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Passion for patients

Driving collaborative innovation

Kilmer Community 2019

Gamma to e-beam/x-ray: fundamentals to practice

Byron J. Lambert, PhD
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Fermilab

Fermi National Accelerator Laboratory

Midwest Medical Device Sterilization Workshop

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E-BEAM / X-RAY STERILIZATION

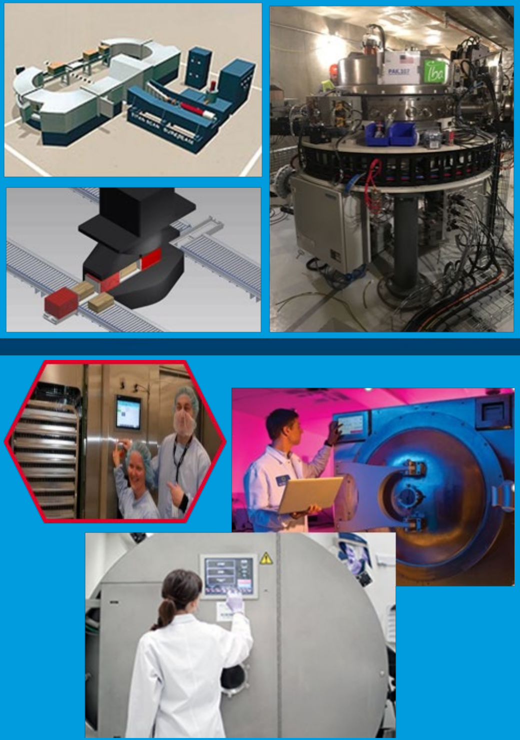
85+%
of the sterilization market

EO

Gamma

ALTERNATIVE GAS STERILIZATION (AGS)

Innovation Over Decades



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OBJECTIVE – facilitate success: Gamma → E-beam / X-ray

- Leverage fundamental scientific realities of ionizing radiation
- Optimally apply practical industry guidance

AGENDA

- Fundamentals → 'follow the electrons'
- Exercise: interpret guidance in ISO 11137-1 radiation sterilization standard
- Practical guidance – AAMI TIR17: material compatibility potential & pitfalls
- Summary

Intensive Course On Irradiation Effects

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Professor Mohamad Al-Sheikhly

Section 1 - Introduction

January 24-30, 2019

J. Silverman, *Radiation processing: The industrial applications of radiation chemistry*, J. Chem Ed 58 (1981) 168–173, https://doi.org/10.1021/ed058p168 Accessed 17Sep'19

AAMI TIR17:2008

Guidance –AAMI TIR17:2008 Compatibility of Materials Subject to Sterilization

November 19, 2009
Presented by

AAMI

Association for the Advancement of Medical Instrumentation

Sterility Assurance

Module 4:
Packaging and material compatibility
Maintenance of validation

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Senior Associate Fellow,
Sterilization
Abbott Vascular

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Manager, Engineering
Sterilization
Abbott Vascular

AdvaMed
Advanced Medical Technology Association

May'19; Potentially available in the future

Types of Ionizing Radiation

Penetration
- needs to be managed
- outside the scope of this talk

Max Acceptable Dose
- needs to be managed
- outside the scope of this talk

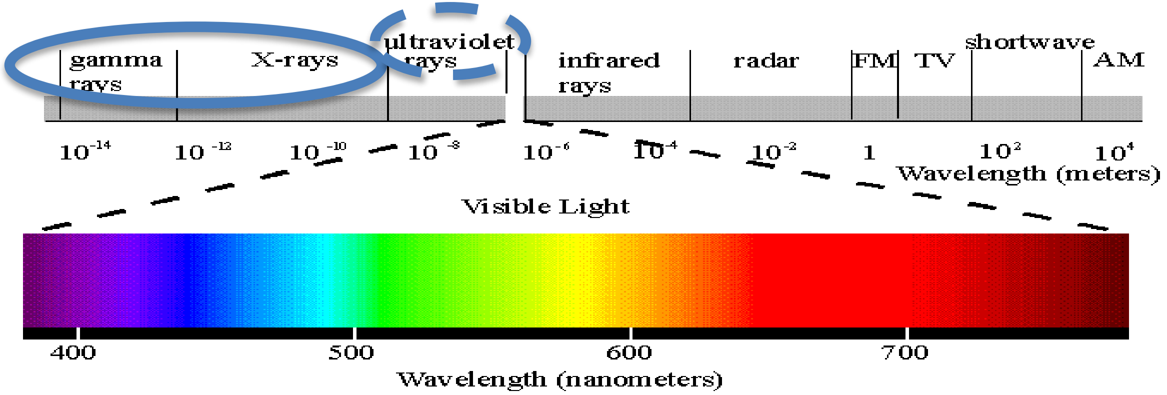
- Alpha
  - He^{2+}

  Very shallow penetration depths

- Beta
  - Electrons

  Penetration depends on energy

- Photons
  - Gamma
  - X-ray
  - UV light



Interaction of Ionizing Radiation with Matter

10^{-18} 10^{-15} 10^{-12} 10^{-9} 10^{-6} 10^{-3} 1 sec

Energy deposition

- Formation of ionized and excited molecules localized along tracks
- Ions and excited molecules react/dissociate forming free radicals. Electrons solvated in polar media

Chemical Processes

- Radicals and solvated electrons diffuse from track zones, react with other molecules.
- Chemical changes to substrate occur.

'Follow the electrons'

Gamma, E-beam and X-ray deposit energy through the SAME MECHANISM, IONIZATION by ELECTRONS

- **Direct Effect**
  - M $\rightsquigarrow$ M^+, e^-, M^* (Ionization, excitation)
- Indirect Effect
  - Secondary reactions of solute with primary species formed by solvent

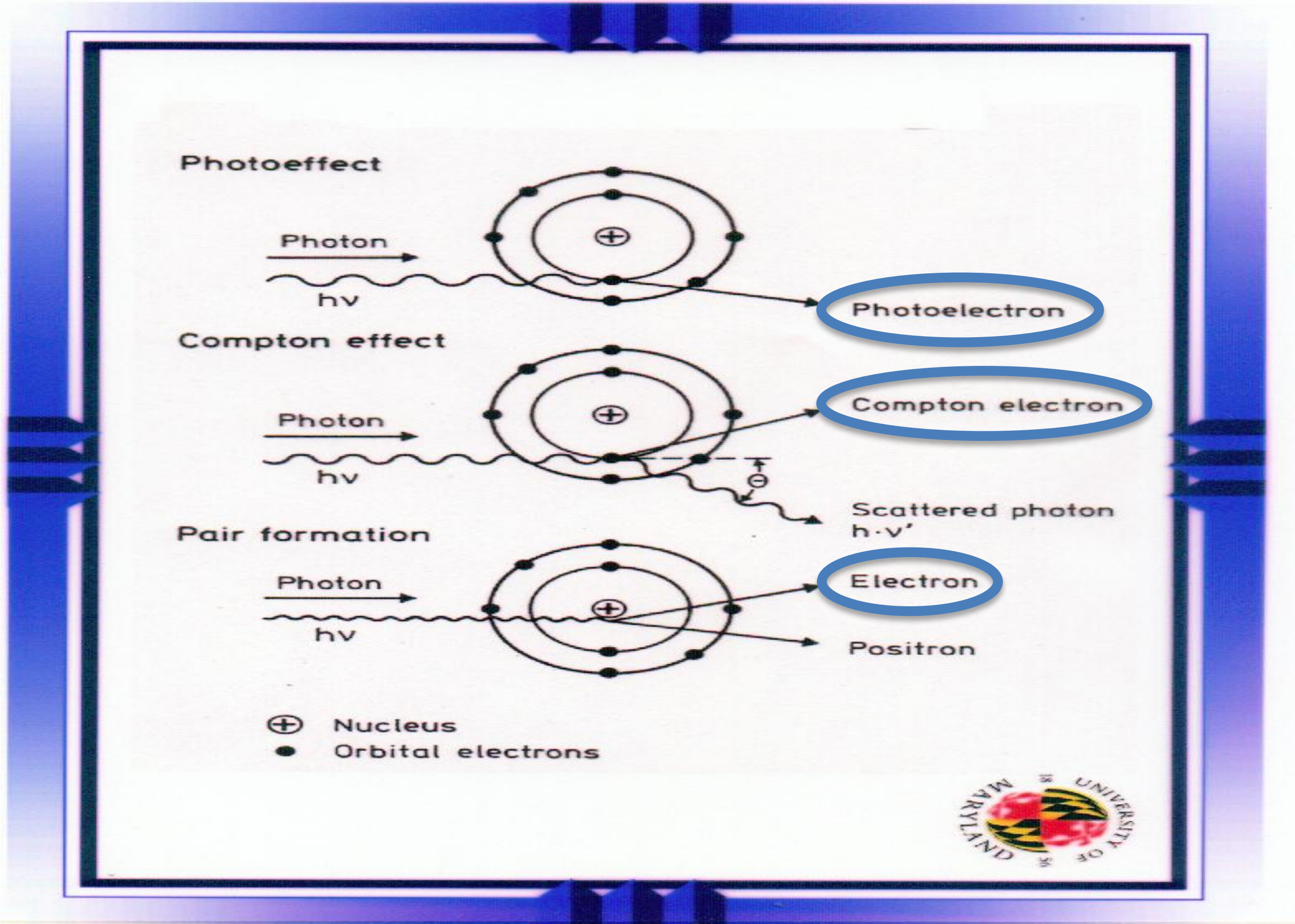
Gamma Radiation - Possible "Energy Deposition" Interactions of Photons

Radiation dose

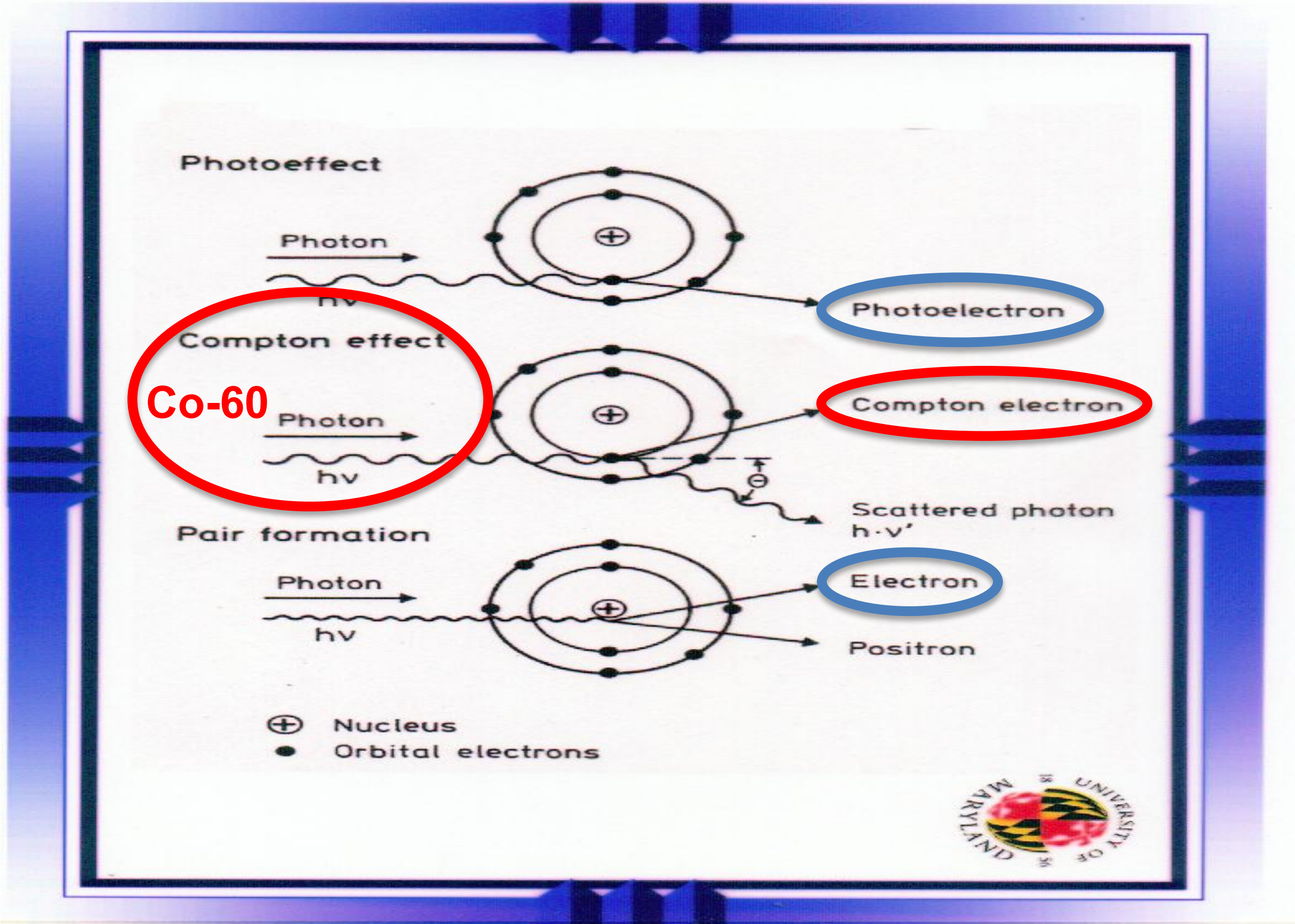
kGy

kJ/kg

Energy deposition into mass of materials



Gamma Radiation - Possible "Energy Deposition" Interactions of Photons



Compton Scattering - Gamma Sterilization with Co-60

In Compton scattering, an incoming photon makes contact with an orbital electron and transfers some of its energy to it. The result is a free "recoil" electron travelling at an angle υ and the photon deflected at angle θ.

Co-60 Compton electron: ≈ 0.5 MeV
≈ 500,000 eV

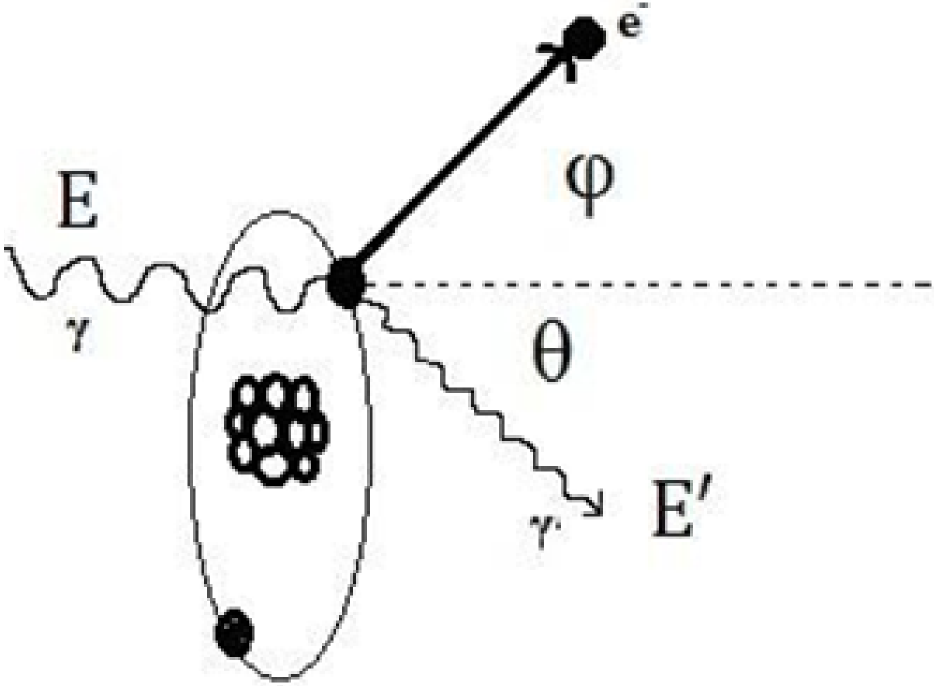


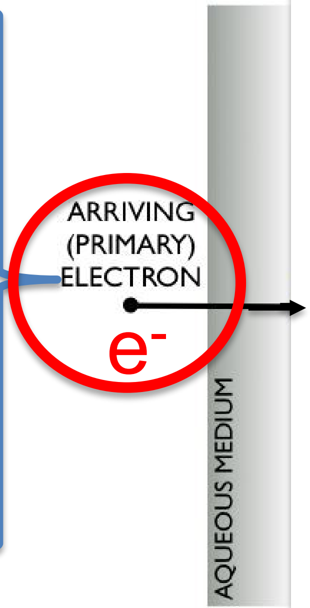
Figure 2.2.5 Compton Scattering

Energy Deposition by Electrons, e$^-$

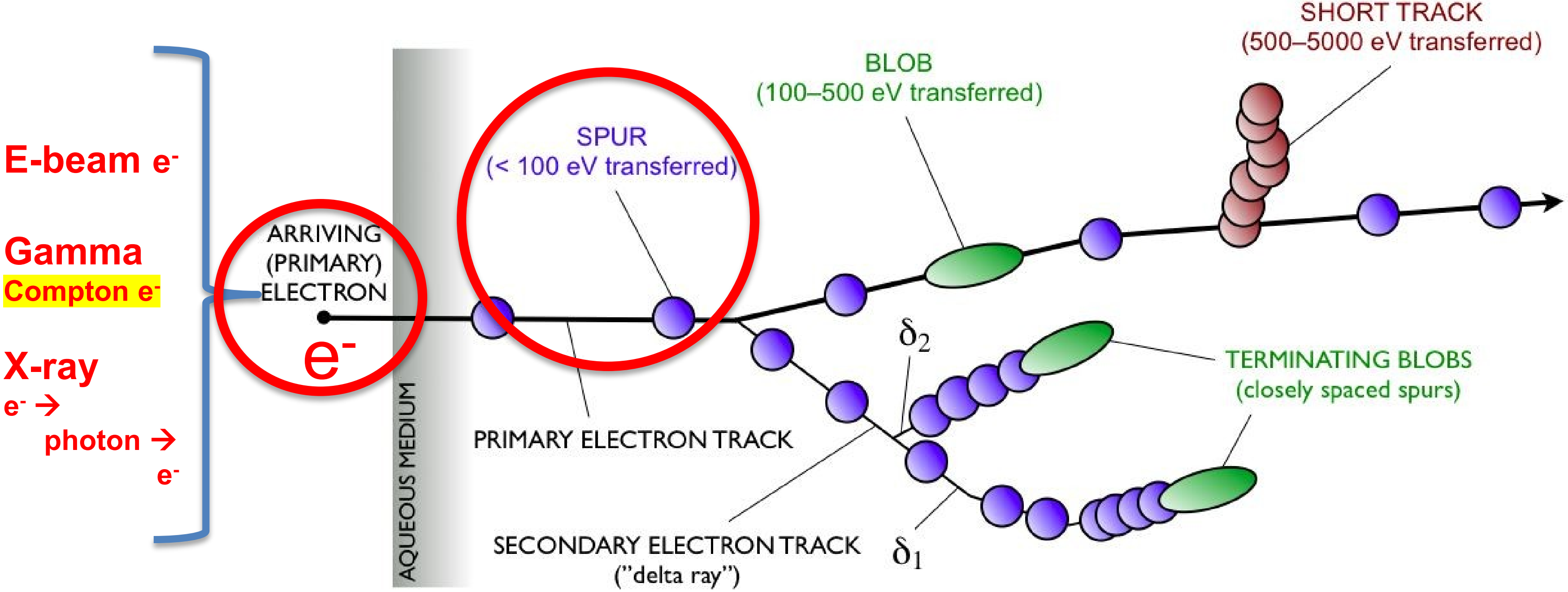
E-beam e$^-$

Gamma
Compton e$^-$

X-ray
e$^-$ →
photon →
e$^-$



Energy Deposition by Electrons, e⁻



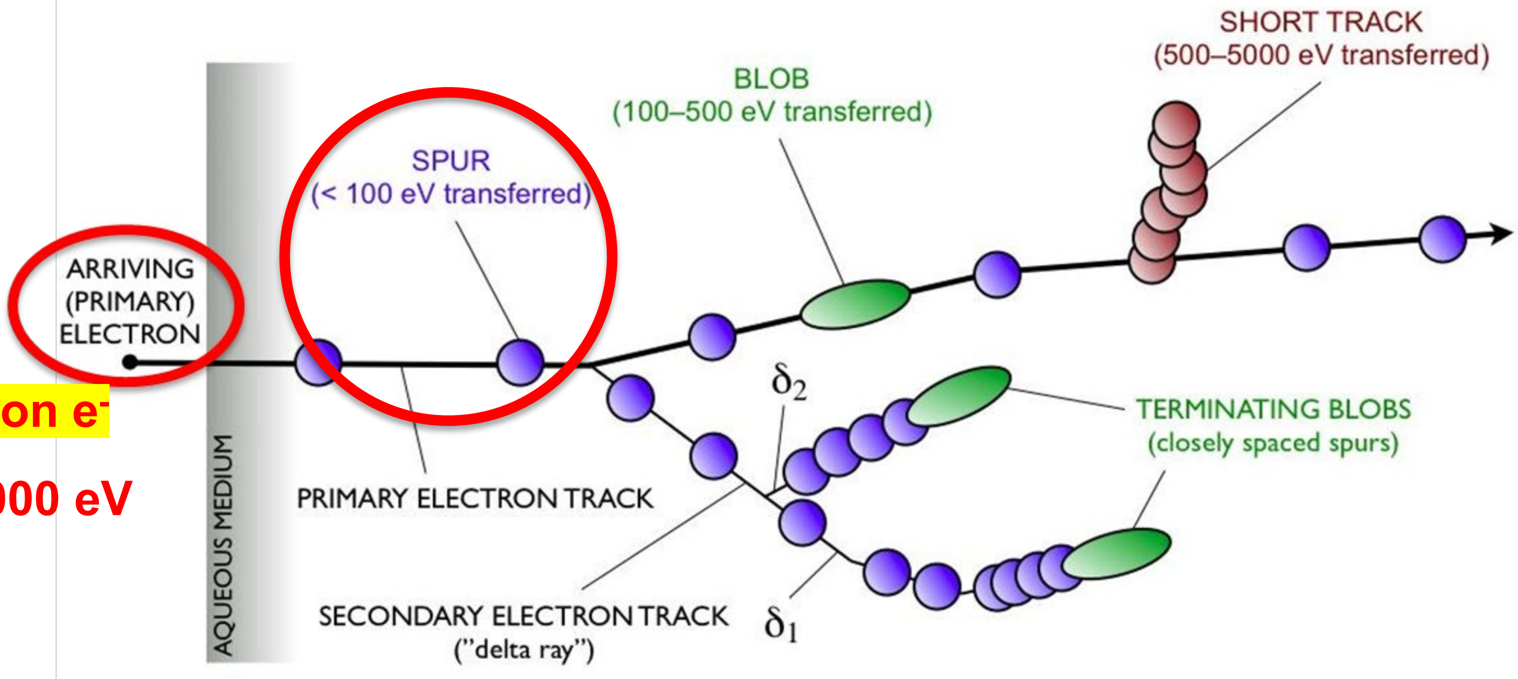
Energy Deposition by Electrons, e^-

… dominates radiation effects

Co-60

Compton e^-

≈ 500,000 eV



One Co-60 photon → one Compton e^-

≈ 500,000 eV = [(100 eV/spur) * (5,000 spurs)]

Dose, dose rate & temperature normalized radiation effects **are identical** between Gamma, E-beam and X-ray

American National Standard

ANSI/AAMI/ISO 11137-1:2006

Sterilization of health care products—Radiation— Part 1: Requirements for development, validation, and routine control of a sterilization process for medical devices

AGENDA

- Fundamentals → 'follow the electrons'
- **Exercise: interpret guidance in ISO 11137 radiation sterilizat'n standard**
- Practical guidance – AAMI TIR17: material compatibility potential & pitfalls
- Summary

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8.4 Transference of maximum acceptable, verification, or sterilization dose between radiation sources

8.4.1 Transference of maximum acceptable dose

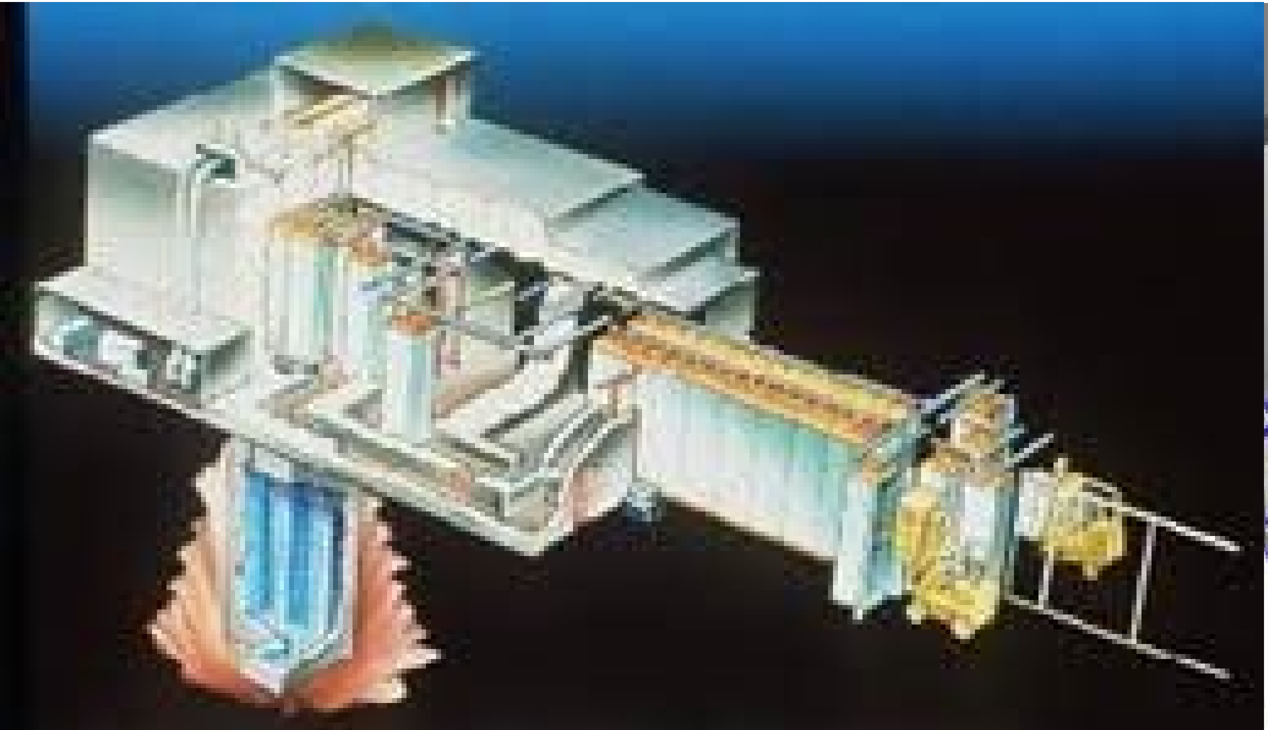
In transferring a maximum acceptable dose to a radiation source different from that on which the dose was originally established, an assessment shall be made demonstrating that differences in irradiation conditions of the two radiation sources do not affect the validity of the dose. The assessment shall be documented and the outcome shall be recorded (see 4.1.2).

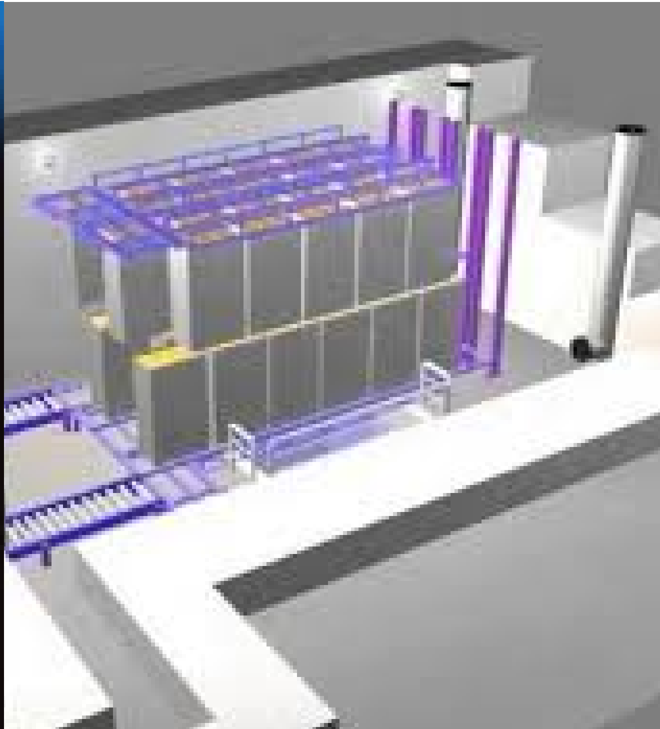
Gamma E-beam X-ray

Abstract: Specifies requirements for validation, process control, and routine monitoring in the radiation sterilization for health care products. It applies to continuous and batch type gamma irradiators using the radionuclides 60 Co and 137 Cs, and to irradiators using a beam from an electron or X-ray generator.

8.4 Transference of maximum acceptable, verification, or sterilization dose between radiation sources

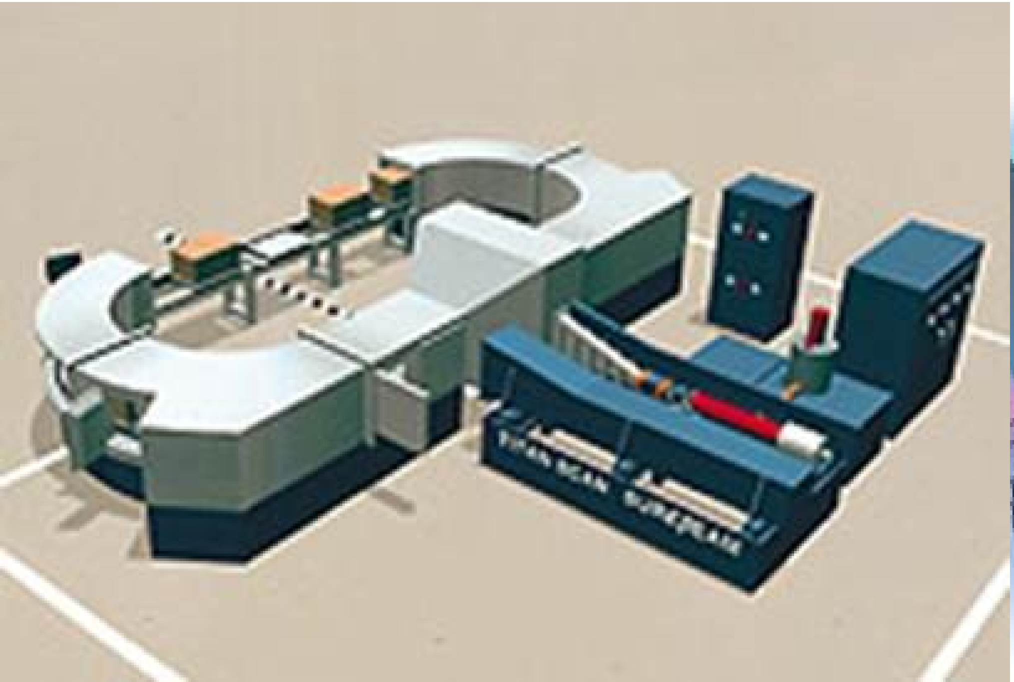
Gamma

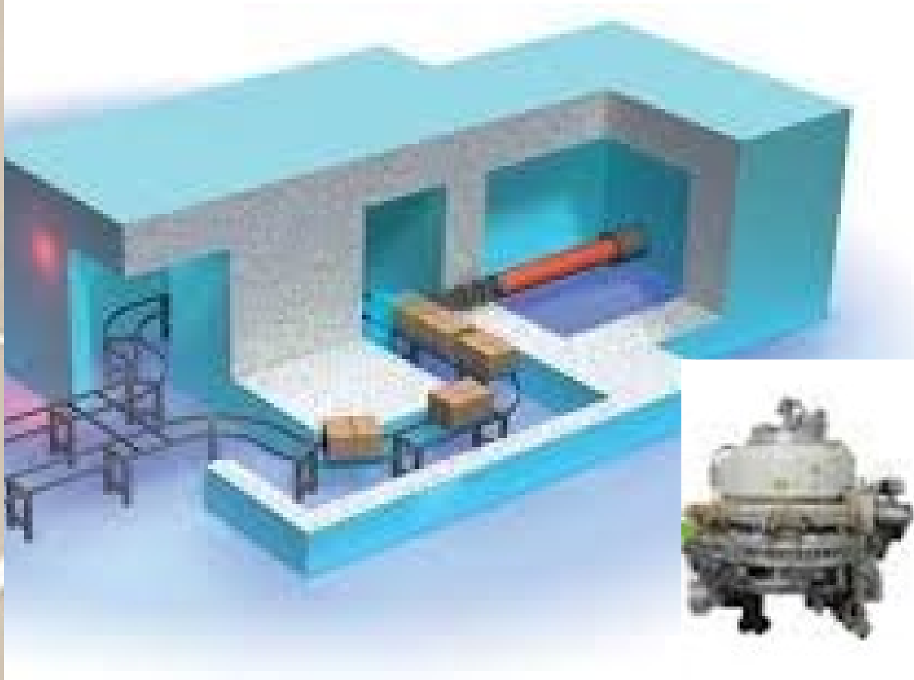




8.4 Transference of maximum acceptable, verification, or sterilization dose between radiation sources

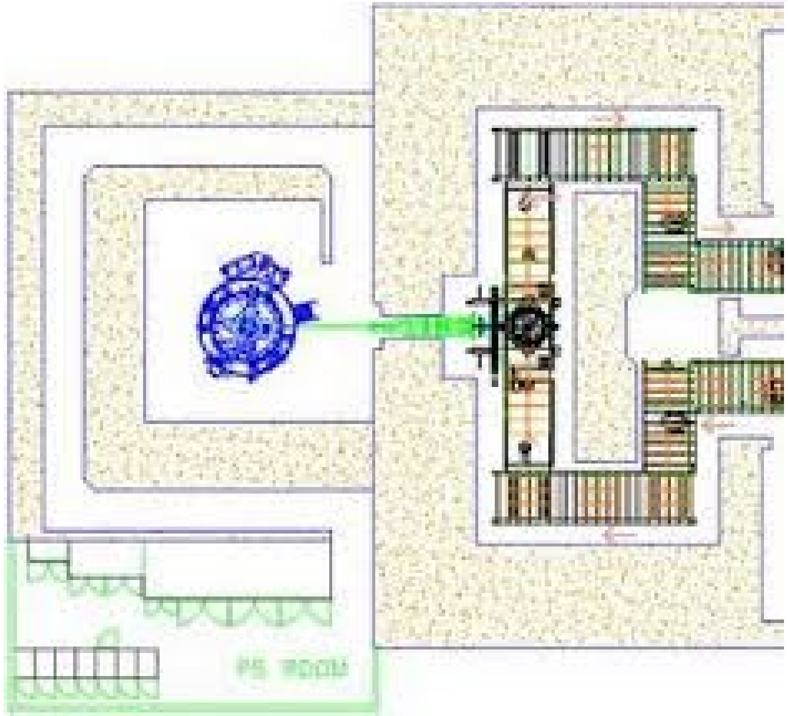
Electron Beam (E-beam)

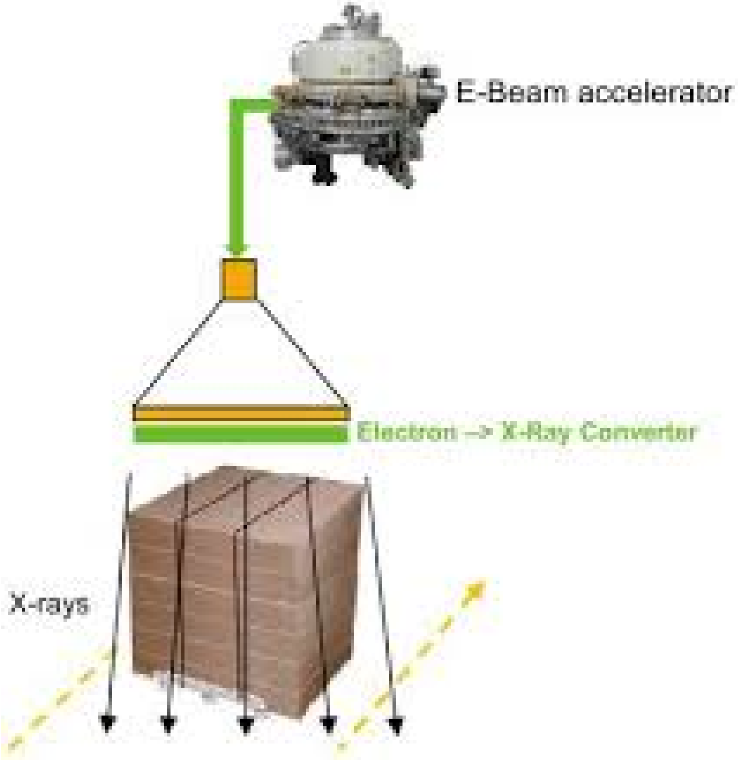




8.4 Transference of maximum acceptable, verification, or sterilization dose between radiation sources

X-ray





8.4 Transference of maximum acceptable, verification, or sterilization dose between radiation sources

8.4.1 Transference of maximum acceptable dose

A.8.4 Transference of maximum acceptable, verification, or sterilization dose between radiation sources

A.8.4.1 Transference of maximum acceptable dose

The assessment of the validity of the maximum acceptable dose for a radiation source other than that on which the dose was originally established should take into consideration dose rate and product temperature during irradiation. For example, the higher the dose rate, the lower the unwanted effects upon product.

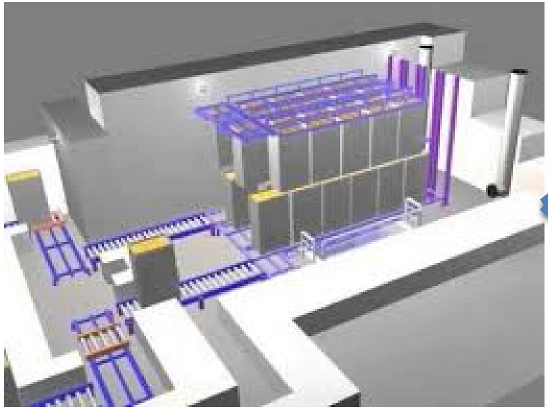
A product qualified at a low dose rate (gamma or X-rays) will typically require minimal qualification to demonstrate material compatibility at a higher dose rate (electron-beam). Conversely, a material qualified at a high dose rate may require more substantial qualification in the low dose rate application.

If dose rate and product temperature are equivalent, transfer between the same type of radiation sources is appropriate.

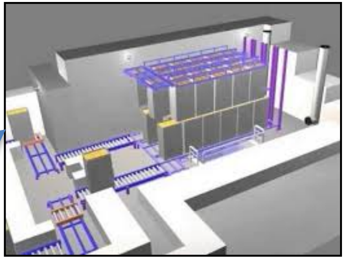
ANSI/AAMI/ISO 11137-1:2006

8.4 Transference of maximum acceptable, verification, or sterilization dose between radiation sources

DOSE RATE

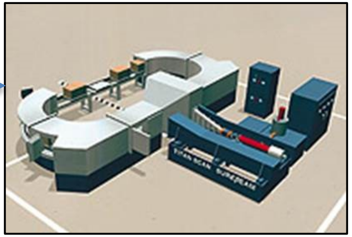


Gamma – approx. 2 Gy/s
E.g., 25 kGy in **4 hours**

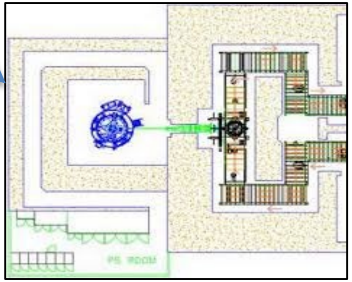


Gamma – approx. 2 Gy/s
E.g., 25 kGy in **4 hours**

Delta is 3-4 Orders of magnitude



E-beam – approx. 6,000 Gy/s
E.g., 25 kGy in **4 seconds**



X-ray – approx. 10–1,000 Gy/s
E.g., 25 kGy in **1 min to 1 hour**

8.4 Transference of maximum acceptable, verification, or sterilization dose between radiation sources

8.4.1 Transference of maximum acceptable dose

In transferring a maximum acceptable dose to a radiation source different from that on which the dose was originally established, an assessment shall be made demonstrating that differences in irradiation conditions of the two radiation sources do not affect the validity of the dose. The assessment shall be documented and the outcome shall be recorded (see 4.1.2).

Differences in irradiation conditions

1. Dose rate – why is this important? C/o radiation-oxygen effects
2. Temperature – important c/o product sensitivities, e.g., T_g
3. Environment - an inert gas, e.g., N_2, in a non-permeable package can mitigate radiation-oxygen effects

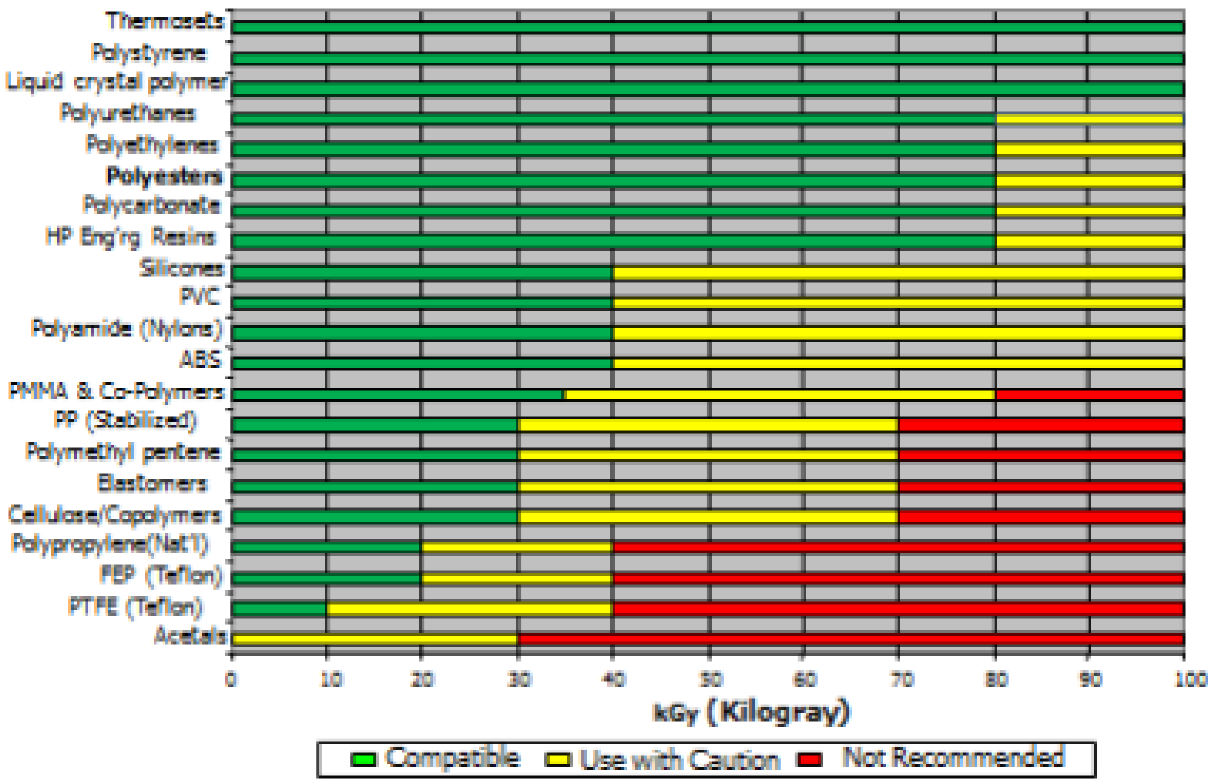
AGENDA

- Fundamentals → 'follow the electrons'
- Exercise: interpret guidance in ISO 11137 radiation sterilization standard
- **Practical guidance –AAMI TIR17: material compatibility potential & pitfalls**
- Summary

AAMI TIR 17:2017

Compatibility of Materials Subject to Sterilization

1. **Material Selection Guidance**
2. Material Processing & Design Considerations
3. Clinically Relevant Material Testing
4. Accelerated Aging Programs



AAMI TIR 17:2017

Compatibility of Materials Subject to Sterilization

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Annex A - Radiation

(•) = poor
(• •) = fair
(• • •) = good
(• • • •) = excellent

→ Circles represents the grade of material compatibility for each material

(NL) = not likely
(L) = likely
(U) = unknown

→ Materials are graded on single use cycle which is less than 50 kGy. This label indicates whether materials are likely to be compatible after multiple sterilization cycles (<100kGy)

Table 1 - Material compatibility table, given a single processing

7 Classes; 63 Families of Materials

Table 1— … given a single processing

Key: (•) = poor; (• •) = fai… excellent; (U) = unknown

Material			Moist heat	Dry heat	Hydrogen peroxide	Ozone
Thermoplastics						
Acrylonitrile butadiene styrene (ABS)	• • •	• • • •	• to • •	• to • •	• • • •	• •
Fluoropolymers						
Polytetrafluoroethylene (PTFE)	•	• • • •	• • • •	• • • •	• • • •	• • • •
Perfluoro alkoxy (PFA)	•	• • • •	• • • •	• • • •	• • • •	• • • •
Perchlorotrifluoroethylene (PCTFE)	• • • to • • • •	• • • •	• • •	• • •	• • • •	• • • •
Polyvinyl fluoride (PVF)	• • •	• • • •	• • to • • •	• • to • • •	• • • •	U
Polyvinylidene fluoride (PVDF)	• • • to • • • •	• • • •	• • •	• • •	• • • •	• • • •
Ethylenetetrafluoroethylene (ETFE)	• • • to • • •	• • • •	• • •	• • •	• • • •	• • • •
Fluorinated ethylene propylene (FEP)	• •	• • • •	• • • •	• • • •	• • • •	• • • •
Polyacetals (e.g., polyoxymethylene)	•	• • • •	• • to • • •	• • to • • •	• • • •	• • •
Polyacrylates (e.g., polymethylmethacrylate)	• • to • • •	• •	• to • •	• to • •	• •	• • •
Polyamides (e.g., nylon)	• • to • • •	• • • •	• to • • • •	• to • • • •	• • •	• • •
Polycarbonate (PC)	• • • to • • • •	• • • •	• to • • •	• •	• • • •	• • • •

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AAMI TIR 17:2017

Compatibility of Materials Subject to Sterilization

1. Material Selection Guidance

2. **Material Processing & Design Considerations**

3. Clinically Relevant Material Testing

4. Accelerated Aging Programs

Examples:

- Processing conditions:
  Impact strength decreases by **20 times** in ABS material simply by lowering the mold temperature from 185°F to 85°F
- Polymer Molecular Weight, MWD
- Additives

AAMI TIR 17:2017

Compatibility of Materials Subject to Sterilization

1. Material Selection Guidance
2. Material Processing & Design Considerations
3. **Clinically Relevant Material Testing**
4. **Accelerated Aging Programs**

Case Study # 1

PTFE is on the bottom of everyone's list of radiation compatible materials

An e-beam sterilized PTFE coating on a stainless steel wire does not fail

… What are the clinically relevant stresses?

Case Study # 2

Polyamide / Polyether blends are relatively high on the list of radiation compatible materials

An e-beam sterilized polyester blend balloon catheter fails

… What are the clinically relevant stresses?

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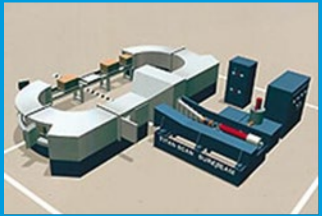
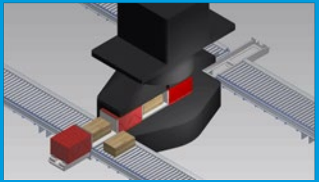
Gamma





- Mechanism of energy deposition is ’ identical – ‘follow the electrons’
- Irradiation time & temperature need to be managed per ISO 11137-1
- A given manufacturer with controlled materials and processes can have confidence in conversion from gamma sterilization to e-beam / x-ray sterilization
- CAUTON leveraging material compatibility data broadly without due diligence

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Dose audit

8.4.2 Transference of verification dose or sterilization dose

8.4.2.1 Transference of a verification dose or a sterilization dose to a radiation source different from that on which the dose was originally established shall not be permitted unless:

a) data are available to demonstrate that differences in operating conditions of the two radiation sources have no effect on microbicidal effectiveness

or

b) 8.4.2.2 or 8.4.2.3 applies.

ANSI/AAMI/ISO 11137-1:2006

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Product with no water:

8.4.2.2 For product that does not contain water in the liquid state, transference of the verification dose or sterilization dose is permitted between:

25 kGy in 4 hr

a) one gamma irradiator and another gamma irradiator,

25 kGy in 4 sec

b) one electron beam generator and another electron beam generator

or

c) one X-ray generator and another X-ray generator.

ANSI/AAMI/ISO 11137-1:2006

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b) one electron beam generator and another electron beam generator

or

c) one X-ray generator and another X-ray generator.

Product with water:

8.4.2.3 For product that contains water in the liquid state, transference of the verification dose or sterilization dose is permitted between:

a) one gamma irradiator and another gamma irradiator,

Dose rate actors of 10 or less can make a difference

b) two electron radiation sources operating under identical operating conditions

or

c) two X-ray radiation sources operating under identical operating conditions.

Ordinary Light	2eV
Bond Energy	4eV
Metal ionization potential	10Z eV
CRT, TV	25,000eV = 25keV
Co-60 gammas	1,250keV = 1.25MeV
Electron Accelerators	0.2 - 15MeV