BPSA℠

2023 Single-Use Pulse Webinar Series

IMPLEMENTATION OF X-RAY STERILIZATION OF SINGLE-USE SYSTEMS: WHAT TO EXPECT

Thursday, March 9, 2023

10 - 11:30 AM EST

Presenters

Samuel Dorey, Sartorius

James Hathcock, Pall Corporation

Created in Cooperation With…

socma
SOLUTIONS FOR SPECIALTIES

BPSA
Bio-Process Systems Alliance
Advancing Single-Use Worldwide

CPMA
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solvias

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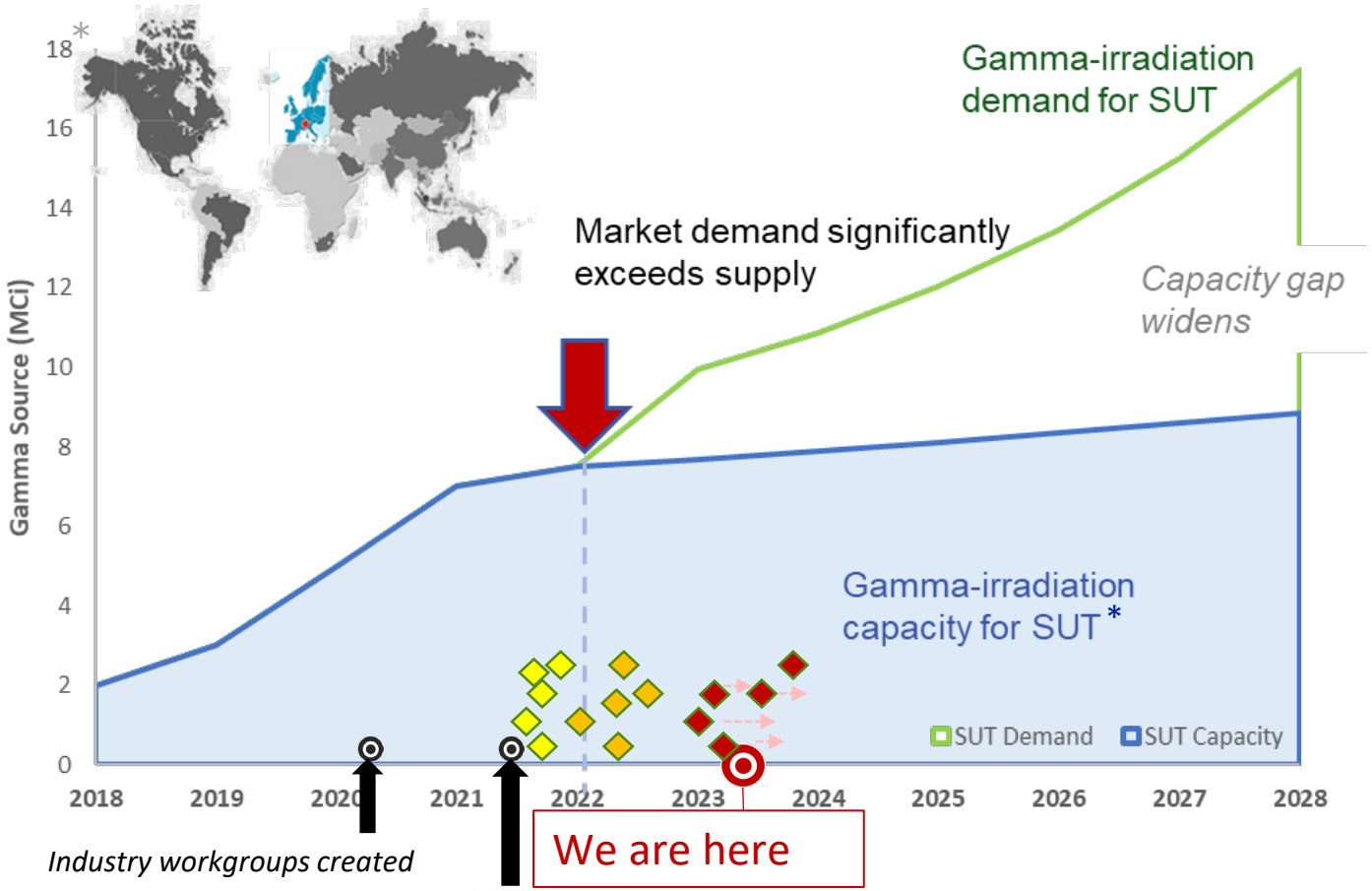
Implementation of X-ray for Single-Use

- Implementation Ramp-Up, Capacity & Risks
- BPSA X-ray Qualification Testing Paper
- Regulatory Perspectives
- Staying Current

Implementation Ramp-Up

Contract Irradiation Capacity Bottle-Neck for Single-Use



2021 BPSA White Paper. X-ray Sterilization of Single-Use Bioprocess Equipment: Part I – Industry Need, Requirements, and Risk Evaluation.

Timelines

- Integrators Pre-change Notification Issued
- Change Notifications Issued
- Implementation Targets

Challenges

- Regulator Uncertainty
- Capacity Buildout

Mapping of Irradiation Sites and Key Risks

- Opening Dates
  - Steris, Daniken (Switzerland) - open
  - Steris, Venlo (Netherland) - open
  - Steris, Libertyville (USA) – June 2023 (TBC)
  - Steris, Chomburi (Thailand) – Summer 2023 (TBC)
  - Steris, Suzhou (China) – planned
  - Others in pipeline
- Risks: additional delays
- Dose Mapping performed as within gamma sites
- Potential tension to Cobalt-60 supply due to current sanctions

Implementation of X-ray for Single-Use

- Implementation Ramp-Up, Capacity & Risks
- **BPSA X-ray Qualification Testing Paper**
- Regulatory Perspectives
- Staying Current

Sterilization Modality or Technology

Sterilization Modalities

Heat

Chemical

Technologies / Processes

Gamma

γ

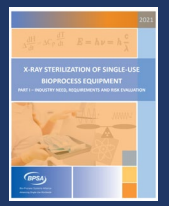
X-Ray

x

Beta / E-beam

β

Ionizing Radiation



2021 BPSA X-ray Assessment White Paper

Responses to radiation for different polymers intrinsically related to the chemical structures of the polymers

Bags & Film

Sensors

Tubing (TPE, Silicone)

Filters

Aseptic Connectors

- Focus on polymers with limited irradiation compatibility (worst case)
- Couple material-science assessments with component testing
- Not retest every component.
- Demonstrate existing data packages remain valid for X-ray

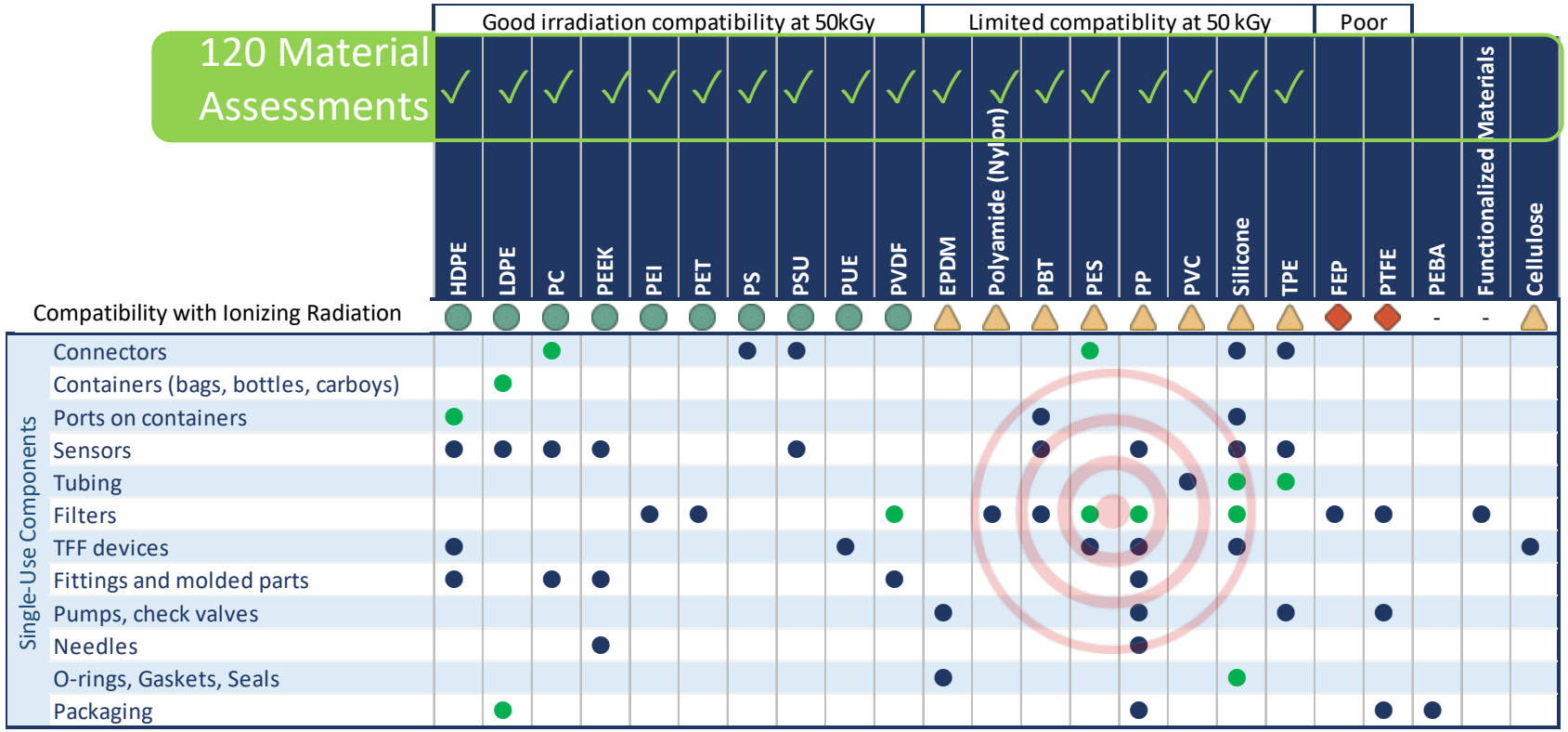
		Good irradiation compatibility at 50kGy										Limited compatiblity at 50 kGy								Poor				
		HDPE	LDPE	PC	PEEK	PEI	PET	PS	PSU	PUE	PVDF	EPDM	Polyamide (Nylon)	PBT	PES	PP	PVC	Silicone	TPE	FEP	PTFE	PEBA	Functionalized Materials	Cellulose
	Compatiility with Ionizing Radiation	●	●	●	●	●	●	●	●	●	●	▲	▲	▲	▲	▲	▲	▲	▲	◆	◆	-	-	▲
Single-Use Components	Connectors			●				●	●						●			●	●					
	Containers (bags, bottles, carboys)		●																					
	Ports on containers	●												●				●						
	Sensors	●	●	●	●				●					●		●		●	●					
	Tubing																●	●	●					
	Filters					●	●				●		●	●	●	●		●		●	●		●	
	TFF devices	●								●					●	●		●						●
	Fittings and molded parts	●		●	●						●					●								
	Pumps, check valves											●				●			●		●			
	Needles				●											●								
	O-rings, Gaskets, Seals											●						●						
	Packaging		●													●					●	●		

Materials Impact Assessment

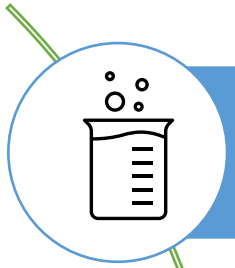
Material Assessments

- **FTIR.** *Chemical fingerprint*
- **DSC.** *Heat flow characteristics (melting temperature, crystallinity)*
- **TGA.** Change in mass with thermal decomposition
- **Mechanical.** (components dependent)
- **DMA.** *Viscoelasticity* (components dependent)

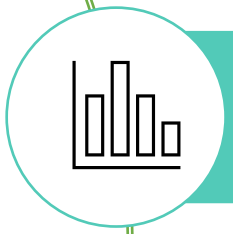
1st investigation level to assess X vs G impacts



Key outputs

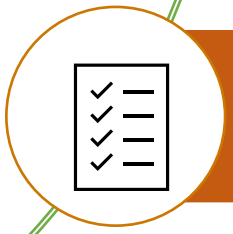


The paper reflects multiple types of testing, data presentation and ways to evaluate the results



A review of multiple datasets, from different components, materials and suppliers, offers a robust holistic perspective

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



It shows the hypothesis mentioned in WP1 is right: same irradiation physics and thus equivalent impact

Part II. Representative Qualification Data

Draft pending BPSA board review

X-Ray Sterilization of Single-Use Bioprocess Equipment. Part II – Representative Qualification Data

Published by:
Bio-Process Systems Alliance (BPSA)
1400 Crystal Drive
Arlington, VA 22202

Authors & Data Contributors

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CD Feng	Broadley-James
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Timo Neuman	MilliporeSigma
Lise Tan-Sien-Hee	DuPont
Nick Troise	PendoTECH
Andrew Trolio	NewAge
Gabrielle Wilson	Saint Gobain

Acknowledgements

We want to thank the following people for their contribution to the development and review of this guide.

- Executive Summary
- Temperature and Activation with Radiation Processing
- Physical and Functional Component Data
- Chemical Tests
- Materials Assessments
- Biological Tests
- Assembly Integrity
- Conclusions and Next Steps
- Appendices

Part II. Representative Qualification Data

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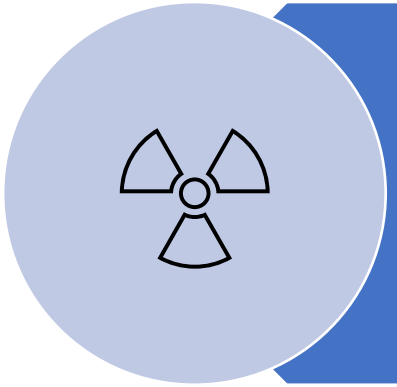
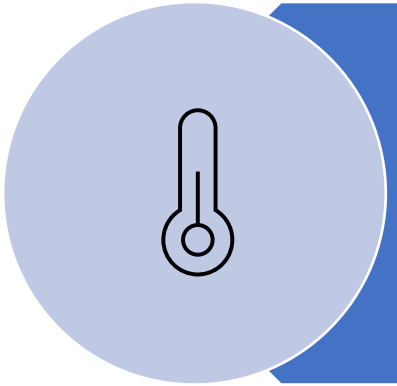
	Primary MOC	Materials	Physical	Functional	Chemical	Biological
Biocontainer						
Flexsafe® bag (S80 film)	PE's/EVOH	●	●	●	●	●
Connector						
Lynx® S2S	PSU, Sil	●	●	●	●	●
AseptiQuik® AQG	PC, PPSU, PE, PES, Sil	●	●	●	○	○
Filter						
Kleenpak™ EKV Capsule	PP, PES, EPDM	●	●	●	●	●
Sensor						
PendoTECH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

Temperature and Activation Associated with Radiation Processing



Tested materials irradiated at 55-80 kGy show no reports of significant activation



Average maximum temperatures experienced during gamma irradiation were 35-45°C vs 30-40°C with X-ray irradiated samples at 50±5kGy

Overall assessment

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

Physical and Functional Component Data ✓

Chemical Tests ✓

Materials Assessments ✓

Biological Tests ✓

Implementation of X-ray for Single-Use

- Implementation Ramp-Up, Capacity & Risks
- BPSA X-ray Qualification Testing Paper
- **Regulatory Perspectives**
- Staying Current

Regulator Engagement & Alignment

FDA ETT CDER Engagement ❶ Dec 2021 ❷ Sept 2022

- X-ray appears new concept
- Need cross functional expertise & data
  - Physicists, Single-use SMEs, Pharma manufacturers
- Good vibes
  - Sterility assurance ✓
  - Functionality assessment ✓
- Continued engagement
  - Extractables (low/high pH)
  - Case Studies
- MHRA/EMA Engagement Critical

Transitioning from Gamma to X-ray

- **ISO 11137 "**Sterilization of Healthcare Products" **covers** gamma and **X-ray**
  - ✓ No change to dose window *(transfer of dose)*
  - ✓ Dose mapping required for new radiation sources/sites
  - ✓ Sterility dose audits with X-ray will demonstrate continued effectiveness
  - ✓ Activation studies demonstrate no meaningful radioactivity
  - ✓ No impact to sterility assurance level (SAL)

> *"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."*

BPSA WhitePaper 2

Transitioning from Gamma to X-ray

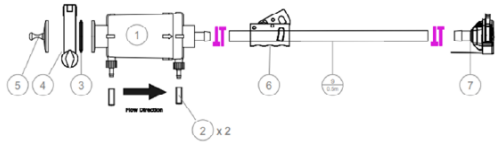
- **Fundamental physics** of gamma and x-ray are equivalent
  - ✓ Gamma to X-ray is not a “modality” change *(heat, radiation, gas)*

- **Sponsor risk-assessment** based on
    - ✓ Irradiation physics understanding
    - ✓ Evaluation of wide range of representative materials
    - ✓ Limited testing to “verify” equivalence, but not revalidate
  - USP <665> “moderate risk” testing to assess leachables risk
  - Case study Risk Assessments for post-approval changes

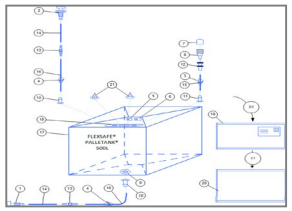
Case Study Risk Assessment & Regulatory Notification Action

Case Study	Gamma mentioned in approved filing
Case A: Single-use filtration assembly in final sterilizing-grade filtration step of monoclonal antibody product	No
Case B: Single-use storage bag assembly for mixing and/or storage of formulation buffer	No
	Yes
Case C: Low risk applications (e.g. associated with or upstream of clearance steps)	No

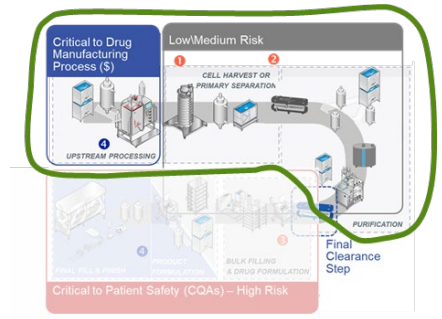
A



B



C



Authors Note: The assessments included in this document represent the consensus opinions of recognized subject matter experts in the pharmaceutical industry who have been actively engaged in industry groups and review panels focused on risk assessment and qualification of X-ray. This includes three team members currently employed in related risk assessment roles at different pharmaceutical manufacturers, and two team members from different single-use providers. Authors names and affiliations are indicated where allowed per company policy. As part of this process additional subject matter experts within companies have been consulted and existing regulatory filings reviewed to ensure in good faith and to the best of our ability that these case studies and assessments are largely representative of those expected in 2023 and beyond. These opinions represent those of the authors, and in most cases have not been formally reviewed and endorsed by their companies or industry organizations in which they participate

Case Study Risk Assessment & Regulatory Notification Action

Case Study	Gamma mentioned in approved filing	Final Risk Determination (Gamma → X-ray)	Regulatory Notification Action
Case A: Single-use filtration assembly in final sterilizing-grade filtration step of monoclonal antibody product	No	Low Risk	Annual report
Case B: Single-use storage bag assembly for mixing and/or storage of formulation buffer	No	Low Risk	Annual report
	Yes	Low Risk	CBE-30
Case C: Low risk applications (e.g. associated with or upstream of clearance steps)	No	Low Risk	Non reportable

Agency Feedback
Annual Report*

*Such changes, where compliant to ISO 11137 including dose mapping and sterility dose audit studies, may be documented in annual product quality review.

Case Study Risk Assessment & Regulatory Notification Action

Case Study	Gamma mentioned in approved filing	Final Risk Determination (Gamma → X-ray)	Regulatory Notification Action
Case A: Single-use filtration assembly in final sterilizing-grade filtration step of monoclonal antibody product	No	Low Risk	Annual report
Case B: Single-use storage bag assembly for mixing and/or storage of formulation buffer	No	Low Risk	Annual report
	Yes	Low Risk	CBE-30
Case C: Low risk applications (e.g. associated with or upstream of clearance steps)	No	Low Risk	Non reportable

Agency Feedback
Annual Report*

In Scope SUS & Applications

- ✓ Formulation buffer mixing & storage
- ✓ Final sterilizing filtration
- ✓ Many inherently low risk applications involving wide range of materials

Not Yet in Scope

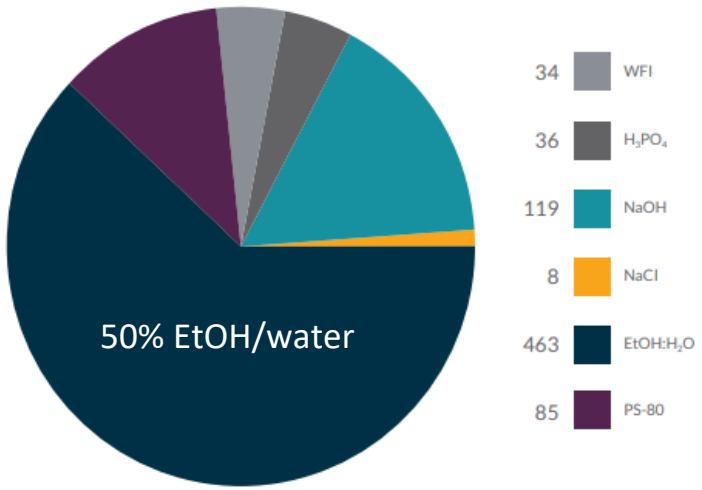
- × Final filling
- × BDS storage
- × Container closure *(not SUS)*

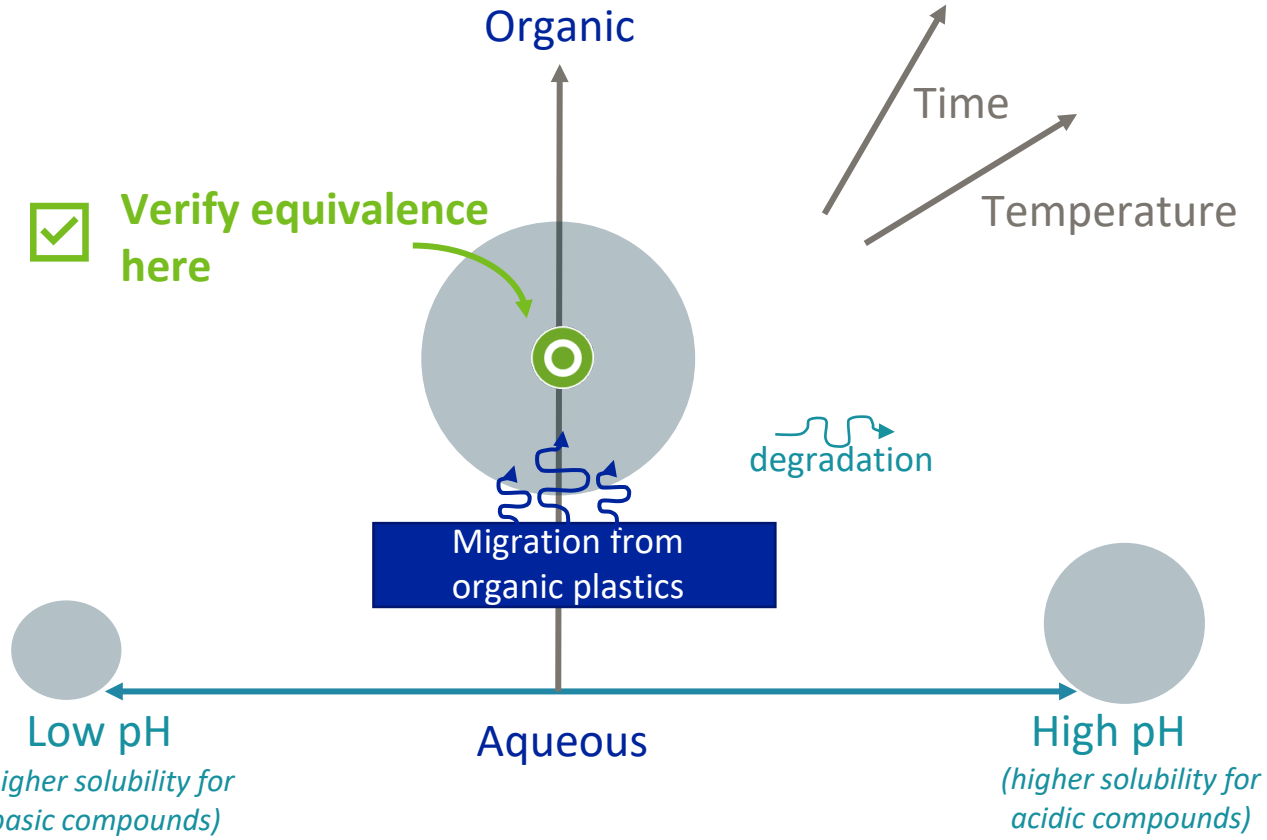
** will likely be implemented at future date*

Rationale for <665> Moderate Risk

50% EtOH/water extraction profile (referred to as <665> expanded baseline testing)

Distribution of unique extractables by solvent





USP <665> Moderate risk testing *of representative materials, coupled with materials testing,* ***VERIFIES*** *our understanding of the irradiation physics that* ***X-ray is equivalent to gamma*** *for single-use materials. The* ***existing E&L risk assessment remains valid for X-ray****.*

Proof-of-concept data (low pH, high pH, high organic) for worst-case components confirm no unexpected effects related to X-ray.

ETT Engagement on X-ray Qualification Expectations for Single-Use Bioprocess Systems

Key points and aligned positions

- Sterility assurance
  1. ISO 11137 approach including activation, dose mapping of new X-ray sites, and sterility dose audits sufficient to justify no impact to sterility assurance level (SAL). [A]
- Categorization of changes
  2. A sponsor risk assessment based on irradiation physics, materials impact assessment, limited component "verification" testing, and knowledge of the drug manufacturing process is appropriate for transition from gamma to X-ray [B]
  3. The case studies and recommended regulatory notification actions *(non-notifiable, annual review, CBE-30)* appear reasonable [B]
  4. Whether CBE-30 (vs Annual review) is expected for post-approval changes of filings that mention "gamma", but the overall risk determination is "low"[B]
- USP <665> Moderate Risk (Level B)
  5. USP <665> "Moderate" risk extractables testing of representative components is suitable to "verify" equivalence, and that existing E&L assessment remains valid (i.e. no impact to E&L.) [C]
- Other groups
  6. While CDER and CBER agree on points above during meeting, official notes from CBER still pending

Regulatory Perspectives & Feedback

FDA ETT Engagement ❶ Dec 2021 ❷ Sept 2022

Executive Summary

ETT Engagement on X-ray Qualification Expectations for Single-Use Bioprocess Systems

1 Executive Summary

Given the urgency to qualify X-ray as an alternative to Gamma for irradiation of single-use systems (SUSs), clear alignment is needed among suppliers, pharmaceutical manufacturers, and regulators on expectations for transition & commercial implementation. On September 8, 2022, a small industry team consisting of members of BioPhorum and BPSA, BARDA and subject matter experts met with the FDA/CDER/Emerging Technologies Team (ETT), including observers from CBER and EMA, to socialize and advocate for the positions published in the 2021 BPSA white paper on X-ray [1], and address concerns expressed by regulators during a prior, December 2021 Type C meeting with the ETT. Specifically, these concerns focused on the need for (I) examples of how sponsors would assess, categorize, and notify authorities when implementing a change, as well as (II) proof-of-concept extractables data for representative worst-case components which verify that there are no unexpected effects under low pH, high pH, or high organic content. The package included (i) the follow-up Type C meeting request which identified key questions on which agency feedback was desired; (ii) the May 2021 BPSA whitepaper; (iii) a recently finished & to-be published technical paper demonstrating the comparability of X-ray and Gamma irradiation physics; (iv) the December 2021 CDER/ETT Type C meeting minutes; (v) a report consisting of 3 primary examples of post-approval changes and additional supporting rationale for the BPSA-recommended approach to extractables & leachables verification testing; and (vi) a general letter of support for the risk-based approach to assessment, verification, and notification of changes from BioPhorum. Following a detailed, interactive discussion on September 8, formal meeting minutes were received from the agency on September 20, 2022. The FDA's summary and description of the consensus met were consistent with the understanding of the industry participants, were regarded as highly positive to the advancement of the initiative, and aligned with the industry's need for practical, risk-based approaches to the transition to X-ray sterilization.

The key questions and responses in the attached meeting minutes address those posed in the meeting request. A brief overview of the key points and aligned positions is below.

A. Sterility assurance

Sterility assurance concerns around transfer of dose from gamma to x-ray may be addressed per ISO 11137 [2] [3]. Specifically, (i) sterility assurance levels may be considered independent of the source-of photon-based irradiation, as established according to ISO 11137-2; (ii) the x-ray minimum dose may be substantiated through sterility dose audit experiments as described in ISO 11137-2, and (iii) dose mapping studies for each process shall establish that the minimum and maximum dose requirements are achieved by operating within established process settings.

The comments also note that if there is a need to increase the irradiation dose range compared to what was validated for a Gamma sterilization process, then additional studies would be warranted. This case, although worthwhile to consider in the hypothetical, is not expected to manifest with transfer from Gamma to X-ray. Regardless, dose mapping studies will confirm that pre-established dose ranges remain unchanged in transitioning processes.

B. Categorization of changes

Post approval changes that follow the requirements of ISO 11137, and are deemed to be low risk as per the biomanufacturer's assessment may be submitted as part of the Annual Product Quality Report (APQR). This applies to changes that may be used in critical applications such as (A) final, sterilizing-grade filtration assemblies, (B1) formulation buffer mixing assemblies, (B2) applications in which "Gamma irradiation" may have been specifically identified in applicable regulatory filings, or (C) assemblies used in inherently low-risk applications distant to the patient and final drug product.

Meeting Minutes:
T) and BARDA (with Pall Corporation and partners)

ɔck, PhD, Sr. Director of Regulatory & Validation Strategy
ion & BPSA Task Force Lead
y, PhD, Principal Scientist of Materials and Irradiations,
lopment
lim Biotech & BPSA Task Force Lead
hD, Director of Research & Development
maceutical Companies of Johnson and Johnson
ritical Material Management Lead, Sanofi S.A.
Sr. Process Engineer, BioMarin Pharmaceutical
, PhD, Applications Physicist and Head of the Neutron
cility, Fermi National Accelerator Laboratory (Fermilab), US

es, Global Sterility Assurance Director, Cytiva Life Sciences
ne Irradiation Panel
lotzbuecher-Cruz, Senior Biomedical Engineer,
DA/PCI/PVPCR Branch
on, PhD, Domestic Alternative Technology Portfolio
E/National Nuclear Security Agency/Office of Radiological

nan, Supply Chain Management Lead,
DA/Division of Pharmaceutical Countermeasures
(PCI)
, Chief of Pandemic Vaccine Preparedness Capabilities &
VPCR) Branch, DHHS/BARDA/PCI
Drug/Vaccine Supply Chain Manager, Tunnell Government
porting DHHS/BARDA/PCI/PVPCR Branch

- Anabela Marca, EMA Liaison to FDA (invited by BARDA)
- Maria Jesus Alcaraz Tomas, Regulatory Science & Innovation Task Force, Supply & Availability of Medicines & Devices, EMA (invited by BARDA)
- Brian Dooley, Pharmaceutical Qualify Office, EMA (invited by BARDA)

- All Meeting summary and minutes available

Implementation of X-ray for Single-Use

- Implementation Ramp-Up, Capacity & Risks
- BPSA X-ray Qualification Testing Paper
- Regulatory Perspectives
- Staying Current

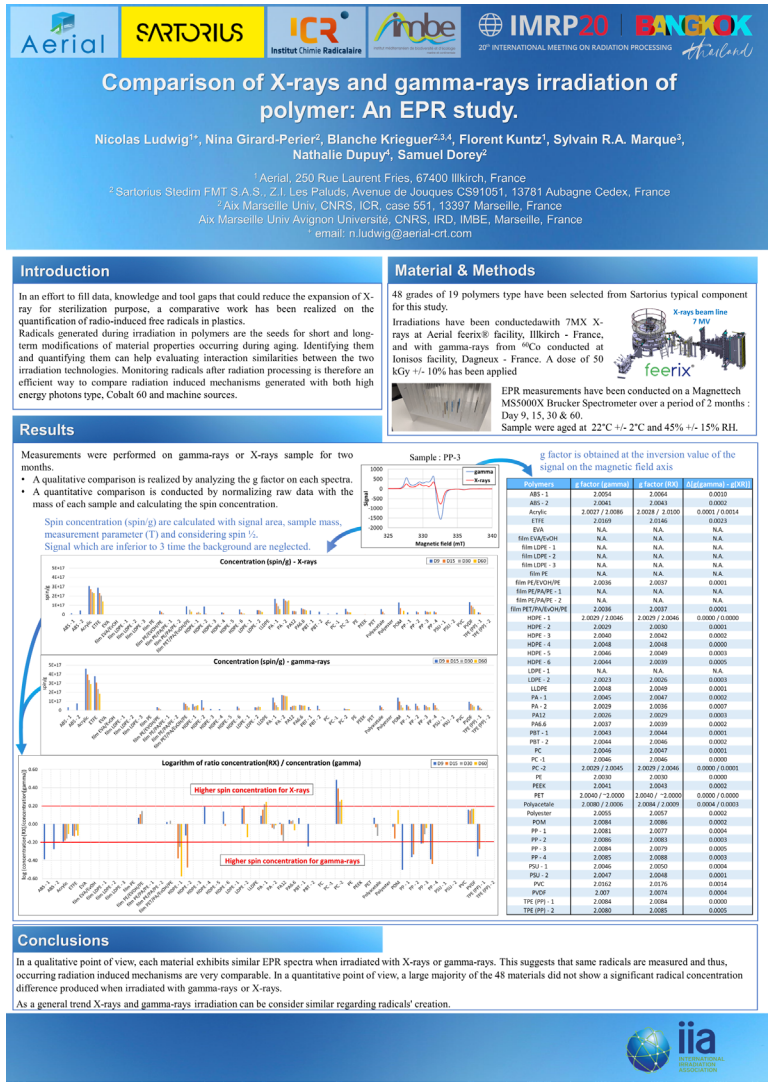
Recent Publications

Arthur Charlesby	• https://doi.org/10.1016/B978-1-4831-9776-0.50007-3 (1960!)
Fermilab	• https://doi.org/10.1016/j.radphyschem.2022.110702 (2023)
Team Nablo	• https://doi.org/10.1016/j.radphyschem.2020.109282 (2021) • https://doi.org/10.1016/j.radphyschem.2021.109505 (2021) • Supplementing Gamma Sterilization – BioProcess (2022) • InternationalBioProcess International (bioprocessintl.com) (2022) • https://doi.org/10.3389/fchem.2022.888285 (2022)
Sartorius	• https://doi.org/10.1039/D1CC02871E (2021) • https://doi.org/10.1002/btpr.3214 (2021) • https://doi.org/10.1016/j.ijpharm.2023.122677 (2023) • https://dc.engconfintl.org/sut_v/55/ (2022)
Pall	• https://dc.engconfintl.org/sut_v/54/ (2022) • Biotechnology Progress *(Grzelak et al., in press)* (2023)
Activation	• https://doi.org/10.2345/0899-8205-55.s3.17 (2021)
Miscelleneous	• https://doi.org/10.1016/j.radphyschem.2007.01.014 (2007) • https://doi.org/10.1016/j.radphyschem.2022.109999 (2022)

Recent Conferences

Single-Use Technologies V Building The Future (Marseille, France, March 2022)	• http://engconf.us/conferences/biotechnology/single-use-technologies-v-building-the-future/
Kilmer (Athens, Greece, June 2022):	• Kilmer Conference
ICARST (Vienna, Austria, August 2022):	• News: Second International Conference on Applications of Radiation Science and Technology (ICARST-2021) | IAEA
IARC (Sept 2022)	• Medical Device Sterilization Workshop *(videos online)*
IMRP (Nov 2022) :	• International Meeting on Radiation Processing (imrp-iia.com)
To be continued in 2023	

Insights in Materials Impact Assessment



Comparison of X-rays and gamma-rays irradiation of polymer: An EPR study.

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Introduction

In an effort to fill data, knowledge and tool gaps that could reduce the expansion of X-ray for sterilization purpose, a comparative work has been realized on the quantification of radio-induced free radicals in plastics.
Radicals generated during irradiation in polymers are the seeds for short and long-term modifications of material properties occurring during aging. Identifying them and quantifying them can help evaluating interaction similarities between the two irradiation technologies. Monitoring radicals after radiation processing is therefore an efficient way to compare radiation induced mechanisms generated with both high energy photons type, Cobalt 60 and machine sources.

Material & Methods

48 grades of 19 polymers type have been selected from Sartorius typical component for this study.
Irradiations have been conductedawith 7MX X-rays at Aerial feerix® facility, Illkirch - France, and with gamma-rays from ^{60}Co conducted at Ionisos facility, Dagneux - France. A dose of 50 kGy +/- 10% has been applied

X-rays beam line 7 MV
feerix

EPR measurements have been conducted on a Magnettech MS5000X Brucker Spectrometer over a period of 2 months : Day 9, 15, 30 & 60.
Sample were aged at 22°C +/- 2°C and 45% +/- 15% RH.

Results

Measurements were performed on gamma-rays or X-rays sample for two months.
- A qualitative comparison is realized by analyzing the g factor on each spectra.
- A quantitative comparison is conducted by normalizing raw data with the mass of each sample and calculating the spin concentration.

Spin concentration (spin/g) are calculated with signal area, sample mass, measurement parameter (T) and considering spin ½.
Signal which are inferior to 3 time the background are neglected.

Sample : PP-3

g factor is obtained at the inversion value of the signal on the magnetic field axis

Concentration (spin/g) - X-rays

Concentration (spin/g) - gamma-rays

Logarithm of ratio concentration(RX) / concentration (gamma)

Higher spin concentration for X-rays

Higher spin concentration for gamma-rays

Polymers	g factor (gamma)	g factor (RX)	Δ(g(gamma) - g(RX))
ABS - 1	2.0054	2.0064	0.0010
ABS - 2	2.0041	2.0043	0.0002
Acrylic	2.0027 / 2.0086	2.0028 / 2.0100	0.0001 / 0.0014
ETFE	2.0169	2.0146	0.0023
EVA	N.A.	N.A.	N.A.
film EVA/EvOH	N.A.	N.A.	N.A.
film LDPE - 1	N.A.	N.A.	N.A.
film LDPE - 2	N.A.	N.A.	N.A.
film LDPE - 3	N.A.	N.A.	N.A.
film PE	N.A.	N.A.	N.A.
film PE/EVOH/PE	2.0036	2.0037	0.0001
film PE/PA/PE - 1	N.A.	N.A.	N.A.
film PE/PA/PE - 2	N.A.	N.A.	N.A.
film PET/PA/EvOH/PE	2.0036	2.0037	0.0001
HDPE - 1	2.0029 / 2.0046	2.0029 / 2.0046	0.0000 / 0.0000
HDPE - 2	2.0029	2.0030	0.0001
HDPE - 3	2.0040	2.0042	0.0002
HDPE - 4	2.0048	2.0048	0.0000
HDPE - 5	2.0046	2.0049	0.0003
HDPE - 6	2.0044	2.0039	0.0005
LDPE - 1	N.A.	N.A.	N.A.
LDPE - 2	2.0023	2.0026	0.0003
LLDPE	2.0048	2.0049	0.0001
PA - 1	2.0045	2.0047	0.0002
PA - 2	2.0029	2.0036	0.0007
PA12	2.0026	2.0029	0.0003
PA6.6	2.0037	2.0039	0.0002
PBT - 1	2.0043	2.0044	0.0001
PBT - 2	2.0044	2.0046	0.0002
PC	2.0046	2.0047	0.0001
PC -1	2.0046	2.0046	0.0000
PC -2	2.0029 / 2.0045	2.0029 / 2.0046	0.0000 / 0.0001
PE	2.0030	2.0030	0.0000
PEEK	2.0041	2.0043	0.0002
PET	2.0040 / ~2.0000	2.0040 / ~2.0000	0.0000 / 0.0000
Polyacetale	2.0080 / 2.0006	2.0084 / 2.0009	0.0004 / 0.0003
Polyester	2.0055	2.0057	0.0002
POM	2.0084	2.0086	0.0002
PP - 1	2.0081	2.0077	0.0004
PP - 2	2.0086	2.0083	0.0003
PP - 3	2.0084	2.0079	0.0005
PP - 4	2.0085	2.0088	0.0003
PSU - 1	2.0046	2.0050	0.0004
PSU - 2	2.0047	2.0048	0.0001
PVC	2.0162	2.0176	0.0014
PVDF	2.007	2.0074	0.0004
TPE (PP) - 1	2.0084	2.0084	0.0000
TPE (PP) - 2	2.0080	2.0085	0.0005

Conclusions

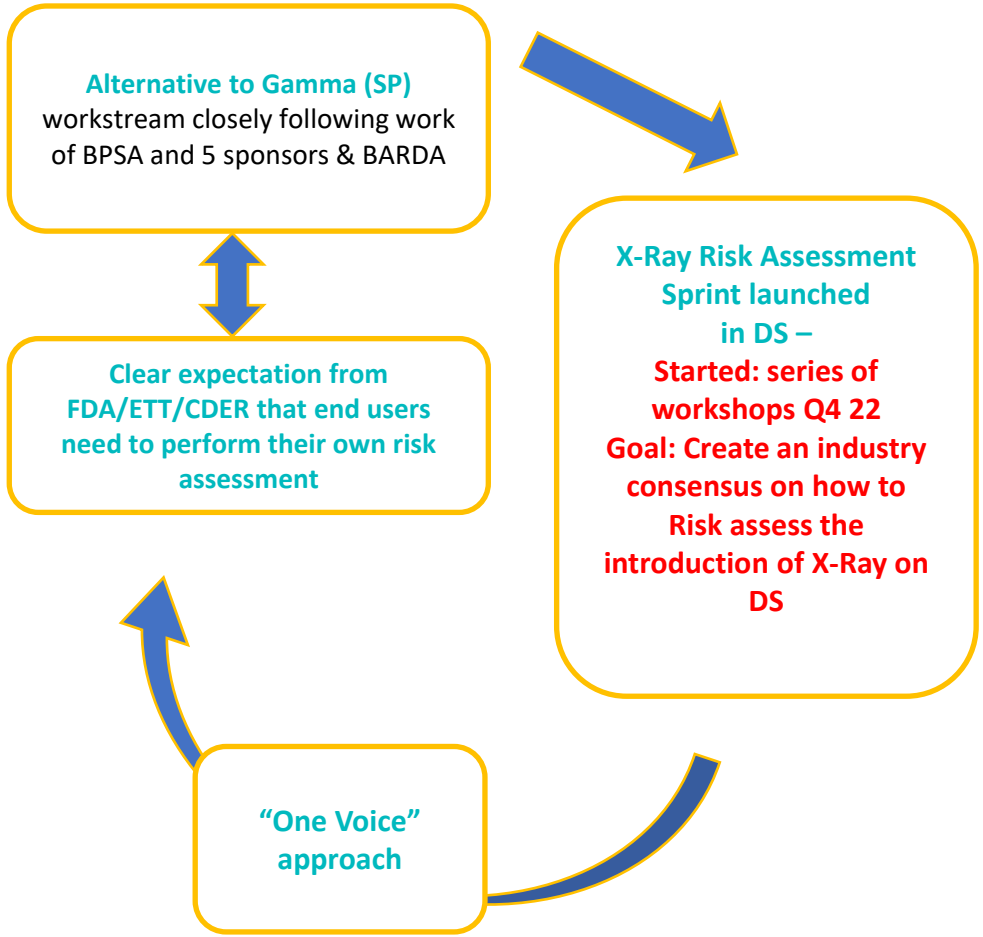
In a qualitative point of view, each material exhibits similar EPR spectra when irradiated with X-rays or gamma-rays. This suggests that same radicals are measured and thus, occurring radiation induced mechanisms are very comparable. In a quantitative point of view, a large majority of the 48 materials did not show a significant radical concentration difference produced when irradiated with gamma-rays or X-rays.
As a general trend X-rays and gamma-rays irradiation can be consider similar regarding radicals' creation.

- Radiation interaction effects between matter and Gamma- & X-ray investigated
- Radicals tracked by EPR (Electron paramagnetic resonance or electron spin resonance (ESR)) spectroscopy
- Same nature of radicals and equivalent quantity after gamma and X-ray irradiation

→ Key interaction outputs equivalent after gamma and X-rays

BioPhorum X-Ray Sterilization Risk Assessment Sprint Workshop

Sharing questions & understanding



- The team are aligned on what we want to deliver
- Want to reach an industry consensus while embracing the viewpoints of all stakeholders (not every company has the same approach to RA)
- Clear decision to focus on low/medium risk (common approach by all biomanufacturers and suppliers) to first implement and to further assess the high risk applications
- Consensus approach in preparation; if not, different approaches can be reported to regulatories
- X-ray implementation on low/medium risks in 2023 and in 2024/2025 for high risks

ASTM Workshop E55/E61

Radiation Processing for the Pharmaceutical and BioPharmaceutical Industries Training Workshop, May 8-9, 2023

- The objective of this workshop is to enhance the knowledge and understanding of the radiation process and critical requirements needed for the sterilization of components and finished products using radiation technologies
- Radiation Processing for the Pharmaceutical and BioPharmaceutical Industries Training Workshop (eventscloud.com)
- This workshop is powered by the ASTM E61 International Workshop on Radiation Processing but focused on and tailored for the individuals supporting the pharmaceutical and biopharmaceutical industries

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Questions & Discussion

- Implementation Ramp-Up, Capacity & Risks
- BPSA X-ray Qualification Testing Paper
- Regulatory Perspectives
- Staying Current

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