two compounds appeared to show markedly higher values with gamma as compared to X-ray. Both compounds, also detected in X-ray, are related to common ethoxylated products of the extraction solvent. One could hypothetically speculate the levels may be attributed to the lower dose rates associated with gamma, and consequently prolonged exposure to oxidative conditions. However, given the level of variation observed and relationship to the extraction solvent, the levels could also be equally attributed to variation in the sample preparation, irradiation processes, and analyses. Please note the error bars are likely smaller than what should be expected for different irradiation treatments, as the error bars are based on replicate samples, placed adjacent to one another in the same box and undergoing the same irradiation process at the same site on the same date.

Compound #4	2-[2-(2-ethoxyethoxy)ethoxy]Ethanol	8.9 µg/mL (gamma)
Compound #18	1,1-Diethoxyethane	5.4 µg/mL (gamma)

Five compounds were detected at levels that could be inferred as noticeably higher with X-ray and thus warranted further assessment.

Compound #1: 2,4-Di-tert-butylphenol (34.3 ppm X-ray vs 25.7 ppm gamma) is a common antioxidant-related compound present at high levels in X-ray and gamma. This compound and related compounds are present at similarly high levels in historic datasets for this component, and any differences are expected related to the sample size and inherent variation associated with the treatment and evaluation.

Compound #7: Ethoxy(methoxy) methylsilane, 1.5 ppm X-ray) is a common extractable related to silicone materials, which were obtained, irradiated, and evaluated in parallel with the TPE tubing. This compound, reported for transparency, is deemed a silicone-related contaminant from a parallel silicone tubing study.

Compound #15: 2,5-Di-tert-butyl-1,4-benzoquinone isomer (0.9 ppm X-ray vs 0.4 ppm gamma) has been previously reported at 0.8 ppm in historical data sets for this component following gamma irradiation, and hence the levels associated with X-ray are expected representative of variation in sample size, testing, and irradiation processing.

Compound #17: Ethyl acetate, an ICH Class 3 (low toxic potential) solvent, was detected in only one of the X-ray extracts (0.86ppm X-ray vs 0.26 ppm LOD gamma). This residual solvent or potential esterification product of the solvent and acetic acid has also been reported in historical datasets for this component and is attributed to process variation and sample size.

Compound #34 and Compound #41: Both benzaldehyde and a structurally similar compound are related to common antioxidant and cross-linked degradation products with reported levels less than 0.25 ppm. These low levels are expected related to inherent variation sample size, testing, and irradiation processing.

Overall, the USP <665> moderate risk extraction profiles, which involved detailed assessment of 52 compounds, indicated no increased risk associated with X-ray, and that extractables profiles associated with gamma irradiation of TPE tubing may be considered representative and bracketing of X-ray irradiated TPE tubing.

Figure 14: Grand summary of organic extractables (ppm) from gamma irradiated and X-ray irradiated and gamma irradiated APAF TPE tubing. For any values at less than detection or quantitation limit, respective limits are shown.

4.1.5 Example (Liveo™ Silicone Tubing [Pt])

Consistent with a product family approach, extraction of gamma and X-ray exposed silicone tubing catalyzed by platinum was conducted using USP <665> conditions of 21 days exposure to one solvent being 50% Ethanol: 50% Water with surface area to volume of 6:1 at 40 °C. The studies characterized Liveo™ Pharma-65 by analytical methods of LC/MS, GC/MS and GC/FID. By all methods, gamma and X-ray samples contained similar species with similar relative intensities in these direct comparisons.

5 Material Assessments

5.1 Visual Observation and Material Color

Many polymeric materials often exhibit a yellow coloration following irradiation exposure. These evaluations look for any apparent differences in X-ray and gamma irradiated samples, as compared to a non-irradiated control. Note that discoloration is a cosmetic observation but does not necessarily translate into physical or chemical modification that may be better assessed through physical or chemical evaluation.

5.1.1 Sensor Example (PREPS and PRESS)

A visual inspection was performed of 3 groups of sensors- control, gamma irradiated, and X-ray irradiated. The Gamma and X-ray irradiated sensors experienced similar changes in material color (Figure 15). There were no clear differences that could distinguish the gamma irradiated group from the X-ray irradiated group, thus demonstrating visual equivalence.

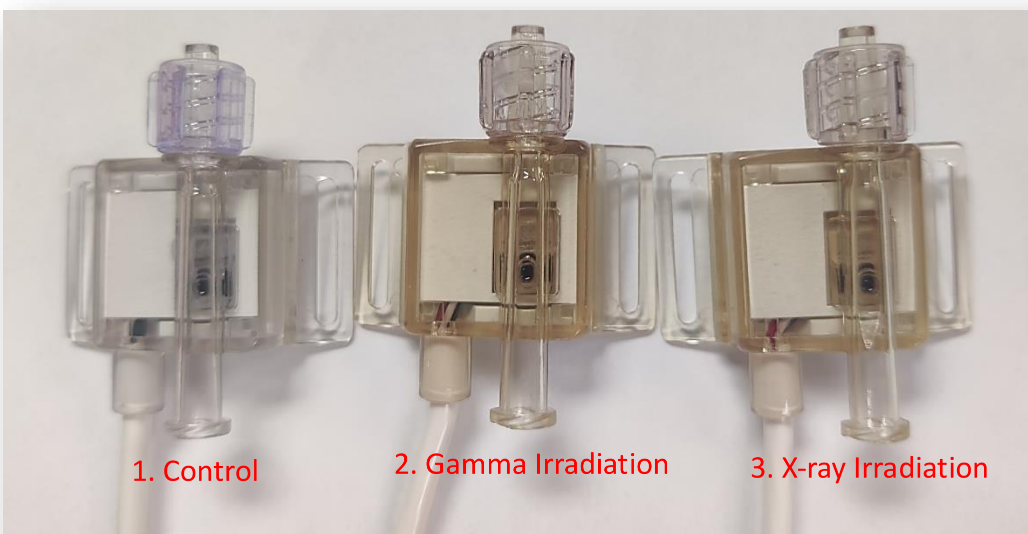


Figure 15: Control, gamma irradiated, and X-ray irradiated single use pressure sensors

5.1.2 Sensor Example (BPC pH Sensor)

All sensors after X-Ray process were visually inspected for any impact from the irradiation.

Table 19: Visual observation summary of pH sensor materials following X-ray

Components	Material	Application Process Contact	Function	Visual Observation
Lever	PPSU	No	Sensor Actuation	No observable impact
Cam Arm	PPSU	No	Sensor Actuation	
Cap	PBT	No	Sensor Actuation	
Bellows	Silicone	No	Sensor Actuation	
Zip tie	HDPE	No	Tamper-proof	Broken
O-Ring	Silicone	No	seal	No observable impact
O-Ring	EPDM	Yes	seal	
Body	PEEK	Yes	construction	
Gasket	Silicone	Yes	seal	
Stem Glass	Sodium Glass	Yes	construction	
pH Sensing Glass	Transition metal glass	Yes	pH sensing	
Ceramic Junction	Alumina Silicate	Yes	pH sensing	
Reference Electrode	Ag/AgCl	Yes	pH sensing	
Storage Solution	Phosphate/KCl	Yes	Self-Calibration	

Visual inspection of the SU800 sensors after X-ray processing found no observable change in any of the sensor component materials, except for cracks at the 90 º bend location of the tamper-proof zip ties. The zip tie cracking at the 90º bent position occurred for gamma treatment as well, indicating it was unrelated to the specific irradiation technology.

5.1.3 Biocontainers Example (Flexsafe®)

Color measurements were performed using the L* (lightness), a* (redness) and b* (blueness-yellowness) space. To evaluate the difference between 2 color measures, ΔE_{00} is calculated between the average of gamma and X-ray irradiated samples according to NF EN ISO 11664-6: 2016. The gamma and X-ray S80 irradiated samples are equivalent in term of color ($\Delta E_{00} < 2$).

5.1.4 Connectors Example (Lynx® S2S)

There were no clear differences that could distinguish the gamma irradiated group from the X-ray irradiated Lynx® S2S connectors, thus demonstrating visual equivalence. Figure 16 shows the similarity in color of the Lynx® S2S male & female parts. The visual inspection and the displayed photograph show that X-ray treated Lynx® S2S connectors do not show any major change in color between X-ray and gamma treated materials

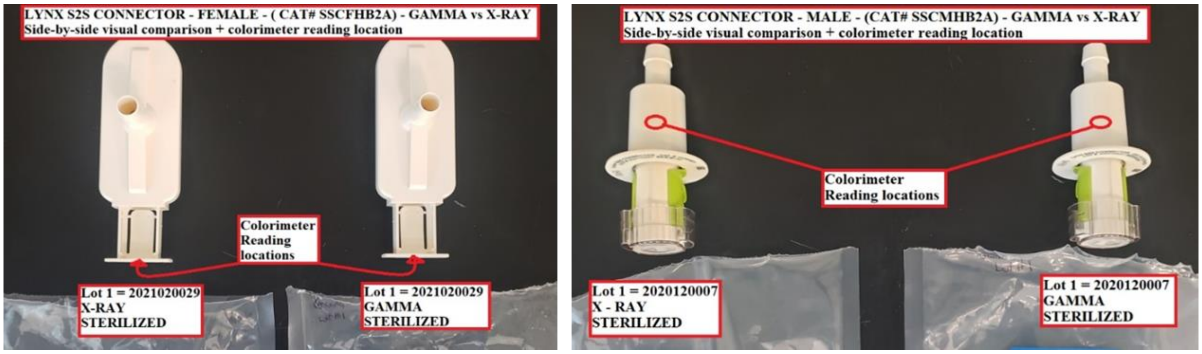


Figure 16: Lynx® male and female S2S connector post gamma & post X-ray

The arrows and circles in Figure 16 indicate the points where yellowness measurements were taken following ASTM E313. Table 20 shows the yellowness index measurement results. Measurements are for information only. Measurements were taken at the same point three times respectively.

Table 20: Yellowness Index Measurements

Tested Part	Irradiation	Yellowness Index
Male Lynx® S2S Connector Lot 1 & 2 2020120007, 2021020020	X-ray	18,6
Male Lynx® S2S Connector Lot 1 & 2 2020120007, 2021020020	Gamma	17,6
Female Lynx® S2S Connector Lot 1 & 2 2021020029, 2021020031	X-ray	17,7
Female Lynx® S2S Connector Lot 1 & 2 2021020029, 2021020031	Gamma	17,5

The results generated through yellowness index measurements clearly suggest that there are no major differences between X-ray and gamma treated Lynx® S2S connectors. The difference in yellowness indexes is within the fluctuation of results, that were observed for the two lots that were tested.

5.1.5 Connector Example (Aseptiquik®)

Samples of X-rayed Connector components and connector materials were visually inspected compared to virgin equivalents (Appendix Table 32.). Little to no color variation was observed. The membranes on the AQG, AQG HT, and AQG PPSU were visually inspected for observations not considered normal. No abnormal observations were observed.

5.1.6 Filter Example (Kleenpak™ capsules)

Visual inspection of gamma irradiated, X-ray irradiated, and non-irradiated filter capsules showed no discernible differences in the KA3EKVP1 filter capsule materials or packaging (Figure 17). For this evaluation, filters were cut apart to evaluate the impact to individual materials of construction comprising the filter capsule. Irradiated materials demonstrated gold coloring (typical of irradiation), but there were no discernible differences between X-ray and gamma irradiated materials.

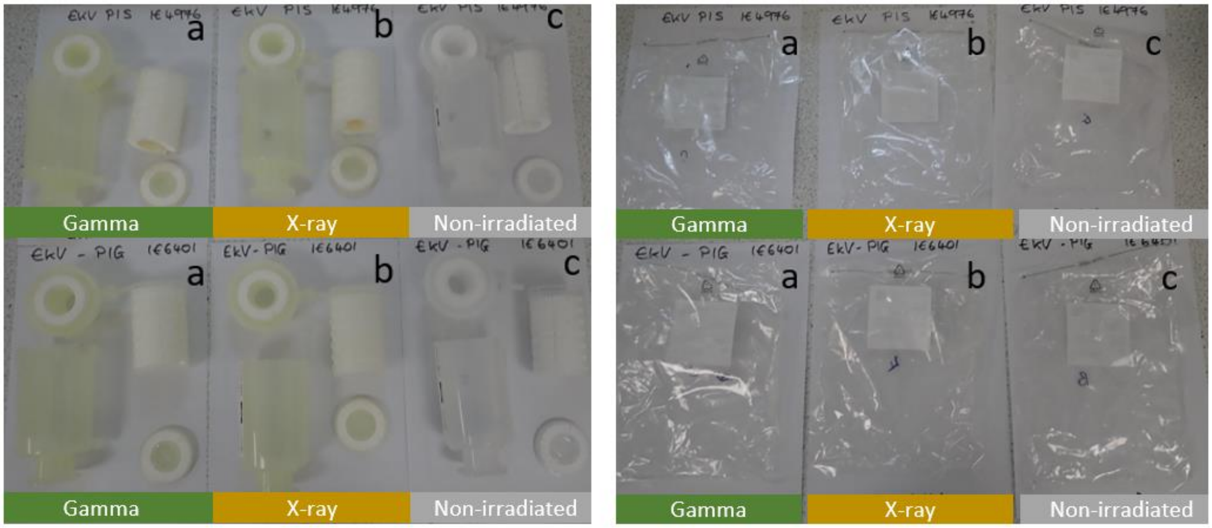


Figure 17: Visual inspection of (left) sectioned KA3EKVP1G filter capsules and (right) component packaging materials

5.1.7 Tubing Example (Pumpsil®)

There was no distinguishable visual difference between the tube materials (Pumpsil®, Bioprene® or PureWeld® XL) or the radiation type (non-irradiated, X-ray or gamma). The connectors that form part of the LoadSure® products though did show a noticeable, visual difference between the irradiated and non-irradiated samples. The colour of the LoadSure® connectors changed from opaque-white to a brown-orange, see Figure 18, but this was equivalent between gamma and X-ray irradiated samples.

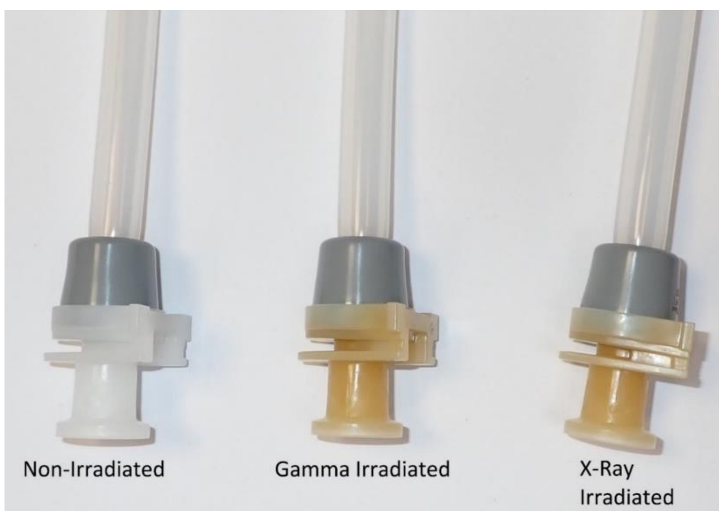


Figure 18: Visual comparison of Pumpsil® LoadSure® connectors.

5.1.8 Tubing Example (AdvantaFlex™ TPE)

TPE tubing samples were evaluated for color differences visually in comparison to non-irradiated, gamma and X-ray irradiated exposures. Little to no color difference was observed between X-ray and gamma irradiated tubing as shown (Figure 19).

Untreated X-ray Gamma

Figure 19: Visual observation and color of the APAF TPE tubing

5.1.9 Tubing Example (Liveo™ Pharma)

Silicone tubing variants catalyzed by platinum were evaluated for color difference visually in comparison to non-irradiated, gamma and X-ray irradiated exposures. Little to no color difference was observed for X-ray and gamma tubing samples as shown (Figure 20).

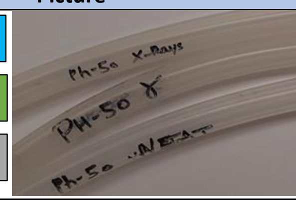
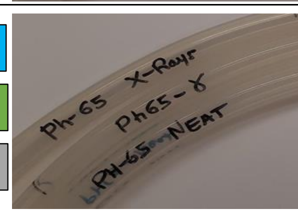
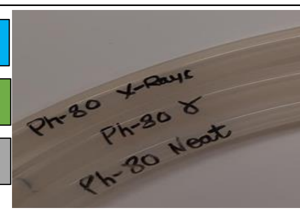
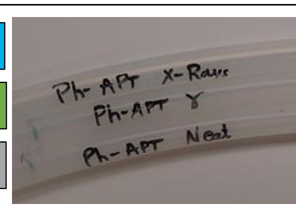
Material Sample	Results	Picture
Liveo™ Pharma 50 Silicone (Pt)	Minimal visual variation in color	X-Ray Gamma Non-irradiated 
Liveo™ Pharma 65 Silicone (Pt)	Minimal visual variation in color	X-Ray Gamma Non-irradiated 
Liveo™ Pharma 80 Silicone (Pt)	Minimal visual variation in color	X-Ray Gamma Non-irradiated 
Liveo™ Pharma Advanced Pump Tubing Silicone (Pt)	Minimal visual variation in color	X-Ray Gamma Non-irradiated 

Figure 20: Visual observation and color of the Liveo™ materials

5.1.10 Tubing Example (C-Flex 374)

Opacity and yellowness were measured on C-Flex® 374 following gamma and X-ray irradiation and compared to a control. The yellowness value of the tubing that was gamma irradiated was higher than the tubing that was X-ray irradiated as seen in the table below. A visual inspection was performed and there was little to no difference between the gamma and X-ray sample sets.

Table 21: Visual inspection of C-Flex 374 tubing

C-Flex® 374	Yellowness Index (Average of 10)	Standard Deviation (Sample set of 10)	Opacity (Average of 10)	Standard Deviation (sample set of 10)
Control	2.15	0.20	20.16%	0.52
Gamma	3.89	0.20	19.45%	0.54
X-ray	2.96	0.20	19.41%	0.37

5.1.11 Tubing Example (Sani-Tech® Ultra-C)

Opacity and yellowness were measured on Sani-Tech® Ultra-C following gamma and X-ray irradiation and compared to a control. The yellowness value of the tubing that was gamma irradiated was higher than the tubing that was X-ray irradiated as seen in the table below. A visual inspection was performed and there was little to no difference between the gamma and X-ray sample sets.

Table 22: Visual inspection of Sani-Tech tubing

Sani-Tech® Ultra-C	Yellowness Index (average of 10)	Standard Deviation (sample set of 10)	Opacity (average of 10)	Standard Deviation (sample set of 10)
Control	5.56	0.37	16.64	0.43
Gamma	6.20	0.26	16.81	0.49
X-ray	5.86	0.50	17.42	0.49

5.2 Differential Scanning Calorimetry (DSC)

Differential scanning calorimetry evaluated the heat flow characteristics in and out of the material as they heated and cooled. These assessments can provide insights into glass transition temperatures (Tg), melting temperature (Tm), degree of crystalline structure of the polymer, and thermal history.

In the examples below from different laboratories, various approaches are used for comparison and evaluation of the DSC curves, including visual inspection and overlay of the curves and/or evaluating calculated transition temperatures inferred from the curves.

5.2.1 Example (PREPS/PRESS Sensors)

Key transition points for PSU and PC are tabulated in Table 23 and an example of an overlay curve for the PC material shown in Figure 21. No discernable differences were observed in the glass transition temperature (Tg) between the control and the irradiated samples. Differences in numbers are related to extrapolation of the curves and points picked for analysis, every attempt was made to be consistent within the groups during analysis.

Table 23: Thermal transitions of the polysulfone and polycarbonate: control, gamma and X-ray irradiated samples

Sample	Polysulfone 2nd heat – Tg (inflection) (°C)	Polycarbonate 2nd heat – Tg (inflection) (°C)
Control	190.7	147.3
X-ray exposure	191.1	144.9
Gamma exposure	190.9	145.4

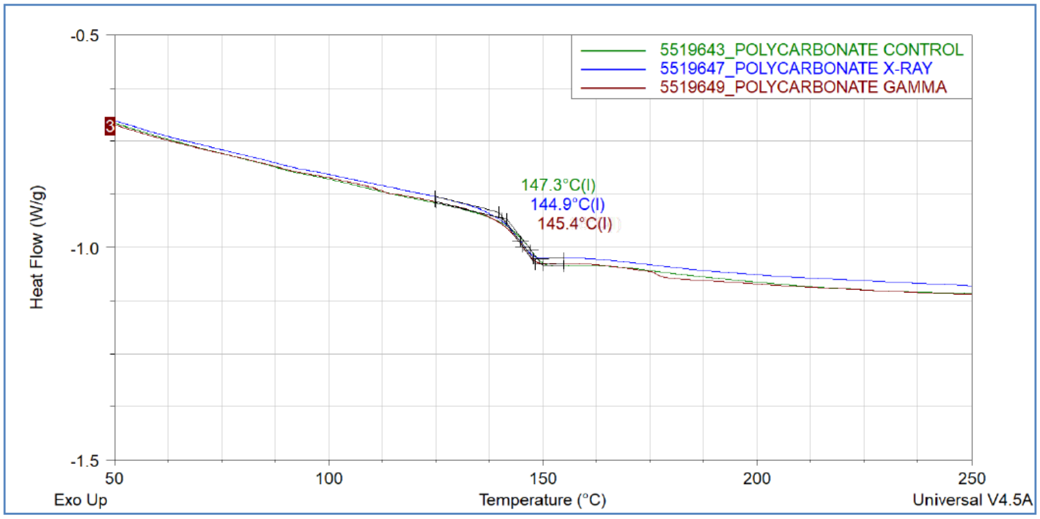


Figure 21: DSC thermograms of polycarbonate sensor material: control, gamma and X-ray irradiated

5.2.2 Example (Flexsafe® biocontainer)

An example of a thermogram for Flexsafe®' S80 film is displayed in the Figure 22. The average data obtained for the melting peak temperatures from 2nd heat of the S80 film according to different irradiation technologies and to different ageing are also displayed in Figure 22 and more detailed in appendix in Table 33. The data representing 3 years ageing is supplemental information. The melting peak temperature values of the samples either irradiated by Gamma or X-ray are distributed within the 5°C equivalence interval per statistical evaluation (i.e. per equivalency test performed with the Minitab® software). The thermal properties of the S80 film are equivalent after either irradiation by gamma or X-ray.

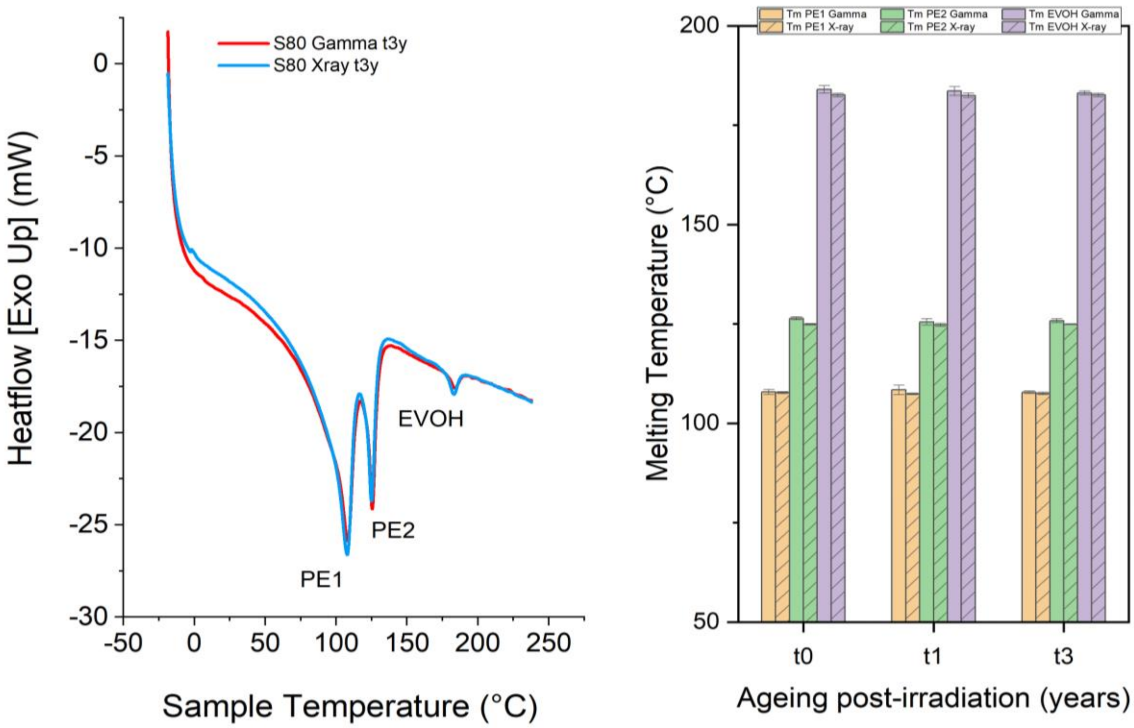


Figure 22: (left) Example of DSC thermograms (2nd heating) obtained for the S80 film after gamma and X-ray irradiation. (right) Melting temperatures of the materials of construction of the S80 film (PE1: yellow; PE2: green; EVOH: purple).

5.2.3 Example (Kleenpak™ filters)

Following irradiation, Kleenpak™ filters were sectioned, and the individual materials evaluated. DSC analysis, performed on each unique material of construction within the filter, was evaluated during the initial heating curve, followed by a cooling cycle, and then a secondary heating cycle thereby generating tremendous amounts of data characterizing the polymeric structure of each material. Figure 23 shows the first heating curve for a polypropylene filter support materials that enables uniform ingress and egress access of the filtered fluid to the filter membrane. This thermal analysis clearly shows changes to the melting behavior of the material upon irradiation. However, the thermal characteristics of the X-ray and gamma irradiated materials are identical. Hence for this material, DSC analysis was a powerful tool that readily detected changes to the polymer structure upon irradiation, and confirmed the same changes occurred regardless of X-ray or gamma.

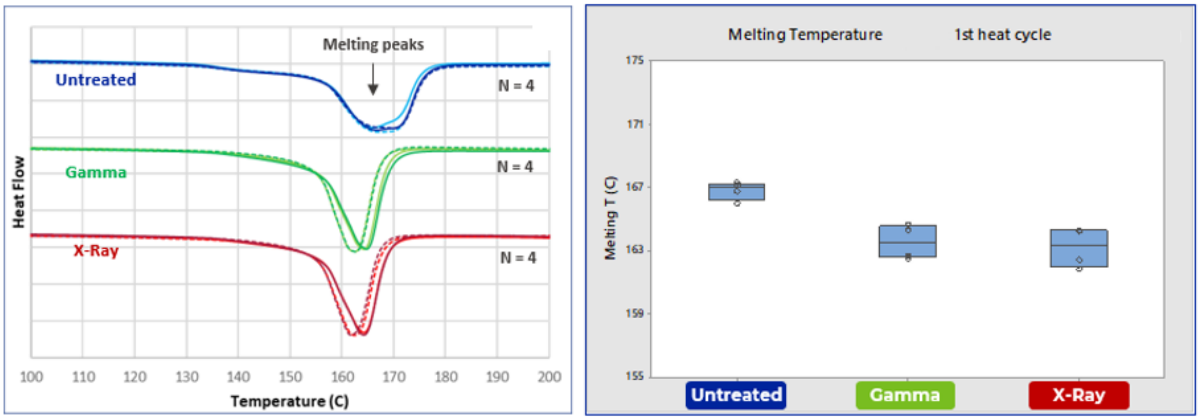


Figure 23: (left) First heating DSC curve for polypropylene filter support material for untreated(blue), gamma (green) and X-ray(red). Melting temperatures. (right) melting temperatures

5.2.4 Example (C-Flex® Tubing)

Plots collected as part of the DSC testing completed on all sterilization types of C-Flex® 374 are seen below in Figure 24 as well as the noted transition temperatures for each. The midpoint for the glass transition of each sterilization type falls approximately at the same temperature, regardless of sterilization type. No changes were observed to the glass transition behavior of C-Flex® 374 after either gamma or X-ray irradiation.

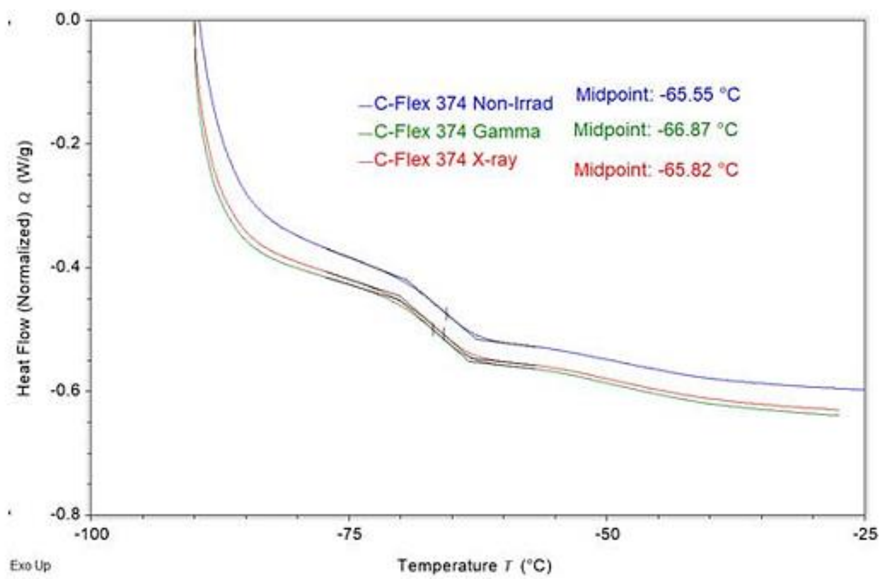


Figure 24: DSC of C-Flex® 374 Tubing

5.3 FTIR

Attenuated Total Reflectance-Fourier Transform Infrared Spectroscopy (ATR-FTIR) is a classic technique to characterize the infrared spectrum absorption by a polymer, which can be used to infer key characteristics of the chemical composition. Similar techniques have historically been used to verify the identity of polymers and to scout for extractables associated with the material.

5.3.1 Example (PREPS/PRESS Sensors)

FTIR spectra from the materials used in PendoTECH sensors are all consistent with typical PSU (Figure 25) and PC FTIR spectra (Figure 46, in appendix). PSU & PC X-ray exposure presented no significant functional group or structural changes that are measurable by FTIR inspection. PSU and PC gamma exposure presented no significant functional group or structural changes that are measurable by FTIR inspection.

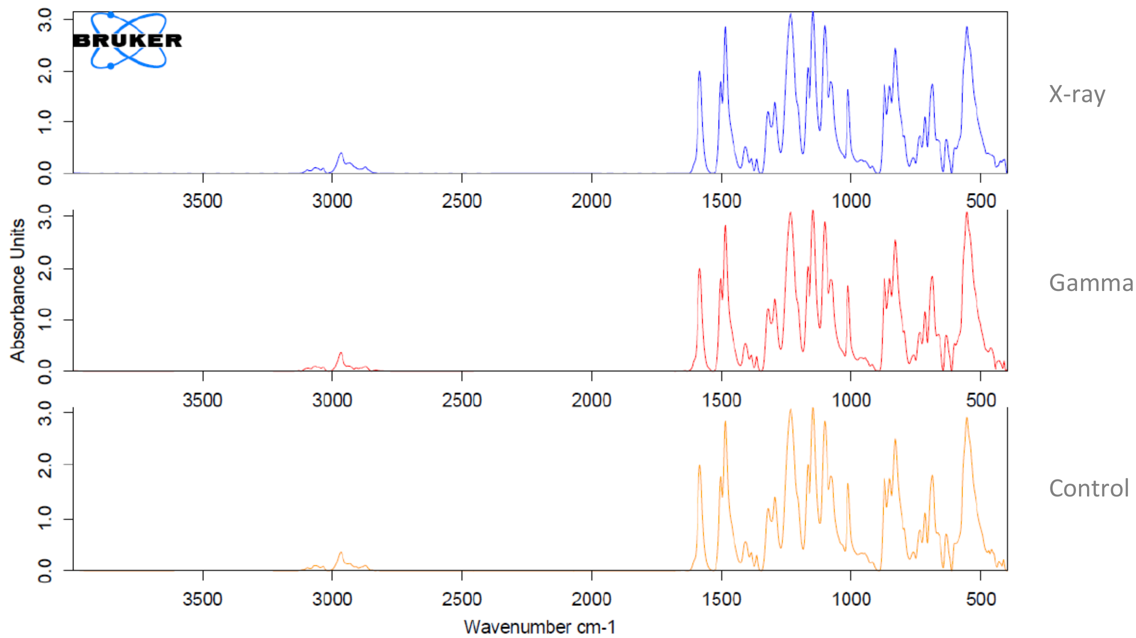


Figure 25: FTIR Spectra of PSU used in single use pressure sensors

5.3.2 Example (Flexsafe® biocontainer)

Figure 26 represents the FTIR spectra of the S80 film (Lot 1+Lot 2) after AsLS (asymmetric least squares) baseline correction and SNV (Standard Normal Variate) normalization using the SIMCA 17 software. Principal Component Analysis (PCA) on gamma and X-ray FTIR spectra reveals no difference due to the irradiation technologies. There is no peak appearance or disappearance on the spectra, and there is no shift of the main peaks. For the effect of irradiation technology, no trends were observed for X-ray in comparison to gamma irradiation.

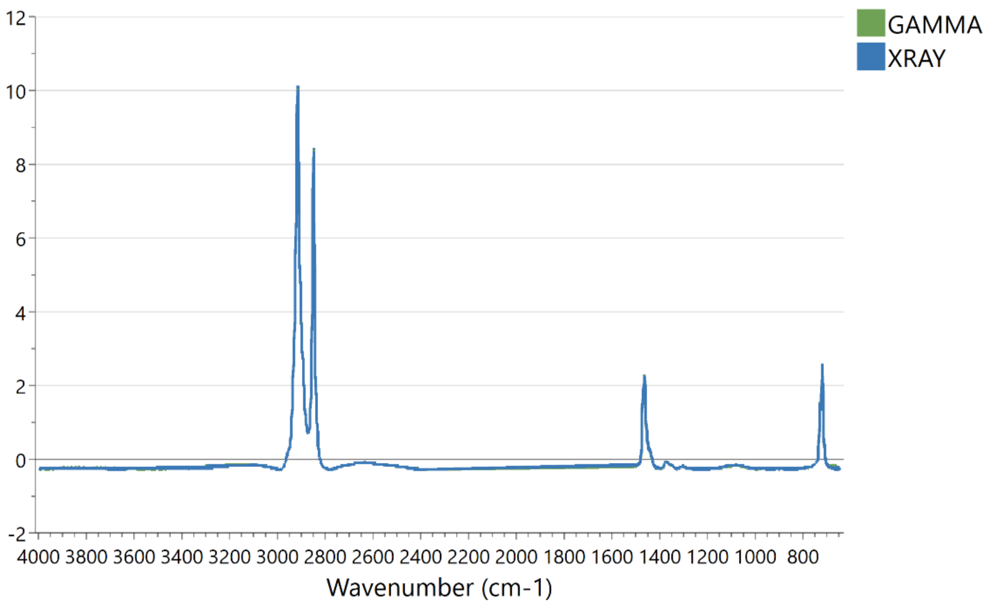


Figure 26: ATR-FTIR spectra for S80 film after AsLS (asymmetric least squares) baseline correction and SNV (Standard Normal Variate) normalization

5.3.3 Example (Lynx® S2S connector)

ATR-FTIR was conducted to show similarity of the main material of construction of the Lynx® S2S connector (polysulfone (PSU)), that has been treated with gamma and X-ray irradiation respectively. To show similarity ATR-FTIR tests were conducted on one female (Figure 27) and one male (Appendix Figure 43) Lynx® S2S lot. The ATR-FTIR results show there is no difference between gamma and X-ray treated polysulfone used to manufacture Lynx® S2S connectors.

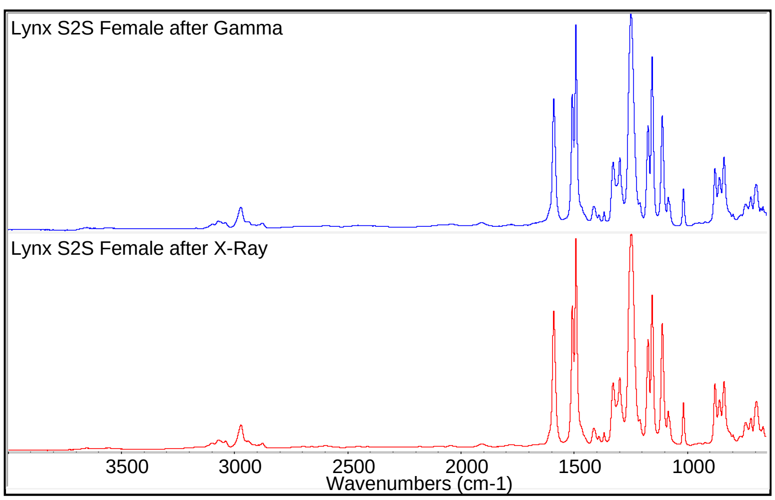


Figure 27: ATR-FTIR spectra on Lynx® connectors (female)

5.3.4 Example (Liveo™ tubing)

Silicone tubing [Pt] was characterized by ATR-FTIR to compare the effects of gamma and X-ray exposures. Testing of Liveo™ Pharma-50, Pharma-65, Pharma-80 and Pharma Advanced Pump Tubing did not identify any removal of nor creation of peaks.

5.4 Thermogravimetric Analysis (TGA)

5.4.1 Example (Lynx® S2S connector)

For Thermogravimetric Analysis (TGA) two approaches were conducted to show similarity of the main material of construction of the Lynx® S2S connector (polysulfone (PSU)) that has been treated with gamma and X-ray irradiation respectively. First the TGA mass and temperature measurements were plotted on top of each other and compared for the female (Figure 28) and male connectors (Appendix Figure 44). Second, the temperatures at 2 % weight loss were compared. Tests were conducted on one female and one male Lynx® S2S lot.

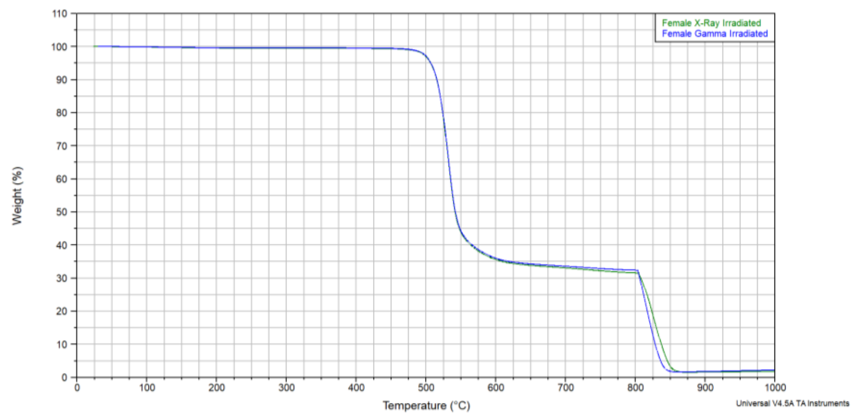


Figure 28: Thermogravimetric analysis of Lynx® S2S (female) connector. Heating 10 C/min.

Table 24: Thermogravimetric Analysis (TGA) results

Batch	Irradiation	Temperature at 2% weight loss (N=1) PASS / FAIL
Lot 1 Male – 2020120007	X-ray	494°C - Pass
Lot 1 Male – 2020120007	Gamma	495°C - Pass
Lot 1 Female – 2021020029	X-ray	494°C - Pass
Lot 1 Female – 2021020029	Gamma	495°C - Pass

Both approaches described the comparison of TGA plots as well as the comparison of the temperature at 2% weight loss suggest that there is no major difference between Gamma and X-ray treated polysulfone used to manufacture Lynx® S2S connectors

5.4.2 Example (PREPS/PREPS Sensor)

Several transition points are tabulated in

Table 25 and overlay curves for visual comparison are displayed for the PSU (Figure 29) and PC (Appendix Figure 47) sensor materials. We do not see any significant differences in rate of weight loss or degradation points between control and the irradiated samples. Differences in numbers are related to extrapolation of the curves and points picked for analysis, every attempt was made to be consistent within the groups during analysis.

*Table 25: Thermogravimetric Analysis (TGA) results of control,
X-ray irradiated, and gamma irradiated polysulfone and Polycarbonate used in pressure sensors*

Sample	Initial rate of weight loss (%/°C)	Degradation onset temperature (°C)	Degradation rate (%/°C)	Ash content at 800°C (%) in N_2	Final Residual content (%) in Air
Polysulfone (PSU) Control	-0.0008	505.7	-1.674	34.0	0.7080
PSU X-ray exposure	-0.0010	507.0	-1.613	34.1	0.6117
PSU gamma exposure	-0.0011	505.6	-1.605	33.1	0.6635
Polycarbonate (PC) control	-0.0030	484.0	-1.667	21.1	0.5598
PC X-ray exposure	-0.0054	490.0	-1.839	22.1	0.5595
PC gamma exposure	-0.0041	485.6	-1.755	21.8	0.6708

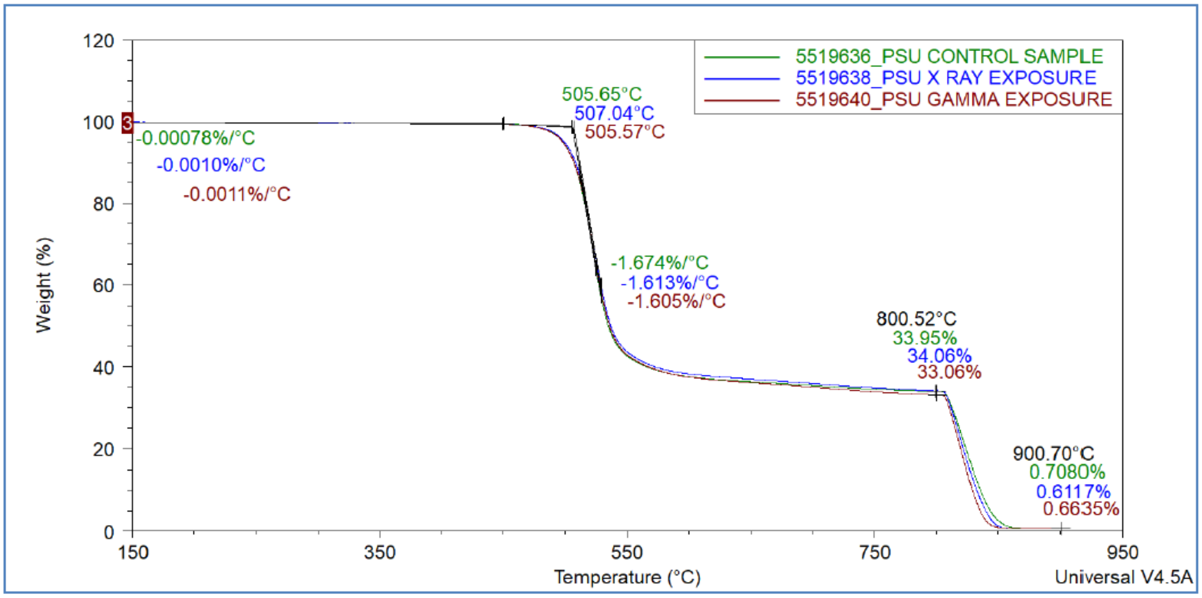


Figure 29: TGA curves of PSU sensor material

5.5 Mechanical Evaluation of Materials

5.5.1 Durometer

Durometer is a measurement of hardness that is often performed on elastomeric materials.

(1) AdvantaFlex™ (TPE) Tubing

Shore hardness A is measured via a durometer and characterizes the penetration hardness of materials such as rubbers and elastomers. Samples of X-ray (n=5) and gamma (n=5) irradiated materials were evaluated for hardness in accordance with ASTM D2240 with the results shown in Figure 30. Values were within the expected ranges from the manufacturer and the were no meaningful differences between X-ray and gamma irradiated samples. Regarding shore hardness, both X-ray and gamma irradiated samples appeared equivalent.

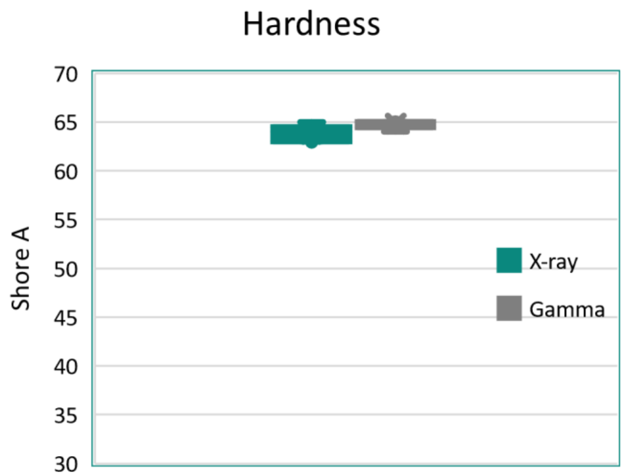


Figure 30: Hardness (Shore A) properties of X-ray (blue) and gamma (orange) irradiated TPE tubing samples.

(2) C-Flex® 374 (TPE) Tubing

The durometer of C-Flex® 374 was measured on 10 samples after gamma and X-ray irradiation. The results demonstrate equivalence between samples that were gamma and X-ray irradiated. As seen in the Table 26, the durometer of C-Flex® 374 decreases with both gamma and X-ray irradiation. The results suggest an equivalence between gamma and X-ray irradiation.

Table 26: Durometer of C-Flex® 374

Batch	Shore A Durometer	Standard Deviation (Sample set of 10)
C-Flex® 374 – Control	55	0.28
C-Flex® 374 – Gamma	53	0.43
C-Flex® 374 - X-ray	53	0.51

(3) Sani-Tech® Ultra-C (Pt. Cured silicone) Tubing

The durometer of Sani-Tech® Ultra-C was measured on 10 samples after gamma and X-ray irradiation. The results demonstrate equivalence between samples that were gamma and X-ray irradiated. As seen in the Table 27, the durometer of Sani-Tech® Ultra-C increased after both gamma and X-ray irradiation, typical of silicone materials due to cross-linking.

Table 27: Durometer of Sani-Tech® Ultra-C

Batch	Shore A Durometer	Standard Deviation (Sample set of 10)
Sani-Tech® Ultra-C – Control	47	0.74
Sani-Tech® Ultra-C – Gamma	52	0.53
Sani-Tech® Ultra-C - X-ray	50	0.12

(4) Liveo™ (Pt. Cured silicone) Tubing

Durometer (Shore A) ASTM D2240 measurements were performed on non-irradiated, gamma irradiated, and X-ray-irradiated materials, and measures plotted relative to non-irradiated values (Figure 31).

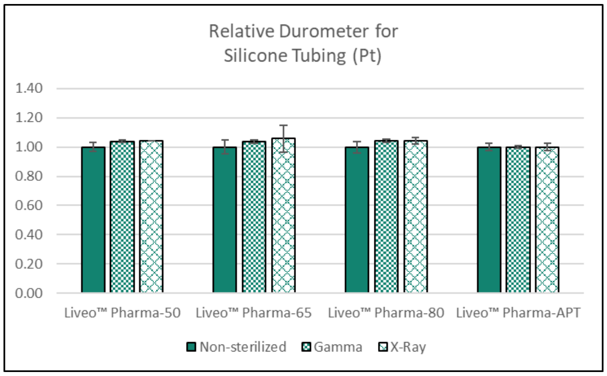


Figure 31: Relative durometer of the Liveo™ Silicone tubing.

(5) Pumpsil®, Bioprene®, PureWeld® Tubing

Five samples of each tubing product were treated as follows: non-irradiated, gamma irradiated, and X-ray irradiated. Furthermore, the tests were conducted at two aging points: unaged and aged to five-years equivalence according to ASTM F1980-21. Aging data are regarded as supplemental. The hardness tests showed that the irradiation type had an equivalent effect on the hardness of the tube material, see Figure 32. The average results were all comparable between gamma and X-ray and the standard deviations of the data were very similar.

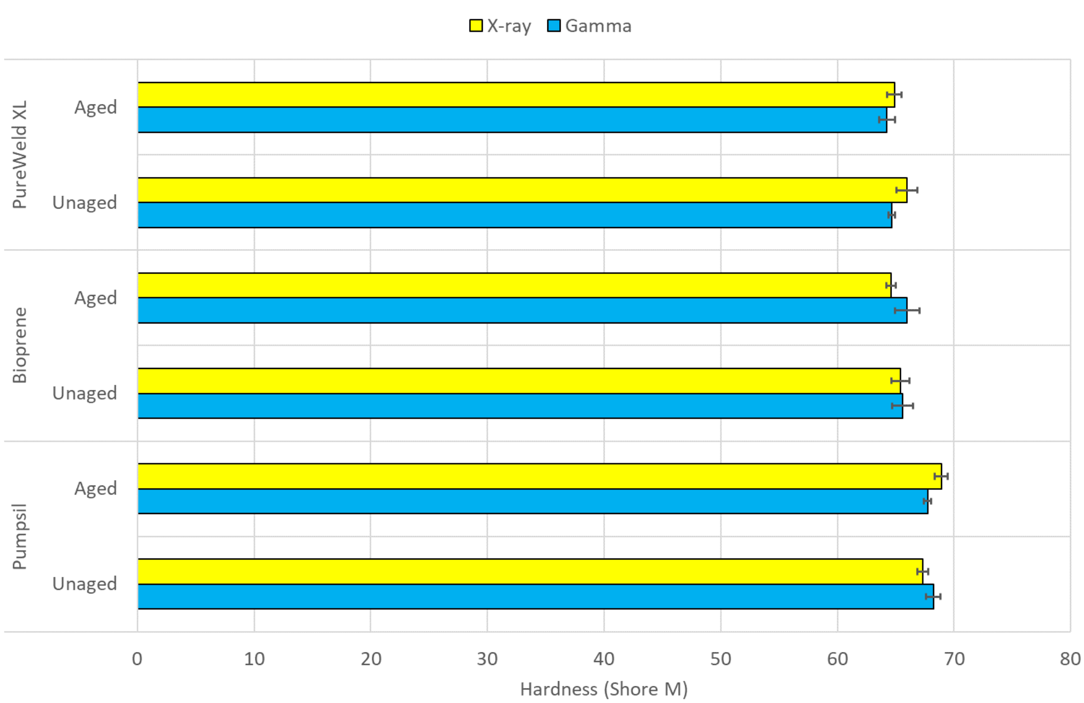
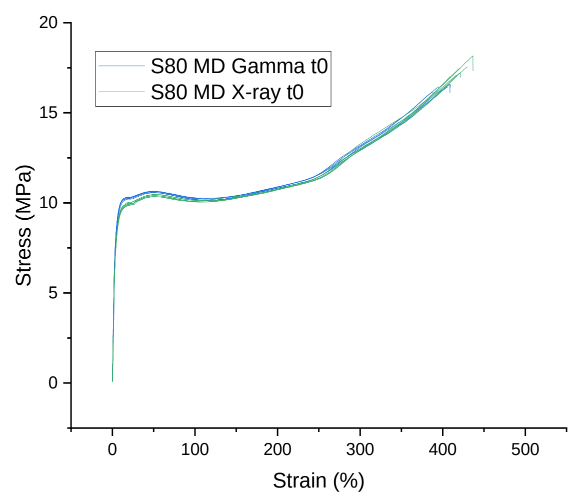


Figure 32: Bar chart of the hardness results in Shore M for unaged, and aged (supplemental) samples. (error bars show one standard deviation).

5.5.2 Tensile strength

(1) Example (Flexsafe® biocontainer)

The stress-strain curves of the S80 film in both directions (MD, machine direction; TD, transverse direction) follow the same behavior for materials either gamma or X-ray irradiated (example in MD in Figure 33). The statistical evaluation shows that UTS and elongation at Fmax data for samples either irradiated by Gamma or X-ray are within the equivalence interval defined with equivalency criteria (35% for UTS Ultimate tensile stress and 25% for the elongation at Fmax) and calculated with Minitab® software (TOST (two one-sided t-tests) equivalency testing[7]). Equivalence can be claimed on those properties as per statistical evaluation and as per polymer viewpoint.



	Elongation at Fmax (%)		Ultimate tensile stress (UTS) (MPa)	
	Gamma	X-ray	Gamma	X-ray
Mean µ	436±32	435±16	17.1±0.7	17.6±0.5
Ratio μ_{Xray}/μ_{Gamma}	0.99		1.03	
Equivalence test outputs	Can claim equivalency		Can claim equivalency	

Figure 33: (left) Stress-strain curves for S80 film in machine direction (MD) (t0) – (right) Elongation at Fmax and ultimate tensile stress (UTS) results

(2) Example (AdvantaFlex™ TPE tubing)

The tensile properties of gamma and X-ray irradiated tubing samples were evaluated in accordance with ASTM D412 Die D. The modulus at 50% elongation (M50), 100% elongation (M100), and 300% elongation (M300) were evaluated as well as the tensile strength (psi) and ultimate elongation (%). Due to variation in the measurement, n=10 gamma- and n=10 X-ray- irradiated samples were employed. Results for the initial elongation modulus (M50<n) tensile strength, and ultimate elongation are shown in Figure 34 and indicate no differences between the X-ray and gamma irradiated samples. Regarding tensile and elastic properties, the X-ray and gamma irradiated samples appear equivalent.

[7] Equivalence test approach is provided in following links: Equivalence Testing for Quality Analysis (Part I): What are You Trying to Prove? (minitab.com) and Equivalence Testing for Quality Analysis (Part II): What Difference Does the Difference Make? (minitab.com)

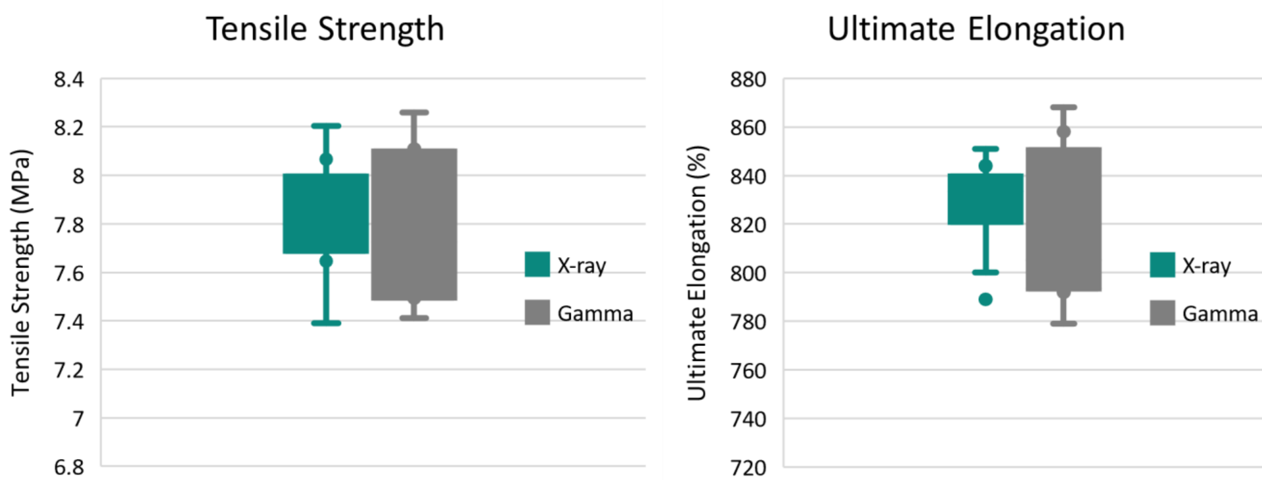


Figure 34: Tensile properties of X-ray (blue) and gamma (orange) irradiated TPE tubing samples.

(3) Example (C-Flex® 374 TPE Tubing)

Tensile Strength and Elongation was measured on 10 samples of C-Flex® 374 after gamma and X-ray irradiation. The results demonstrate equivalence between samples that were gamma and X-ray irradiated.

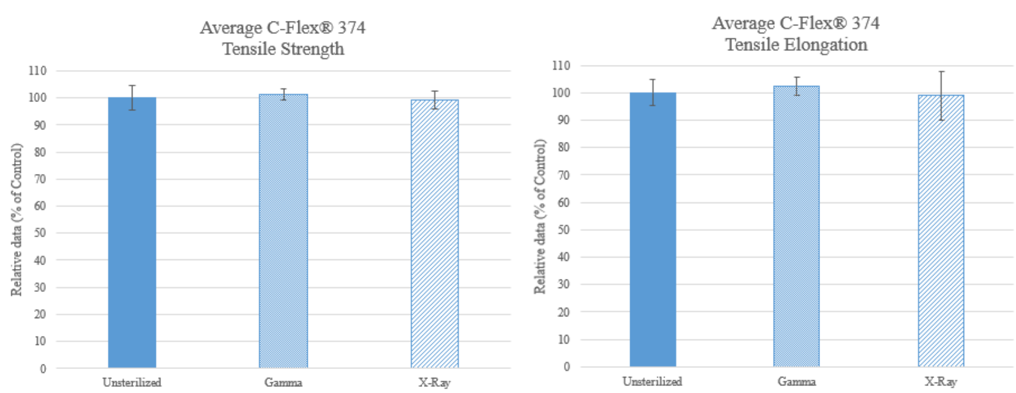


Figure 35: C-Flex® 374 Tensile Strength and Elongation

(4) Example (Liveo™ Tubing)

Cured physical properties of the raw materials used to make each silicone tubing were characterized by measurement of Tensile and Elongation at Break following ASTM D412 (Figure 36). The small sample size and variability of the test methods in some cases resulted in wider distributions of data. From these data, the measured differences between gamma and X-ray exposed samples were not meaningful.

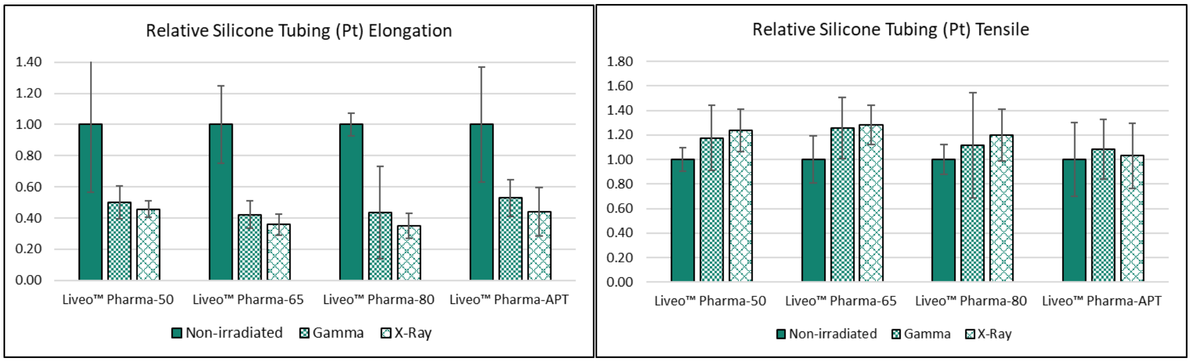


Figure 36: Tensile and elongation at break properties of Liveo™ tubing following irradiation.

5.6 Crosslink Density *(supplemental)*

The cross-linking density is obtained as example on Sanitech Ultra-C Tubing by calculating Mc, the number average molar mass of elastically effective chains between cross-links. A higher value of Mc corresponds to a less cross-linked network. Sani-Tech® Ultra-C experienced an increase in crosslink density after both gamma and X-ray irradiation. As seen in the Figure 37, the effect of gamma and X-ray on the cross-link density was very similar and occurred at almost the same amount. After irradiation, Ultra-C had a 23% increase in crosslink density.

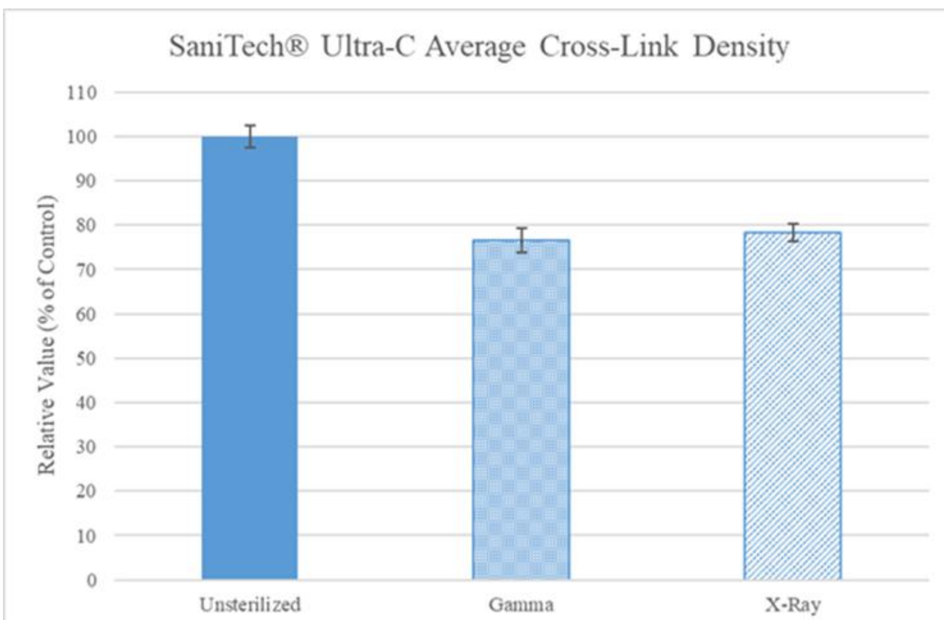


Figure 37: Sani-Tech® Ultra-C relative average cross-link density

5.7 Tear Strength

5.7.1 Example (AdvantaFlex™ Tubing)

Tear strength of thermoset rubbers, elastomers and silicones can be evaluated by ASTM D624, which measures the force per unit thickness required to rupture or start to tear through the sample. N=10 determinations were performed for the gamma- and X-ray irradiated TPE materials. The tear resistance values for X-ray and gamma irradiated materials were overlapping (Figure 38), with both gamma and X-ray samples appearing equivalent.

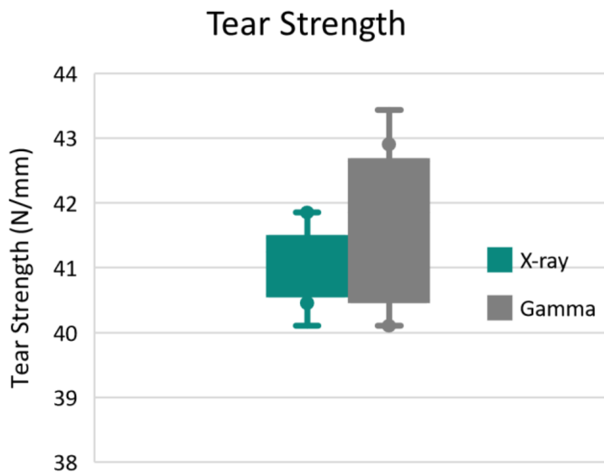


Figure 38: Tear strength properties of X-ray (blue) and gamma (orange) irradiated TPE tubing samples.

5.7.2 Example (C-Flex® 374 Tubing)

Tear strength measures a material's resistance to propagation of a rip or tear once the rip has been initiated. This test is important for rubber and TPEs as they often fail in service due to a rip or tear. As seen below in Figure 39, similar behavior was witnessed after tear resistance testing. Statistical analysis done comparing the tear resistance of the three sterilization types showed no significant difference.

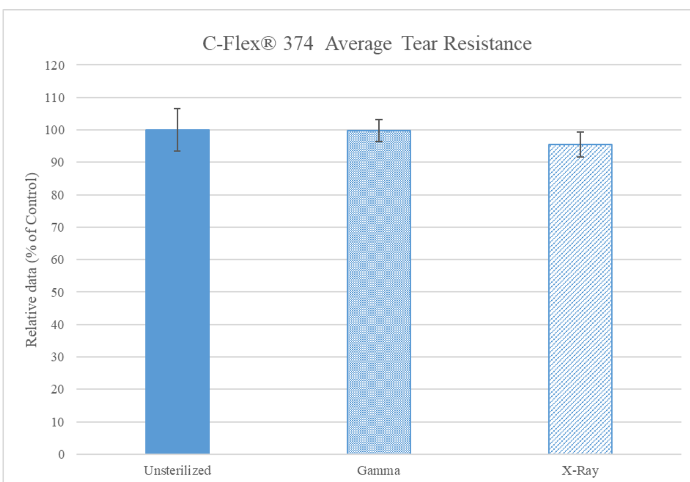


Figure 39: C-Flex® 374 relative average tear resistance results

5.7.3 Example (Liveo™ Tubing)

Tear strength as measured by ASTM D624 was assessed on untreated, X-ray, and gamma irradiated tubing with values reported relative to the non-irradiated tubing (Figure 40). The sample size and variability of the test methods in some cases resulted in wider distributions of data, and the measured differences between gamma and X-ray exposed samples were not meaningful.

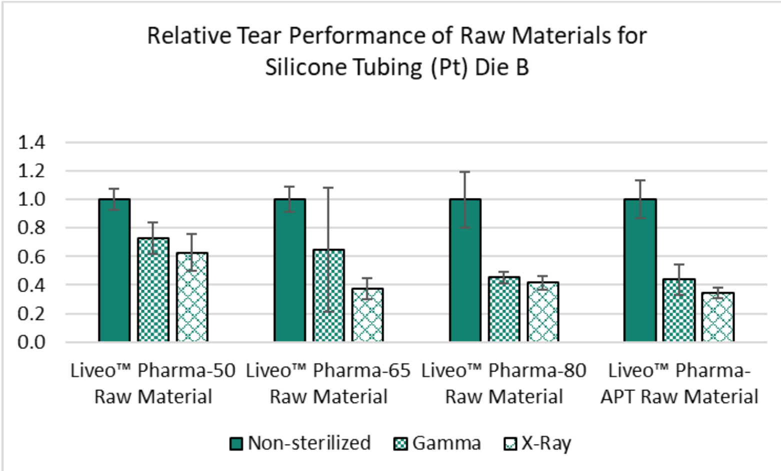


Figure 40: Tear resistance of raw materials for silicone tubing

5.8 Compression Set Testing

5.8.1 Compression Set Testing (C-Flex® 374 Tubing)

Compression set measures the residual deformation after compressive loading under specified conditions. Compression set testing was performed on 10 tubing samples of C-Flex 374® tubing after gamma and X-ray irradiation. The results demonstrate equivalence between samples that were gamma and X-ray irradiated. It is typical for C-Flex® 374 to decrease in compression set % following irradiation. Figure 41 displays the average of the 10 samples from each testing group.

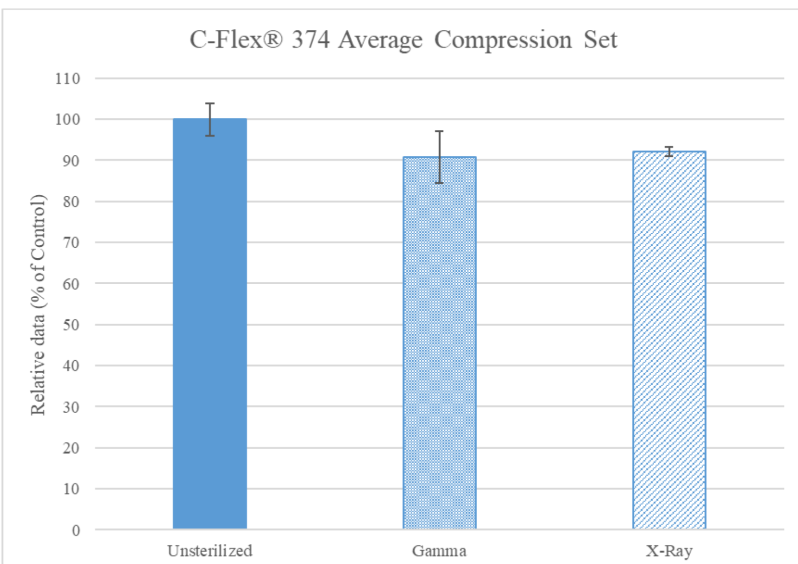


Figure 41: C-Flex® 374 relative average compression set results

5.8.2 Example (Liveo™ tubing)

Compression set testing was performed on non-irradiated, gamma, and X-ray-irradiated samples according to ASTM D395 with values reported relative to the non-irradiated sample (Figure 42). Based on the sample size and variability of test methods, any differences between gamma and X-ray exposed samples were not meaningful.

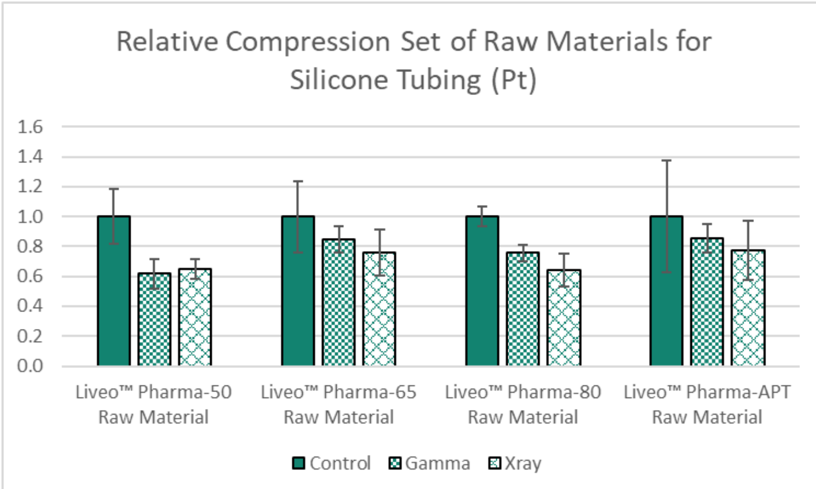


Figure 42: Compression set testing of Liveo tubing materials

6 Biological Tests

6.1 Example (PREPS and PRESS Sensors)

The risk analysis identified sensors to be low risk for biological and chemical testing as they typically contribute very little to the overall surface area of a single-use assembly. However, as a precaution and to generate representative data for the industry, testing was still performed. An *in vitro* biological reactivity test following the guidelines of ISO 10993-5 was completed. All materials were within the requirements considered to not have a cytotoxic effect.

6.2 Example (Flexsafe® Biocontainer)

These studies were conducted to evaluate X-rays and gamma irradiated S80 for potential cytotoxic effects following the guidelines of ISO 10993-5, Biological Evaluation of Medical Devices, Part 5: Tests for In Vitro Cytotoxicity. Results show no cytotoxic potential to L-929 mouse fibroblast cells. X-rays and gamma irradiated S80 films are compliant to the ISO 10993-5 norm.

6.3 Example (Liveo™ Pharma tubing)

The raw materials used to make Liveo™ Pharma-50, Pharma-65, Pharma-80 and Pharma Advanced Pump Tubing were evaluated in duplicate testing by DuPont internal method of direct contact tissue culture following exposure to gamma and X-ray irradiation. The biocompatibility of a material by this method is evaluated by placing a portion of it in direct contact with human embryonic cells. Cytopathic Effect (CPE) is evaluated after a 24 h incubation period. The results of a test are evaluated microscopically against both a positive and negative control. The material being tested is reported as either "Pass" (not producing a cytopathic effect) or "Fail" (producing a cytopathic effect). All Liveo™ Pharma Tubing raw materials passed these tests.

Additional characterization of gamma and X-ray exposed Liveo™ Pharma-50 and Pharma Advanced Pump Tubing by ISO 10993-5 Biological Evaluation of Medical Devices, Part 5: Tests for In Vitro Cytotoxicity was completed and showed no cytopathic effect in any sample tested.

6.4 Example (C-Flex® 374 Tubing (TPE) and Sani-Tech® Ultra-C Tubing (Pt. Cured Silicone))

Biological Reactivity in vitro testing was performed on gamma and X-ray irradiated C-Flex® 374 and Sani-Tech® Ultra-C tubing using the USP <87> MEM Elution method. Results show that neither sample set show cytotoxic potential to L-929 mouse fibroblast cells. Both gamma and X-ray irradiated C-Flex® 374 tubing and both gamma and X-ray irradiated Sani-Tech® Ultra-C Tubing (Pt. Cured Silicone) meet the requirement of the USP <87> of a less than or equal to grade 2 (mild reactivity).

6.5 Example (Kleenpak™ Filter Capsule)

Biological reactivity testing was performed on X-ray irradiated Kleenpak™ PES filter capsules in accordance with the USP <87> MEM elution test. For some evaluations, individual materials of construction of the filter were separated and tested individually. Testing results met the acceptance criteria for USP <87>.

7 Assembly Integrity

An assessment of single-use system integrity, which may leverage much of the testing herein, is critical to the overall risk evaluation. Such assessments often include evaluation by proprietary manufacturer-specific methods that test the strength and integrity of junctions, such as hose barb to tubing connections (see fastener testing example under connectors).

In one case, x-ray irradiated junctions between components, which are normally grouped into material families and tested to demonstrate suitability for use post gamma, were grouped into larger master families with testing performed on representative worst-case junctions (e.g. tubing diameter, wall thickness, material type, etc.) to demonstrate the junctions met pre-established acceptance criteria or exhibited equivalent performance to gamma irradiated junctions. In these cases, there were no observable trends reported where specific types of X-ray irradiated materials or junction types performed worse following X-ray as compared to gamma.

In addition to evaluation of junctions, a general assessment may also be made on non-fluid contact materials and the integrity of the overall single-use primary and secondary packaging.

8 Conclusions, Next Steps, and Other Considerations

Whereas the 2021 BPSA whitepaper on X-ray qualification for single-use focused on the industry need, risk assessment, and testing recommendations, the goal of this paper is to share representative data covering a broad range of materials from different component suppliers. The data shared on the materials evaluated herein, considering variations due to preparation and testing methodologies, have shown equivalent attributes as compared to gamma. The case evaluations detailed in this paper also reflect multiple types of testing, data presentation and ways to evaluate the results. Moreover, a review of multiple datasets, from different components, materials, and suppliers, offers a robust holistic perspective as to the impact of X-ray on materials in general as compared with a myopic examination of strengths and weaknesses of any one particular dataset.

In addition to the materials and component qualification supporting X-ray, other evaluation criteria have been openly shared within the BPSA working group but were outside the scope of this data-based review.

- Dose mapping studies are well-described in ISO11137 and are to be coordinated by the SUS integrator for each unique irradiation site to verify the dose received for their product during routine manufacturing is between the minimum and maximum dose.
- Sterility dose audits, also well described in ISO 11137 are also expected to be performed by the integrator to demonstrate the continued effectiveness of the ionizing irradiation process over time.

Together the data and assessments described herein all verify the understanding that X-ray, when implemented in accordance with ISO 11137, results in an equivalent impact to single-use materials as gamma, with no reports of adverse effects resulting from X-ray as compared to gamma irradiation.

9 Appendix

9.1 Further information on supporting data

For questions or further information related to the supporting data in this document, please see the contact links indicated in the table below.

Component	Name	Further Information
Biocontainer	Flexsafe® bag (S80 film)	Changenotification_AB@sartorius.com
Connector	Lynx® S2S	Monica.Cardona@milliporesigma.com Timo.A.Neumann@merckgroup.com pstechservice@milliporesigma.com
Connector	AseptiQuik® AQG	maria.bollensen@cpcworldwide.com cpcbio@cpcworldwide.com
Filter	Kleenpak™ EKV Capsule	www.pall.com/en/biotech/regulatory/regulatory-dossier.html https://www.cytivalifesciences.com/en/us/support/quality/regulatory-support
Sensor	PendoTECH Single Use Pressure Sensor™	Nick.troise@pendotech.com requests@pendotech.com
Sensor	BroadleyJames pH Sensor	cfeng@broadleyjames.com
Tubing	Pumpsil® Bioprene® Pureweld® XL	Nicole.Hunter@wmfts.com Jim.Sanford@wmfts.com
Tubing	AdvantaFlex™ APAF	compliance@newageindustries.com
Tubing	Liveo™ Pharma Tubing	https://www.dupont.com/liveo/contact-us.html
Tubing	C-Flex® 374 Tubing	Gabrielle.McIninch@saint-gobain.com
Tubing	SaniTech® Ultra-C Tubing	Gabrielle.McIninch@saint-gobain.com

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Trademark	Company
Liveo™	Dupont
Kleenpak™, Supor®	Cytiva
Flexsafe®, Flexel®, Flexboy®	Sartorius
AdvantaFlex™	NewAge Industries
C-Flex® Sani-Tech®	Saint-Gobain
AseptiQuik®	CPC (Colder Products Company)
Lynx® S2S	MilliporeSigma
PendoTECH Single Use Pressure Sensors™	PendoTECH
Pumpsil®, Bioprene®, PureWeld® XL	Watson-Marlow Fluid Technology Solutions

10 Supplemental Component Data

10.1 Connectors Supplemental Data

10.1.1 Lynx® S2S Connector

General information is provided in Table 28.

Table 28: Supplier Report Template

BPSA X-ray Compatibility Assessment - Supplier Report Template	
Controlled Document Identifier:	Customer Summary Report 20727528
Revision:	4.0
Date:	29/11/2022
Author:	Timo Neumann
Suppllier Information	Name: MilliporeSigma
	Address: 400 Summit Drive, Burlington, MA 01803, USA
	Email : Monica.Cardona@milliporesigma.com; Timo.A.Neumann@merckgroup.com ; pstechservice@milliporesigma.com
What is covered by the assessment?	Description of Components Assessed: Lynx® S2S ½ inch; female coupling, Lynx® S2S ½ inch; male coupling
	Component Part Number Assessed: SSCFHB2A24, SSCMHB2A24
	Component Family Addressed (or rationale for coverage): Lynx® S2S product family; same materials of construction
	Materials of Construction: PSU, Silicone
	Maximum Irradiation Dose Evaluated: 45 kGy - 60 kGy
Executive Summary, Rationale and Conclusion	A direct comparison study post X-ray and post gamma between Lynx® S2S connectors was performed.
	The results of these studies demonstrate that there is no difference in the performance of devices between the gamma irradiated and the X-Ray irradiated product.
	In the case that only post X-ray material was tested all results were according to specification.
Quality Approval:	Thomas Brackett

Extractables summary parameters for Lynx® S2S connectors are summarized in Table 29.

Table 29: Summary of part numbers and extraction conditions.

Test Article	Lynx® S2S Connector
Number of Test Articles	Two (2) post gamma irradiation of two (2) solvents compared to two (2) post X-ray samples per each of two solvents = total of eight (8) test specifications
Pre-Change Component	
Component Part Number	SSCFHB2A24, SSCMHB2A24
Lot Number	SSCFHB2A; 2021020029 and 2021020031 post gamma SSCMHB2A; 2020120007 and 2021020020 post gamma
Post-Change Component	
Component Part Number	SSCFHB2A24, SSCMHB2A24
Lot Number	SSCFHB2A; 2021020029 and 2021020031 post X-ray SSCMHB2A; 2020120007 and 2021020020 post X-ray
Pre-Treatment (If applicable)	
Gamma Irradiation	45 – 60 kGy Target. Actual dose 46.5 kGy – 49.9 kGy
X-ray Irradiation	45 – 60 kGy Target. Actual dose 51.7 kGy – 56.2 kGy
Pre-Flush	None (Represents Worst-Case)
Extraction Conditions	
Temperature	40 °C
Time between Sterilization Method & Extraction	< 8 weeks
Extraction Time	24 hours
Total Devices Pooled	16
Solvent Volume (mL)	~12 mL per connector
Conditions	Orbital rotation (50 rpm)

TOC is a test to measure the cleanliness of a component. The organic compounds in the extract solution are oxidized and converted to carbon dioxide. The amount of carbon dioxide detected is converted to a carbon concentration. Results are reported as mg C/component. Only aqueous extracts are tested for TOC.

The TOC results for Lynx® S2S post gamma and post X-ray are comparable. In average TOC results of X-ray irradiated Lynx® S2S connectors are averaged to be 10% lower than Gamma irradiated connectors.

Water extracts of Lynx® S2S connectors were also evaluated using TOC and demonstrated no increase in extractables associated with X-ray. All results are in µg per device.

Table 30: TOC evaluation of water extracts

Solvent	Lynx® S2S						
	Gamma			X-ray			
	Lot 1	Lot 2	Average	Lot 1	Lot 2	Average	%D
Water	33.5	32.1	32.8	30.5	28.2	29.4	-10%

FTIR spectra of Lynx® S2S male connectors following gamma and X-ray.

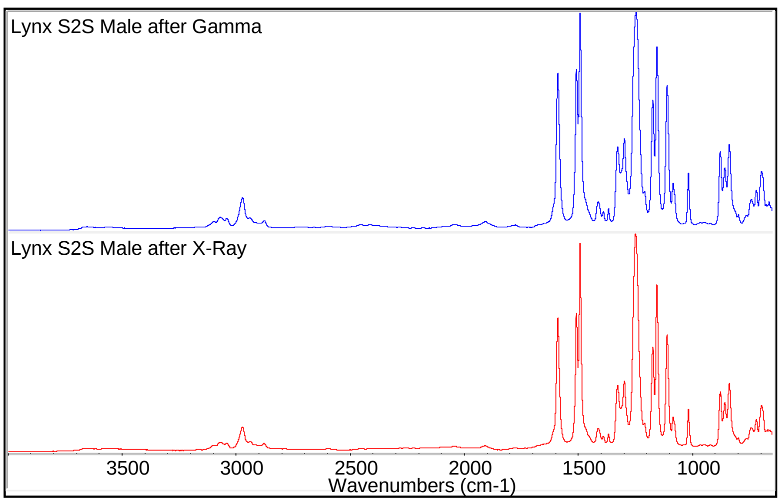


Figure 43: FTIR-ATR spectra on Lynx® S2S connectors (male)

Thermogravimetric analysis (TGA) of Lynx® S2S male connector.

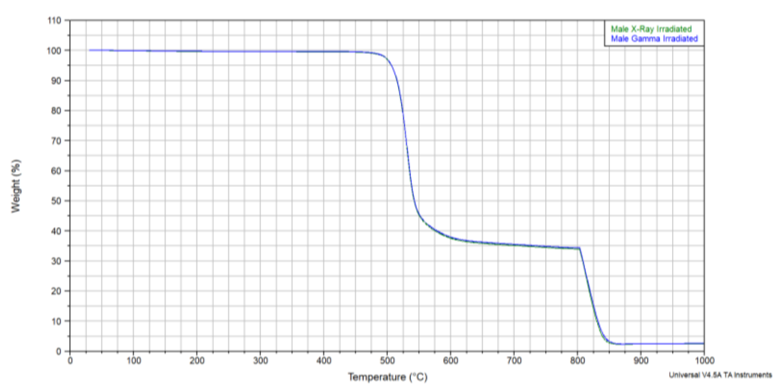


Figure 44: Thermogravimetic analysis of Lynx® S2S (male) connecter. Heating 10°C/min

10.1.2 AseptiQuik® (AQ) Connectors

The table below highlights AQG product lines represented by the connector X-ray qualification study.

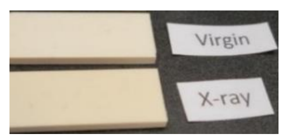
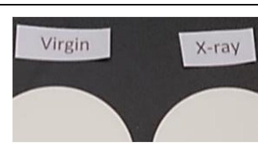
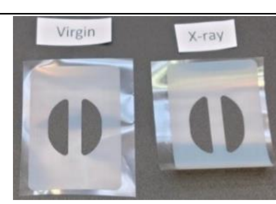
Table 31: Overview of representative part numbers evaluated to support assessment of each product line.

CPC Part Number	Description
AQG17008	½ HB AQG, SAMP
AQG17008HT	½ HT AQG HT, SAMP
AQG17108	½ HB AQG PPSU, SAMP
N/A	White Polycarbonate Sample
N/A	White Polyphenylsulfone Sample
3349200	Seal, AseptiQuik® AQG
3059300	Membrane, PE, Large Format AseptiQuik®
3059400	Membrane, PES, AQX
3402600	Slider, AQX

Note that SAMP parts are considered equivalent to standard production in this case.

Visual inspection of the connector materials demonstrated no abnormal observations.

Table 32: Visual inspection of key connector materials comparing non-irradiated (virgin) to X-ray

Material Sample	Results	Picture
PC	Minimal visual variation in color	
PPSU	Minimal visual variation in color	
Silicone Seal	No visual variation of color	
PE Membrane	No visual variation of color on each side of membrane	 
PES Membrane	No visual variation of color on each side of membrane	 
Slider for PES Membrane	No visual variation of color	

10.2 Flexsafe® Biocontainers Supplemental Data

The Table 33 gathers the average data obtained for the melting peak temperatures of the S80 film according to different irradiation technologies and to different ageing. The melting peak temperature values of the samples either irradiated by Gamma or X-ray are distributed within the 5°C equivalence interval. The thermal properties of the S80 film are equivalent after irradiation either by gamma or X-ray.

Table 33: DSC average data of S80 on its melting temperature (Tm)

Ageing	PE 1 Tm (°C)		PE 2 Tm (°C)		EVOH Tm (°C)	
	Gamma	X-ray	Gamma	X-ray	Gamma	X-ray
t0	107.9±0.6	107.7±0.3	126.4±0.4	124.9±0.2	184.0±0.9	182.6±0.4
t1	108.4±1.2	107.4±0.2	125.5±0.8	124.8±0.4	183.6±1.1	182.5±0.6
t3	107.8±0.3	107.5±0.3	125.8±0.5	124.9±0.1	183.1±0.5	182.6±0.4

[1]t0 = freshly after irradiation (Batch 1 + Batch 2) | [2]t1 = 1 year (Batch 1+Batch 2) | [3]t3 = 3 years (Batch 1 + batch 2)

10.3 Sensors Supplemental Data

10.3.1 PendoTECH Single-Use Pressure Sensors™ (PREPS and PRESS)

Detailed physical leak and burst testing results indicated equivalence of X-ray and gamma.

Table 34: Leak and Burst Test Results of PREPS and PRESS sensors Post X-ray

Part Number	Lot Number	Serial Number	Initial Pressure (psi)[1]	Final Pressure (psi)	ΔP	Pressure Decay (psi/sec)
PREPS-N-025	1191570	29	62.24	62.21	0.03	0.0003
PREPS-N-025	1191570	28	62.51	62.46	0.05	0.0006
PREPS-N-025	1191570	27	61.63	61.60	0.03	0.0003
PREPS-N-025	1191570	32	60.88	60.85	0.03	0.0003
PREPS-N-025	1191570	30	62.25	62.18	0.07	0.0008
PREPS-N-025	1191570	26	61.35	61.33	0.02	0.0002
PREPS-N-025	1191570	31	62.20	62.13	0.07	0.0008
PRESS-S-000	1210050	33	62.26	61.50	0.76	0.0084
PRESS-S-000	1210050	32	61.58	60.76	0.82	0.0091
PRESS-S-000	1210050	31	63.05	62.31	0.74	0.0082
PRESS-S-000	1210050	29	62.29	61.49	0.8	0.0089
PRESS-S-000	1210050	26	62.92	62.02	0.9	0.0100
PRESS-S-000	1210050	27	62.04	61.20	0.84	0.0093
PRESS-S-000	1210050	28	61.27	60.65	0.62	0.0069
PRESS-S-000	1210050	30	61.72	60.97	0.75	0.0083
PREPS-N-000	1203163	41	63.29	63.00	0.29	0.0032
PREPS-N-000	1203163	39	62.01	61.75	0.26	0.0029
PREPS-N-000	1203163	35	62.10	61.87	0.23	0.0026
PREPS-N-000	1203163	36	61.75	60.97	0.78	0.0087
PREPS-N-000	1203163	40	62.46	62.28	0.18	0.0020
PREPS-N-000	1203163	38	61.90	61.67	0.23	0.0026
PREPS-N-000	1203163	37	62.11	61.89	0.22	0.0024

[1]60 psi = 4.14 bars for information

Detailed accuracy and performance testing results show equivalent results for X-ray and gamma treated sensors.

Table 35: Summary of sensor accuracy and performance testing results.

Pre vs Post X-ray Irradiation Difference in Reading								
Part Number	Lot Number	Serial Number	Guage Pressure (psi/bar)					
			10/0.69	20/1.38	30/2.07	40/2.76	50/3.45	60/4.14
			% Difference	% Difference	% Difference	% Difference	% Difference	% Difference
PREPS-N-000	1203163	35	0.00%	0.25%	0.47%	0.59%	0.55%	0.65%
PREPS-N-000	1203163	36	-0.20%	-0.50%	0.43%	0.47%	0.39%	0.50%
PREPS-N-000	1203163	37	0.20%	-0.45%	0.37%	0.40%	0.39%	0.42%
PREPS-N-000	1203163	38	0.00%	0.15%	0.33%	0.40%	0.35%	0.44%
PREPS-N-000	1203163	39	-0.20%	-0.65%	0.13%	0.25%	0.29%	0.36%
PREPS-N-000	1203163	40	-0.40%	-0.80%	0.13%	0.20%	0.25%	0.31%
PREPS-N-000	1203163	41	-0.10%	-0.60%	0.60%	1.09%	1.77%	2.55%
PRESS-N-000	1210050	26	-0.20%	-0.70%	0.20%	0.25%	0.14%	0.13%
PRESS-N-000	1210050	27	-0.10%	-0.65%	0.23%	0.35%	0.22%	0.27%
PRESS-N-000	1210050	28	-0.30%	-0.74%	0.13%	0.12%	0.08%	0.20%
PRESS-N-000	1210050	29	-0.40%	-0.79%	0.17%	0.15%	0.08%	0.23%
PRESS-N-000	1210050	30	-0.10%	-0.50%	0.03%	-0.47%	-1.12%	-1.78%
PRESS-N-000	1210050	31	-0.20%	-0.30%	0.80%	1.34%	1.99%	2.69%
PRESS-N-000	1210050	32	-0.10%	-0.50%	0.13%	-0.07%	-0.47%	-0.69%
PRESS-N-000	1210050	33	-0.10%	-0.50%	0.17%	-0.07%	-0.54%	-0.83%
PREPS-N-025	1191570	26	0.10%	-0.30%	0.33%	0.57%	0.54%	0.63%
PREPS-N-025	1191570	27	0.20%	-0.40%	0.53%	0.57%	0.57%	0.65%
PREPS-N-025	1191570	28	-0.30%	-0.55%	0.33%	0.47%	0.49%	0.58%
PREPS-N-025	1191570	29	-0.20%	-0.40%	0.40%	0.52%	0.55%	0.57%
PREPS-N-025	1191570	30	0.00%	-0.35%	0.37%	0.45%	0.49%	0.48%
PREPS-N-025	1191570	31	-0.20%	-0.40%	0.10%	0.27%	0.31%	0.40%
PREPS-N-025	1191570	32	-0.20%	-0.40%	-0.10%	0.15%	0.20%	0.25%
Average			-0.13%	-0.46%	0.29%	0.36%	0.34%	0.41%

DSC curves of PSU sensor materials are show below, where similar melting curves are observed for untreated, X-ray, and gamma treated sensors.

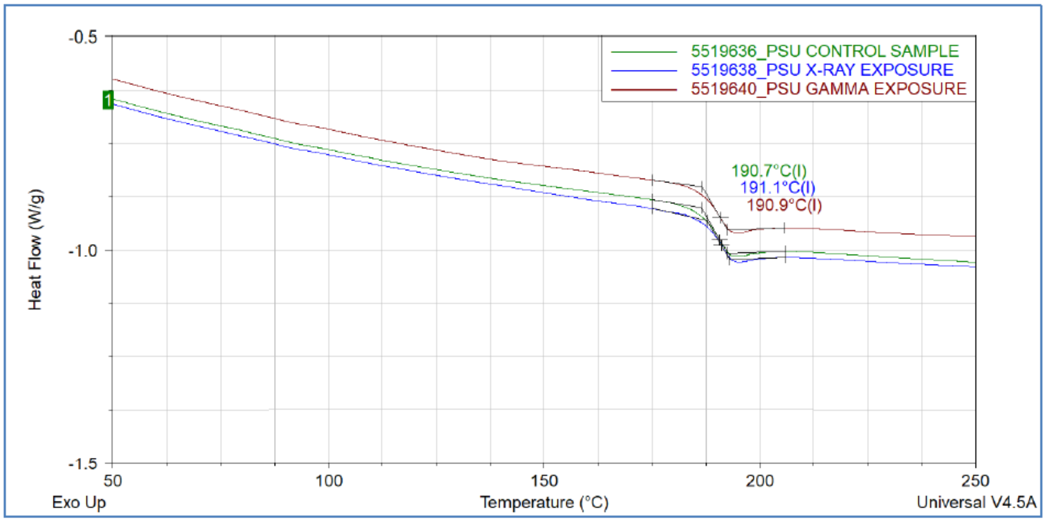


Figure 45: DSC thermograms of polysulfone sensor material: control, gamma and X-ray irradiated

FTIR Analysis of PC material used in PendoTECH sensor.

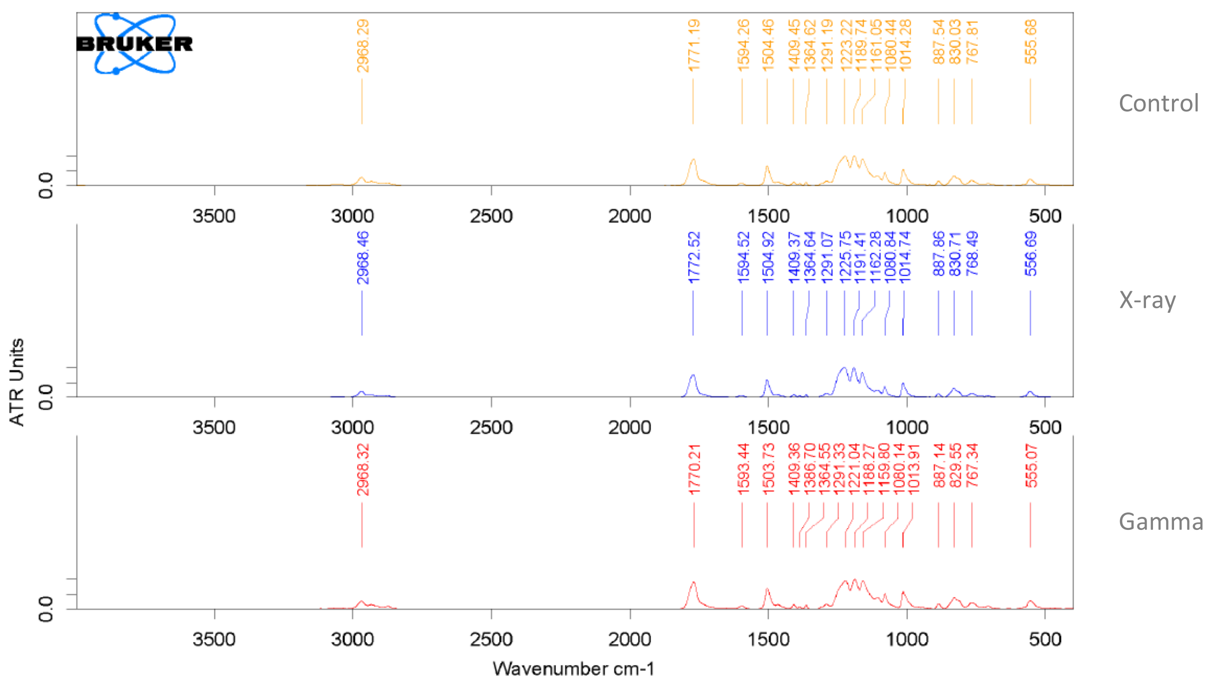


Figure 46: FTIR Spectra of PC used in single use pressure sensors

Thermogravimetric analysis of the PC material associated with the PendoTECH sensor demonstrated equivalent results for gamma and X-ray irradiated samples.

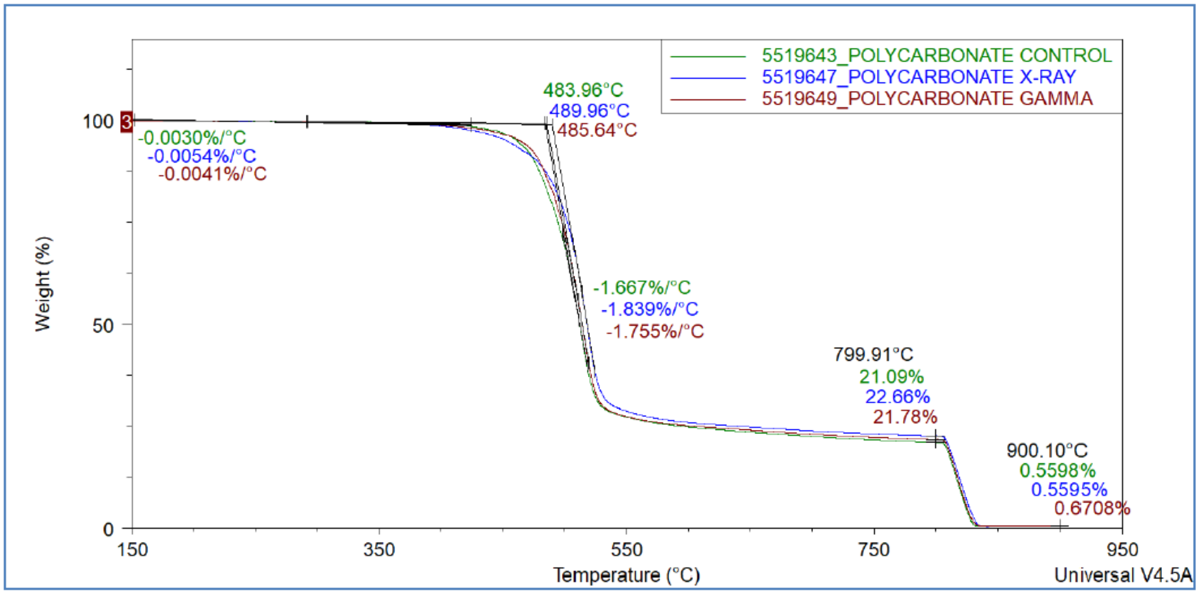


Figure 47: Thermogravimetric analysis of polycarbonate materials in PendoTECH sensor.

10.3.2 Broadley-James Single-Use pH Sensor™ SU800

Study plan and irradiation treatment details are described below.

Products submitted for X-Ray processing	Quantity
SU801-16-V6 (pH)	5
SU110-16 (DO, DCO2)	4
X-Ray Process Output:	
Number of Dosimeters measuring the irradiation	9
Measured Dose from Process Run	
Minimum kGy	47.7
Maximum kGy	51.3
Process Start	15-Mar-2022 8:45am
Process Finish	15-Mar-2022 2:35pm
Process Facility	Steris, 2500 Commerce Dr., Libertyville, IL 60048.
Process ID:	10834-40001881

The Table 36 lists the sensor drift values (The value is accumulative with time) of the sensor reading during the 16 days of a cell culture simulation run. The pH of the media was from 6.93 – 7.13 during the run.

Table 36: pH value drift results

SU800 SN	Sensor drift in simulated cell culture run, pH				
	113	**118**	**120**	**121**	**122**
4/6/2022	0.00	0.00	0.00	0.00	0.00
4/7/2022	-0.04	-0.04	-0.03	-0.02	-0.03
4/8/2022	-0.05	-0.05	-0.03	-0.03	-0.03
4/11/2022	-0.02	-0.02	-0.01	0.00	-0.01
4/12/2022	-0.01	-0.01	0.00	0.00	-0.01
4/13/2022	0.01	0.01	0.02	0.02	0.01
4/14/2022	0.03	0.03	0.04	0.05	0.04
4/15/2022	0.01	0.01	0.02	0.03	0.02
4/18/2022	0.01	0.01	0.02	0.03	0.02
4/19/2022	0.04	0.03	0.04	0.04	0.03
4/20/2022	0.03	0.03	0.04	0.04	0.03
4/21/2022	0.03	0.04	0.05	0.05	0.04
4/22/2022	0.01	0.02	0.03	0.03	0.02

10.4 Filters Supplemental Data

10.4.1 Kleenpak™ Filter with Supor EKV membrane

Particulates evaluation of X-ray and gamma irradiated filters demonstrate no impact of X-ray on particulates.

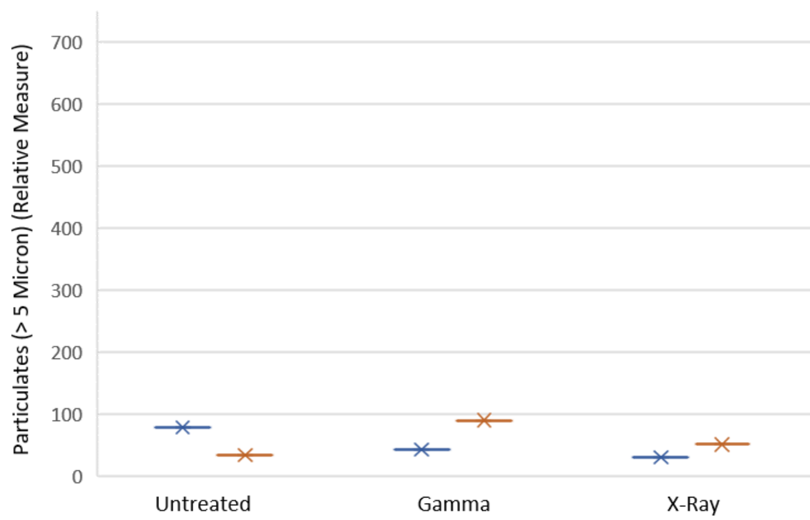


Figure 48: Particulate levels (> 5 micron) in filter effluent evaluated without prior flushing evaluated for non-irradiated, gamma irradiated, and X-ray irradiated filter capsules

Filter integrity testing values in alcohol/water confirm the integrity of the filter and membrane are not impacted by X-ray irradiation as compared to gamma.

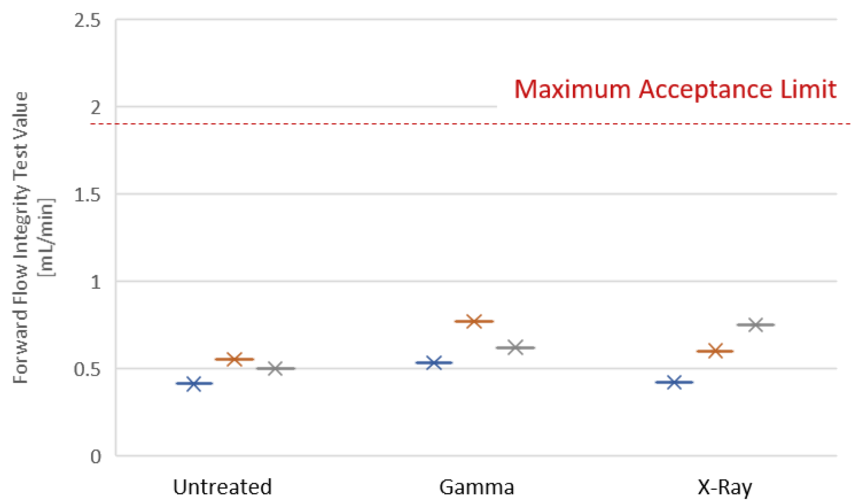


Figure 49: Forward flow test results for untreated, gamma irradiated, and X-ray irradiated KA3EKVPG1 filter capsules wetted with 60/40 IPA/water

10.5 Tubing Supplemental Data

10.5.1 AdvantaFlex™ APAF TPE Tubing

Values for gamma and X-ray- irradiated tubing samples are shown in Appendix Table 37.

Table 37: Bend radius results for gamma and X-ray irradiated TPE tubing samples.

APAF-BP	
Gamma	**X-ray**
1.000	1.125
1.125	1.125
1.125	1.000
1.125	1.125
1.125	1.125
1.125	1.125

Results of the burst testing are shown in Table 38.

Table 38: Burst testing results for gamma and X-ray irradiated APAF TPE tubing samples.

APAF-BP					
Gamma			X-ray		
Temp (°C)	Time (s)	Pressure (psi)[1]	Temp (°C)	Time (s)	Pressure (psi)
16.7	65	79	16.9	61	78
-	62	79	-	64	79
-	62	78	-	60	79
-	66	78	-	64	80
-	62	78	-	67	79
16.7	64	78	16.9	62	79

[1] 80 psi ~ 5.5 bars for information

About BPSA

The Bio-Process Systems Alliance (BPSA) was formed in 2005 as an industry-led corporate member trade association dedicated to encouraging and accelerating the adoption of single-use manufacturing technologies used in the production of biopharmaceuticals and vaccines. BPSA facilitates education, sharing of best practices, development of consensus guides and business-to-business networking opportunities among its member company employees.

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