STERIS Applied Sterilization Technologies

The development in radiation sterilizing methods for single-use systems

ALFLOW Seminar 2023

Speaker

Pierre Reppert
Radiation Technology Centers Senior Manager EMEA-APAC
STERIS Applied Sterilization Technologies

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RADIATION MODALITIES

GAMMA
Exposes product to Cobalt 60 radiation

ELECTRON BEAM
Exposes product to high-energy electrons

X-RAY
Uses ionizing energy from electron beams

GAS MODALITIES

ETHYLENE OXIDE (EO)
Exposes product to gaseous sterilant

VAPORIZED HYDROGEN PEROXIDE (VHP)
Low temp gas process under deep vacuum

TESTING SERVICES

LABORATORY TESTING
Provides microbiological and analytical testing

PRODUCT & PACKAGE TESTING
Provides testing options for the validation of medical devices

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Agenda

- Radiation Technology comparison
- Considerations
- Solutions: Risk based approach
- Publications

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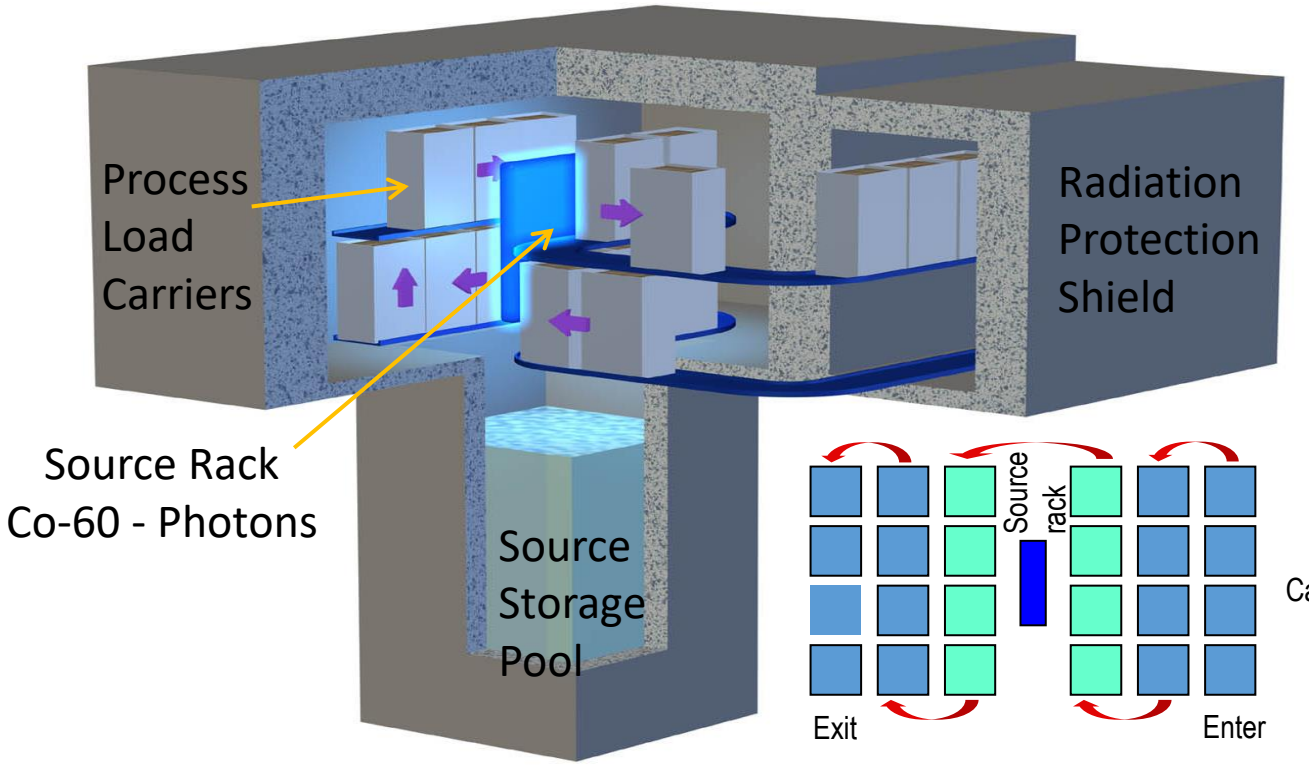
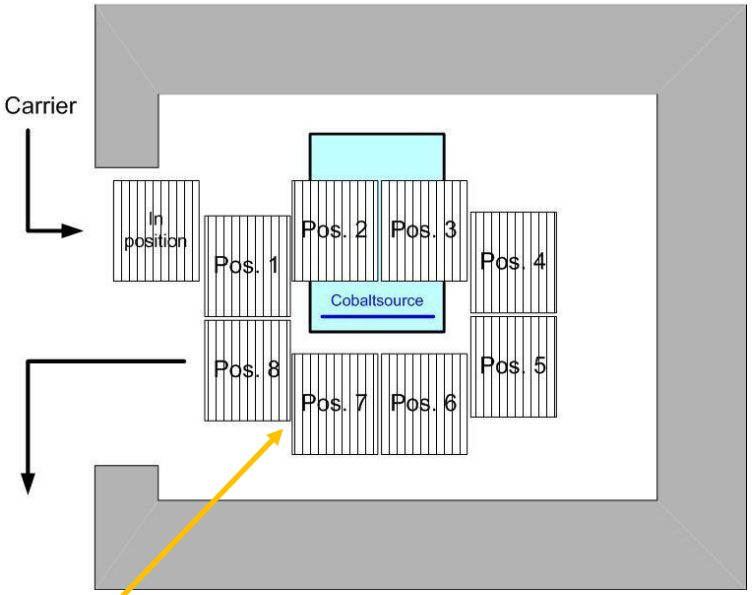
Technology Comparison: Gamma



Irradiation Pathway



Process Load
Pallet

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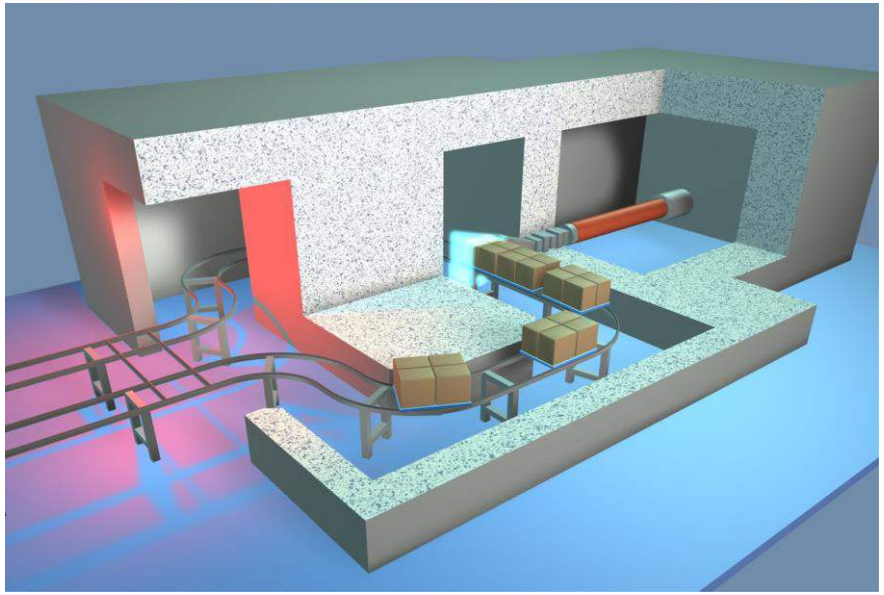
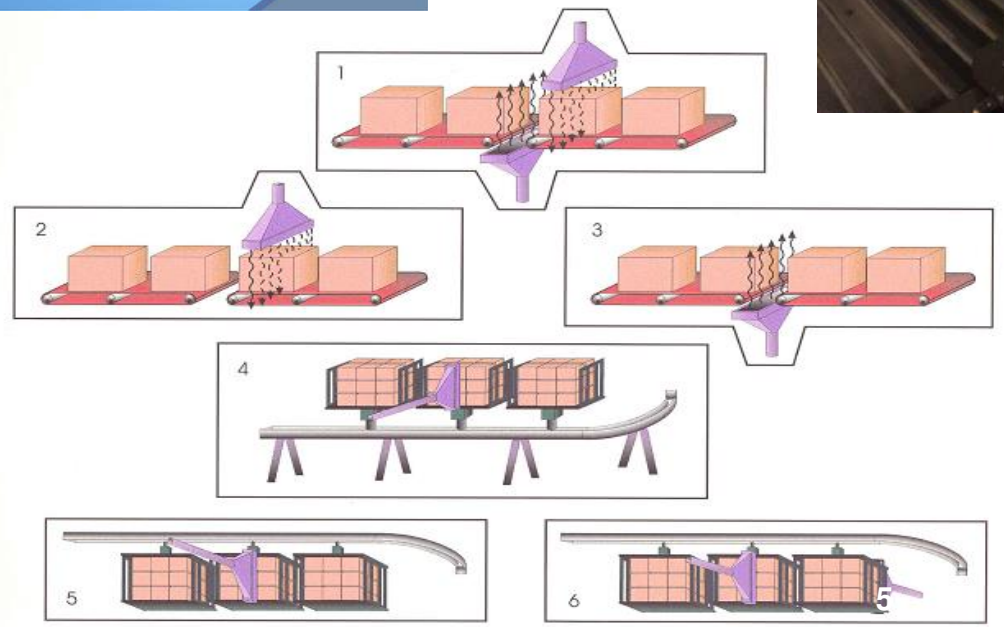
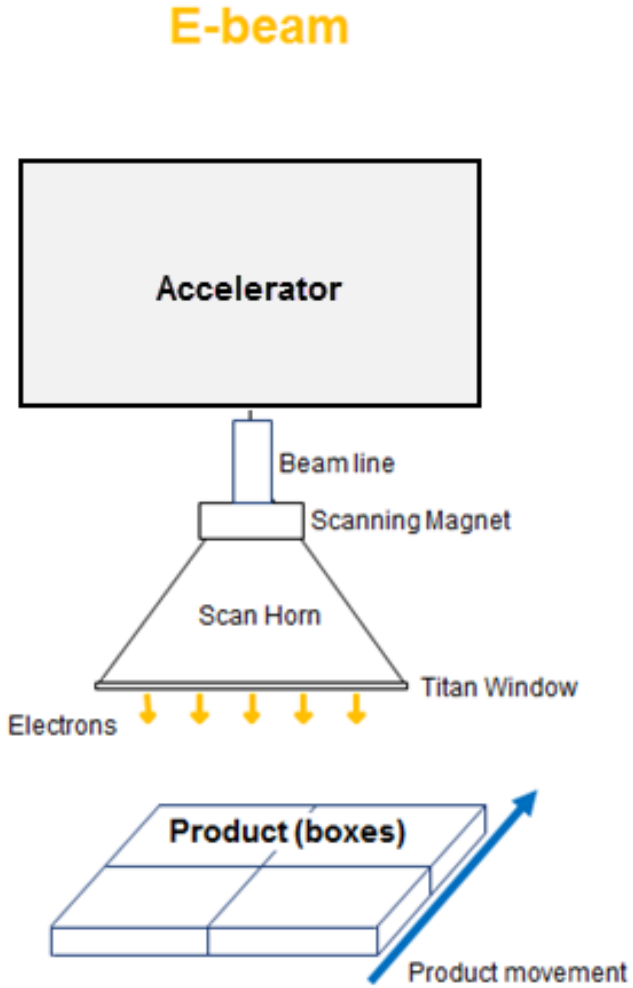
Technology Comparison: Electron Beam







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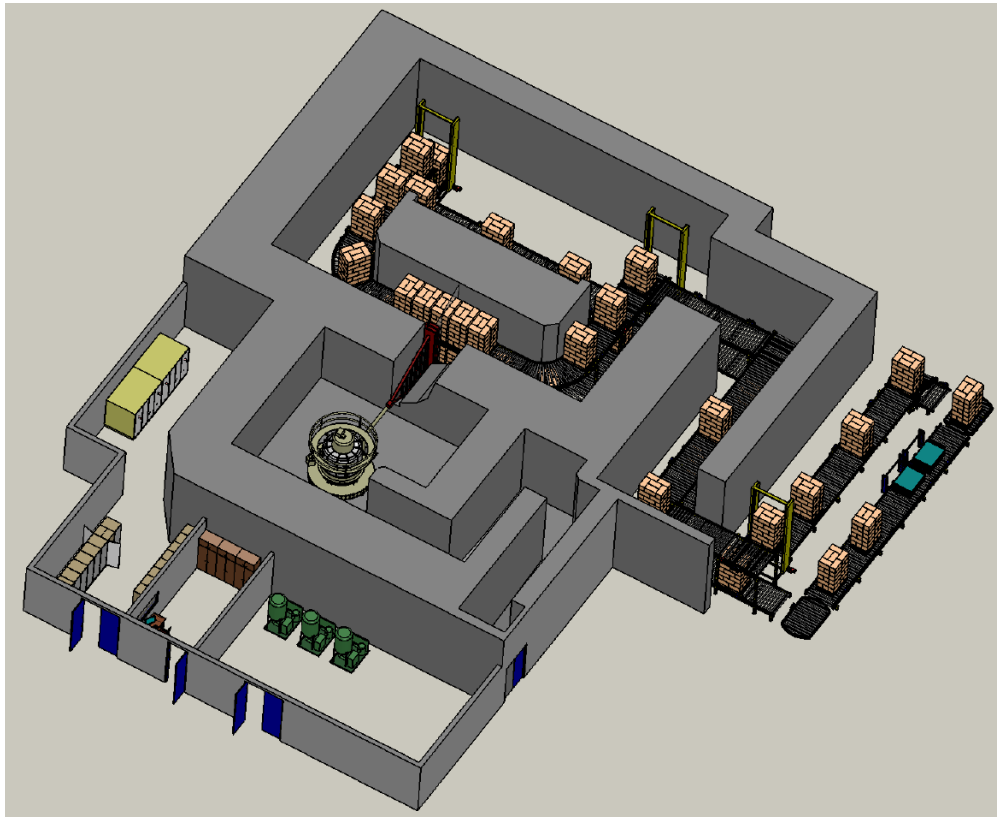
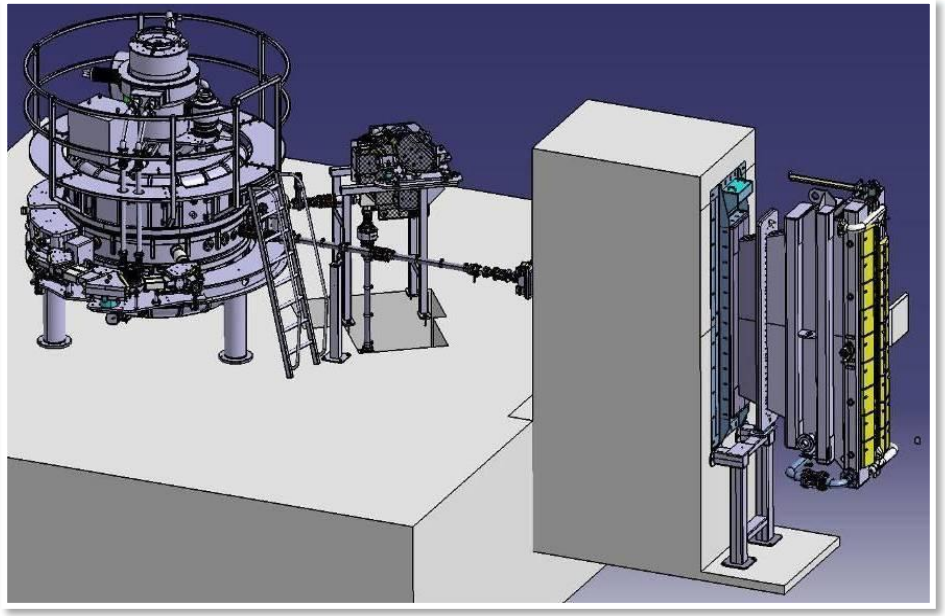
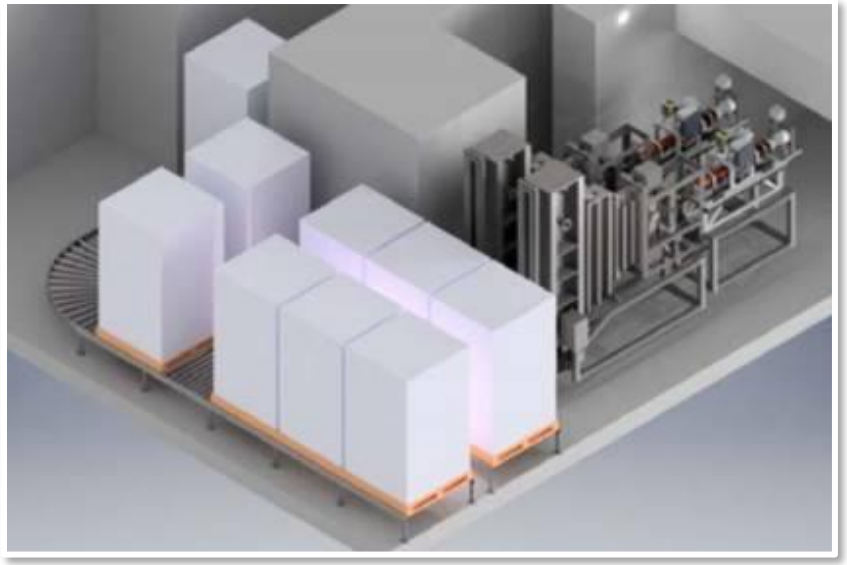
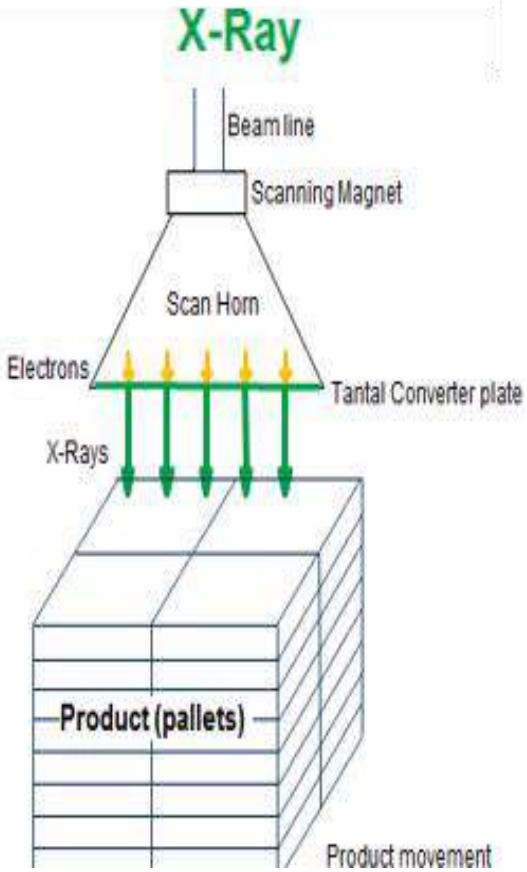
Technology Comparison: X-ray









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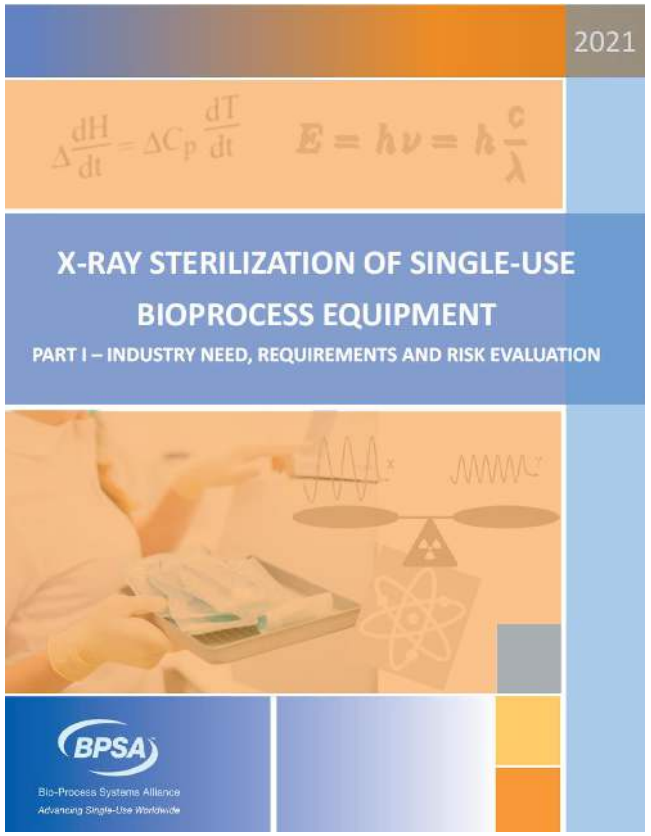
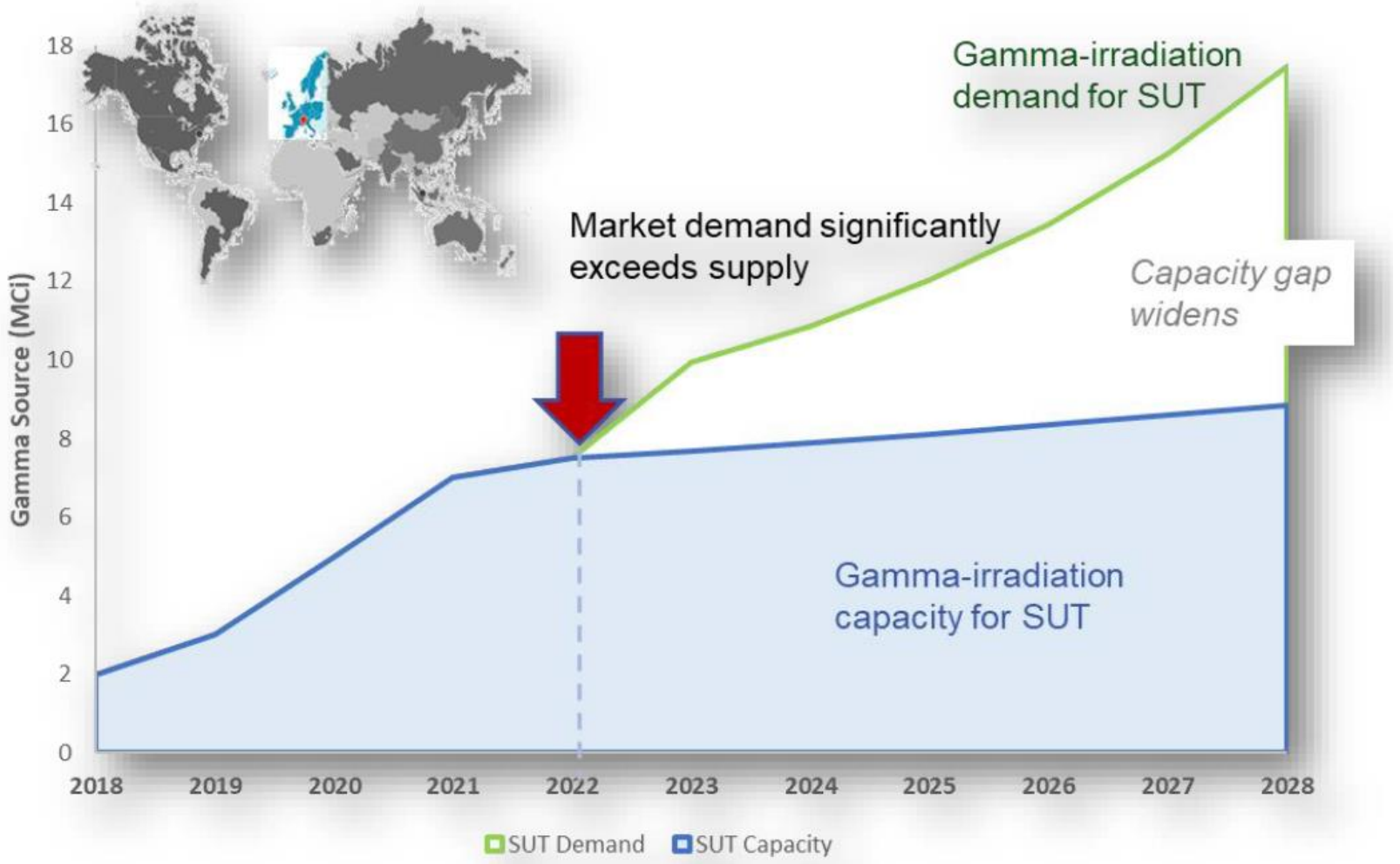
BPSA Publication



BPSA

X-RAY STERILIZATION OF SINGLE-USE BIOPROCESS EQUIPMENT:
PART I – INDUSTRY NEED, REQUIREMENTS AND RISK EVALUATION



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Technology Comparison: Dose is Dose

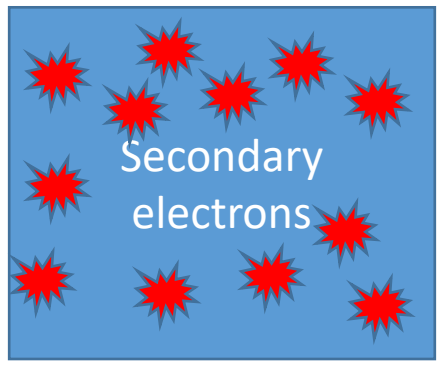
Ionizing Radiation Sources - Dose given by secondary electrons

- All three technologies create ionization of materials
- Each ionization results in electrons distributed in product
- Electrons created ionize additional secondary ionizations further distributing through the product
- Regardless of ionizing source, electrons which are created inside the matters are doing the work

Gamma (photons)

X-Ray (photons)

E-beam (electrons)



→ Dose in kGy

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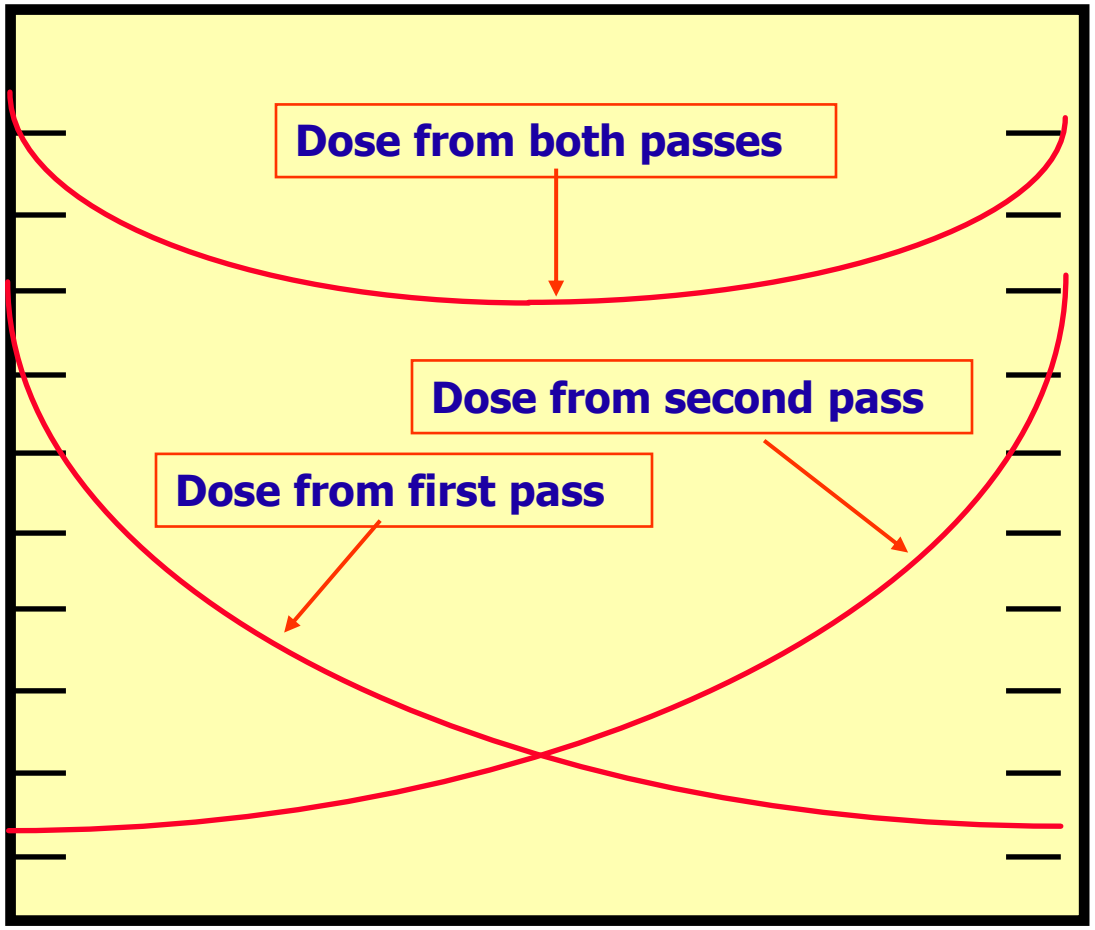
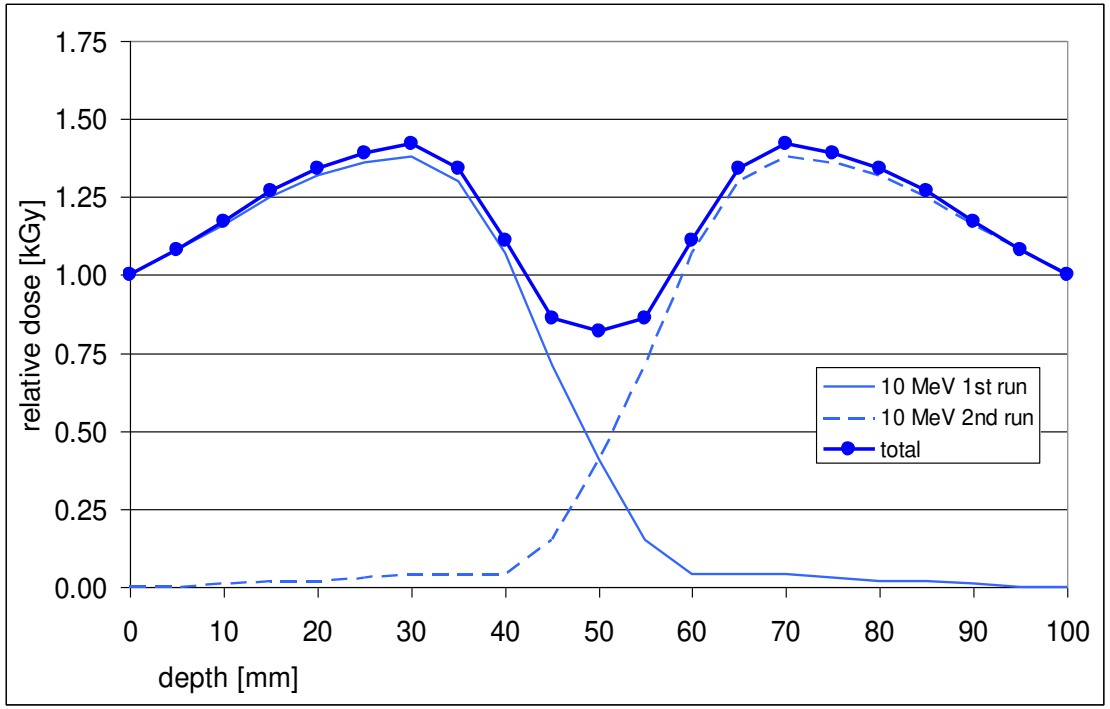
Technology Comparison: Penetration

Photons (Gamma and X-ray)



Electron Beam



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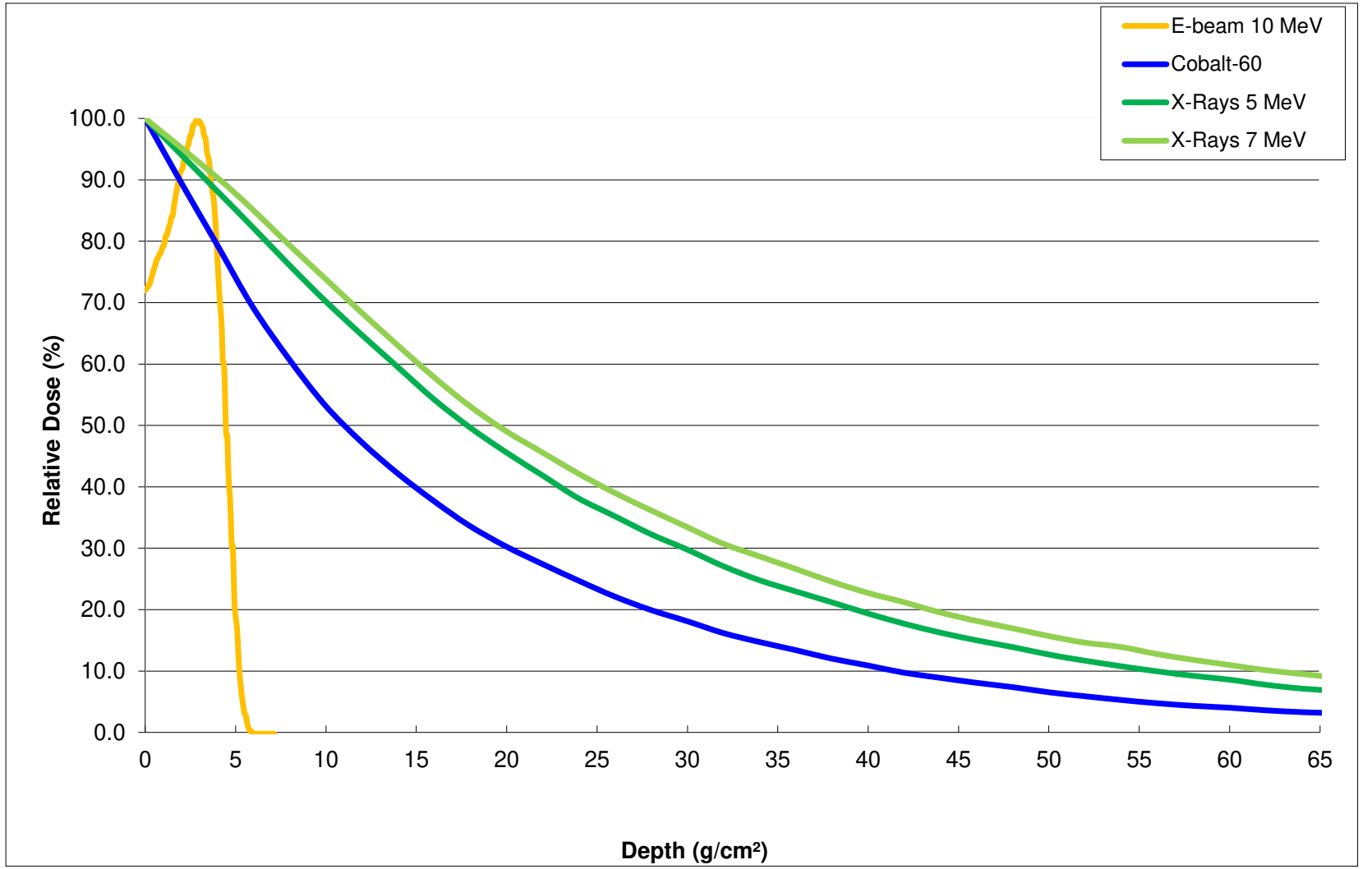
Technology Comparison: Penetration



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Technology Comparison: Summary

Process comparison

Technology	Process	Process Load	Radiation Field Design
Gamma	• Continuous • Batch • Incremental • Multi-pass	• Tote • Pallet	• Product overlapping • Source overlapping
X-ray	• Continuous • Batch • Incremental • Multi-pass	• Pallet	• Product overlapping • Source overlapping
Electron Beam	• Continuous • Batch	• Box • Carrier	• Source overlapping

Critical processing parameters:

- **Dose rate (kGy/h):** Risk of undesirable molecule recombination
- **Exposure time:** Risk of undesirable molecule recombination, ozone impact
- **Process capability:** Maximal dose received to achieve minimal required dose
- **Irradiation temperature**: Impact on some active material

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Technology Comparison: Summary

	Gamma	E-beam	X-ray
Mode of action	Isotropic **Photons**	Electron	**Photons** with almost the same direction
DUR (~ 0.20 g/cc)	Dose range achievable : 25-40 kGy	Dose range achievable : 25-50 kGy	Dose range achievable : 25-35 kGy
	Ideal: 25-50 kGy	**Ideal: 25-60 kGy**	**Ideal: 25-40 kGy**
Dose rate	Variable during process A few kGy/h	Constant during process A few thousand kGy/h	Variable during process A few kGy/h to a few hundred of kGy/h
Temperature	Depends on design and Cobalt activity	Depends on power	Depends on power and design
	Typically, maximum temperature can go to 45 to 50°C	**Typically, maximum temperature can go to 50°C**	**Typically, maximum temperature can go to 35°C to 40°C**

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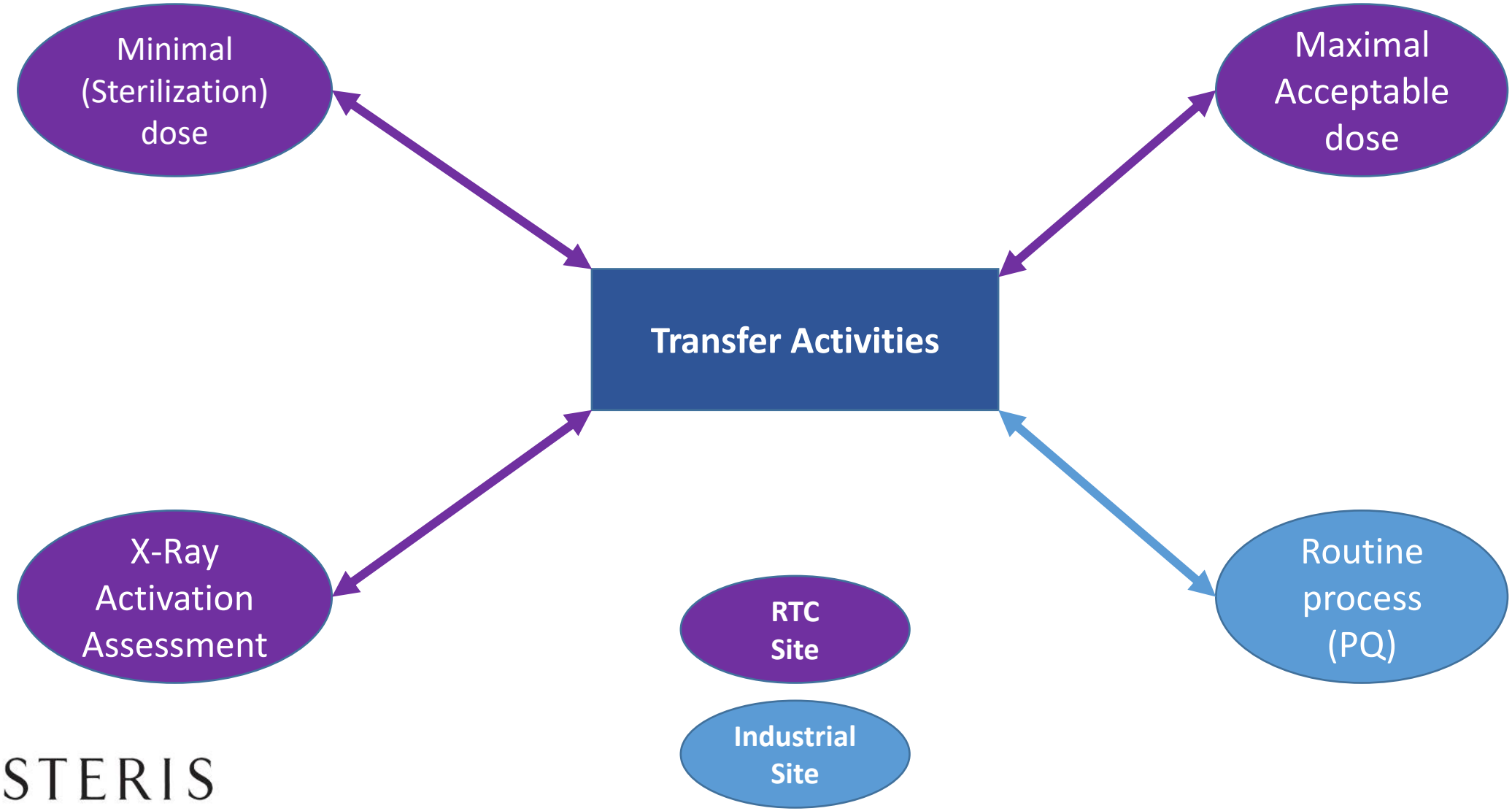
Consideration: Transfer activities



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Consideration: Minimal or Sterilization dose transfer

Transfer of verification dose or sterilisation dose (Section 8.4, 11137-1):

- Product not containing liquid water (dry product):
  - ✓ Transfer between facility operating the same radiation source is permitted without assessment
  - ✓ Transfer to different type of radiation source: assessment required

- Product containing liquid water:
  - ✓ Gamma to gamma is permitted
  - ✓ Two electron or X-ray operating under identical operating condition: permitted
  - ✓ Transfer to different type of radiation source: assessment required

Microbiological effectiveness of all 3 technologies has been demonstrated as equivalent therefore:

→ **ISO 11137: Assessment consist of performing a Dose Audit exercise Other: Minimal dose used at current technology can be used (publication)**

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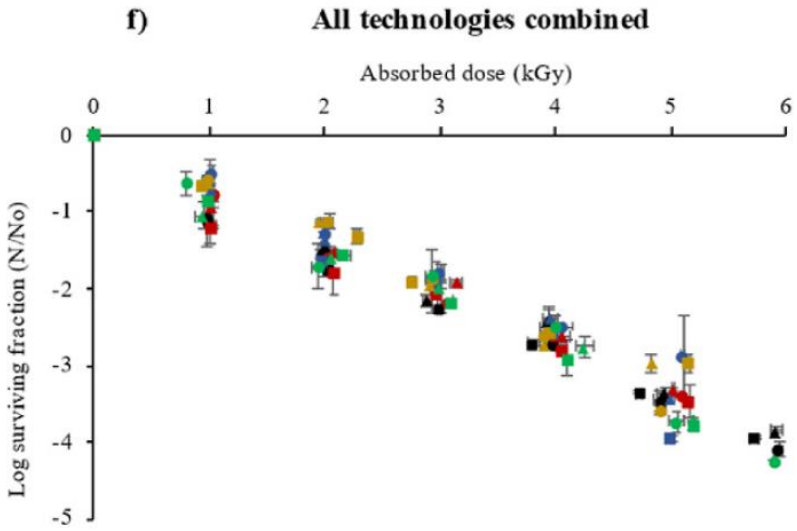
Publications : Minimal / Sterilization dose

Radiation Sterilization: Dose Is Dose

Joyce M. Hansen, Niki Fidopiastis, Trabue Bryans, Michelle Luebke and Terri Rymer
AAMI (2020)

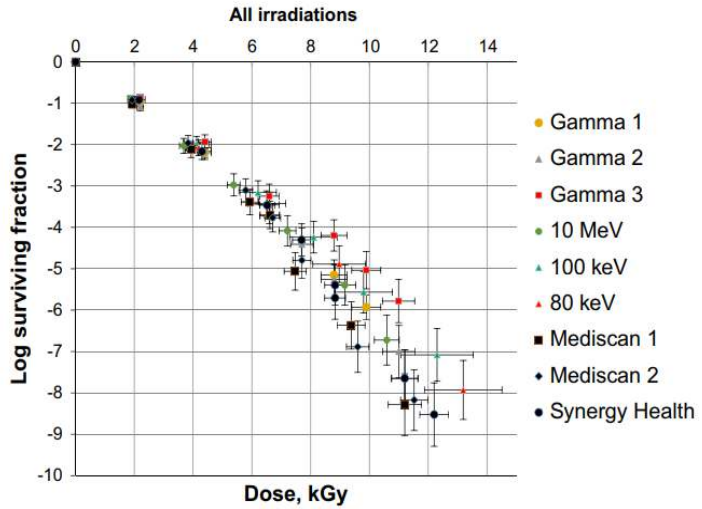


Studies on the comparative effectiveness of X-rays, gamma rays and electron beams to inactivate microorganisms at different dose rates in industrial sterilization of medical devices.

Brian McEvoy, Ana Maksimovic, Daniel Howell, Pierre Reppert, Damien Ryan, Neil Rowan, Herve Michel (2023)
Radiation Physics and Chemistry

Microbicidal effectiveness of X-rays used for sterilization purposes

Tallentire, A. and Miller, A. (2015)
Radiation Physics and Chemistry



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Consideration: Maximal acceptable dose transfer

ISO 11137-1: 8.1.1, The maximum acceptable dose for product shall be established. When treated with the maximum acceptable dose, product shall meet its specified functional requirements throughout its defined lifetime.

This statement is not specific to X-Ray, Gamma or EBeam. It applies to all three.

Clause 8.4.1 states that an assessment must be made to ensure that differences in conditions of two radiation modalities do not affect the validity of the maximum acceptable dose.

→ Assessment to be made → Risk Based Approach

Solutions: Risk based approach – Example 1

Critical processing parameters:

- **Dose rate:** Risk of undesirable molecule recombination
- **Exposure time**: Risk of undesirable molecule recombination, ozone impact
- **Process capability**: Maximal dose received to achieve minimal required dose
- **Irradiation temperature**: Impact on some active material

Processing Parameters	Gamma	X-ray	Electron beam
Dose rate	**3**	**2**	**1**
Exposure time	3	2	1
Maximal dose	2	1	3
Minimal dose	0	0	0
Irradiation temperature	3	1	2
Process capability	2	1	3
Total	**13**	**7**	**10**

0 Equivalent, 1 Best; 2 Medium; 3 worst

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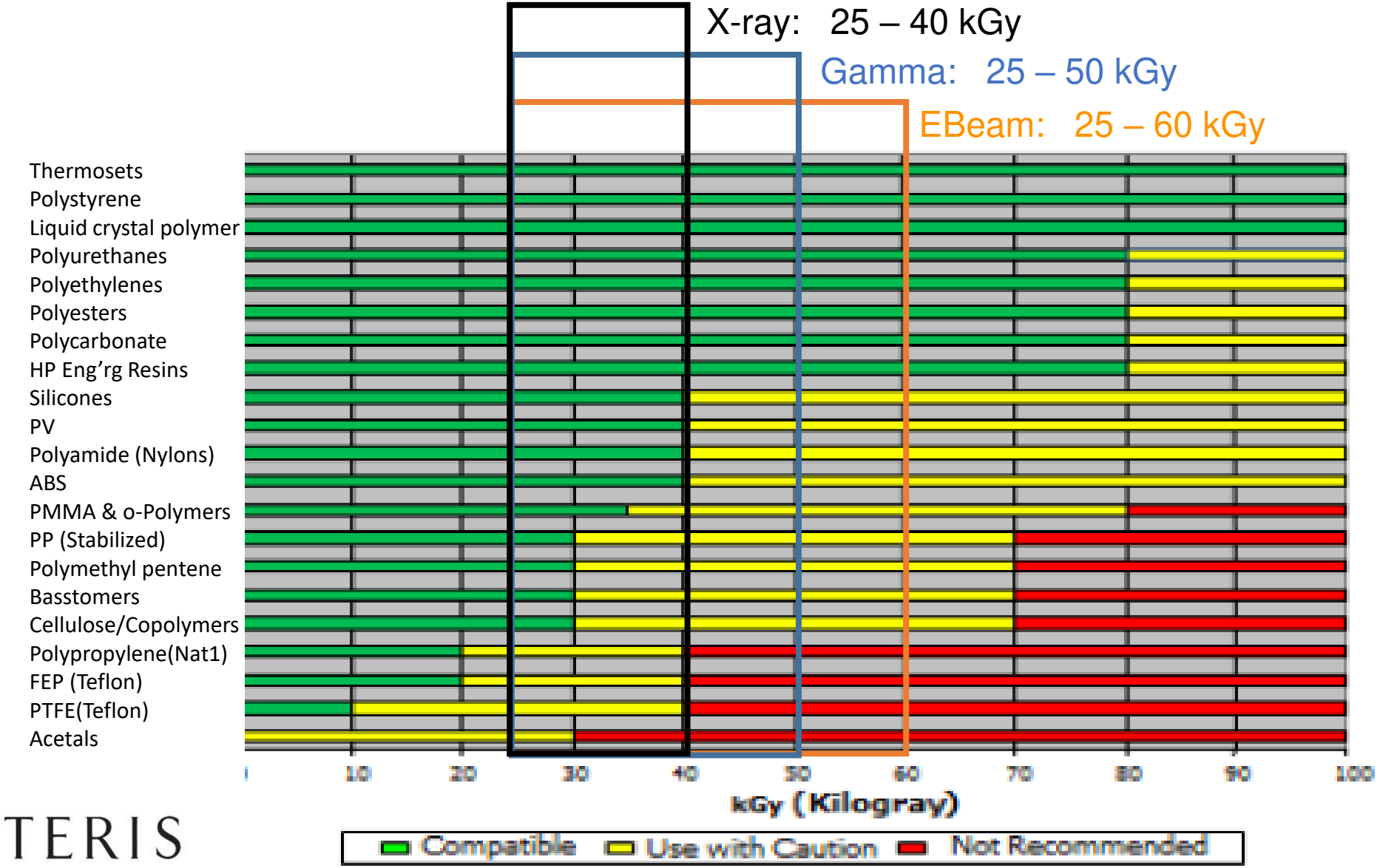
Solutions: Risk based approach – Example 2

Technology transfer - photons to photons
Using a risk-based approach

	X-ray vs Gamma	Risk Evaluation
Sterilization / Minimal Dose	Equivalent	No
Maximal routine dose	Lower or Equivalent	No
Dose rate (kGy/h)	higher	Low
Temperature during process	Lower or Equivalent	Low
Exposure Time	Less	Low
Penetration (DUR)	Better or Equivalent	No
Product handling	Equivalent	No

Publications: AAMI Tir17: Compatibility of Materials subject to sterilization



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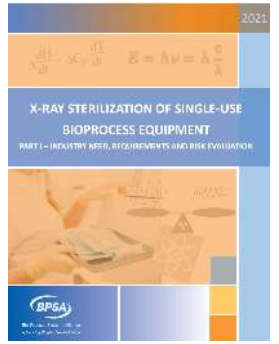
Publications : Maximal Acceptable dose

X-ray: An effective Photon
Brian McEvoy, Hervé Michel, Daniel Howell and Philip Roxby
AAMI 2020



X-RAY STERILIZATION OF SINGLE USED BIOPROCESS EQUIPMENT Part I: Industry need, Requirements and Risk Evaluation
*BPSA (*2021)

Regulatory Approach for Transitioning from Gamma Ray to X-ray Radiation Sterilization
Alan Montgomery, Romain Bolle-Reddat, Shari Formica, Bradley Lundahl and Gerald McDonnell (AAMI 2021)

X-ray sterilization of biopharmaceutical manufacturing equipment
Roberto Menzel, Samuel Dorey, Tanja Maier, Ina Pahl, Armin Hauk
Biotechnology Progress 2021

BIOTECHNOLOGY PROGRESS

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Consideration: Activation assessment

Activation
ISO 11137-1 5.1.1 asks for an evaluation of a potential activation of materials with X-ray irradiation exceeding 5 MeV, or E-Beam with a >10 MeV E-beam treatment, even if the risk of activation of product is very small.

→ All products (Polymers, Implants, Animal feeds, API) tested to date at maximal acceptable dose have been declared as non-activated.

Tests were performed at SUVA (Swiss Government Accredited Laboratory) or at STERIS Libertyville RTC

Potential Induced Radioactivity in Material Process with X-ray Energy above 5 MeV
Hervé Michel, Thomas Kroc, Brian McEvoy, Deepak Patil, Pierre Reppert and Mark Smith – 06/2021

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Consideration: Routine process transfer

Transference of Performance Qualification (mapping)

The transfer of performance qualification results is not possible as almost each installation and site are different

Statement valid for all 3 technologies

→ **PQ must be performed in accordance with ISO 11137 to assure the product specification can be met.**

Conclusions :

Critical processing parameters:

- **Dose rate (kGy/h):** Risk of undesirable molecule recombination
- **Exposure time:** Risk of undesirable molecule recombination, ozone impact
- **Process capability:** Maximal dose received to achieve minimal required dose
- **Irradiation temperature:** Impact on some active material

Considerations:

- Should the transfer from Gamma (photons) to X-ray (photons) be considered as a technology transfer?
- Can Gamma Qualification be considered as a worst-case scenario?

Solutions:

- Risk Based Approach
- Publications

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Thank You!

Don’t hesitate if you have questions in the future…
We are here to help!

Pierre Reppert
STERIS AST
RTC Senior Manager EMEA-APAC
Email: pierre_reppert@steris.com

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