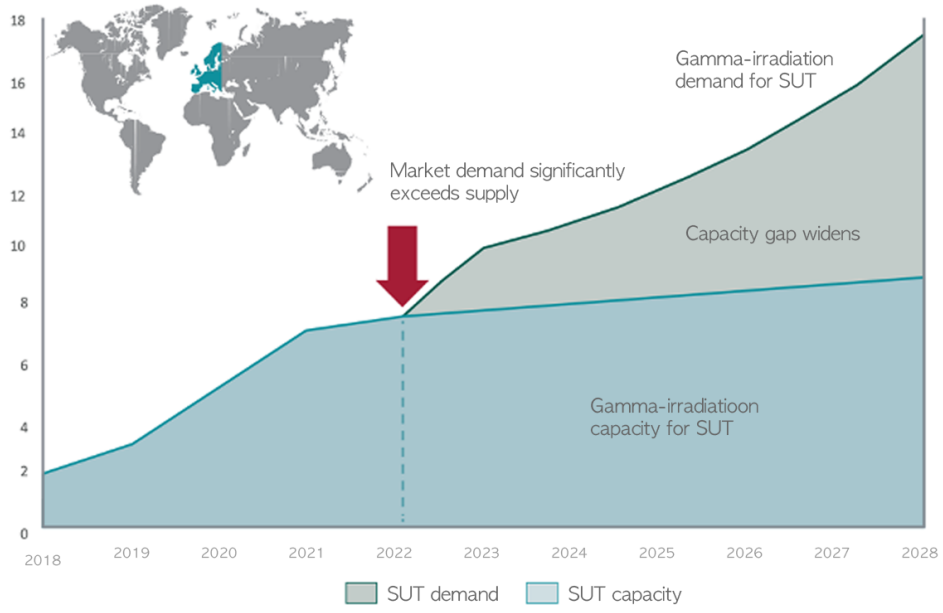
MediZap
Advanced Sterilization

Act Now: Exploring Alternative Terminal Sterilization by Irradiation Methods of E-Beam and X-Ray Compared to Gamma

Introduction:

The primary method for sterilizing medical devices and combination products is gamma irradiation, which is also used for sterilizing pharmaceutical and biopharmaceutical drug products. However, there are concerns regarding the global supply of gamma irradiation due to its various downsides. These downsides include the need for a non-naturally occurring radioisotope (Cobalt-60), lengthy production time, limited global suppliers, logistical challenges, and safety implications. As the demand for terminal sterilization of drug products continues to rise, it is essential to consider alternative modalities such as E-Beam and X-Ray to ensure a reliable supply chain and support drug production.

Source: BioPhorum (August 2021) Data: Bio Process Systems Alliance. Figure: Analysis of Gamma irradiation market demand vs expected market capacity. Vertical axis indicates estimated biotech consumption of Gamma irradiation capacity. Red Arrow indicates expected time in which demand starts to significantly outpace capacity.



Compatibility: E-Beam sterilization is generally compatible with various primary packaging materials, including plastics, rubbers, and metals. However, some clear materials may be sensitive to electron beam radiation, requiring visual compatibility assessment for color change.

Validation and Regulatory Compliance: Like any sterilization method, E-Beam terminal sterilization requires validation to ensure its effectiveness in achieving the desired sterility assurance level. Regulatory agencies, such as the U.S. Food and Drug Administration (FDA), have established guidelines and regulations to ensure proper use in the pharmaceutical industry.

Cost and Infrastructure: Implementing E-Beam sterilization necessitates specialized equipment and infrastructure, including electron beam accelerators, which can be costly to acquire and maintain. Expertise is also required for their operation.

E-Beam

Radiation Source: E-Beam sterilization utilizes an electron beam accelerator to generate and direct high-energy electrons toward the target material. The accelerator's electron energy, measured in MeV, is related to its speed.

Mechanism of Action: E-Beam sterilization exposes pharmaceutical products and medical devices to a beam of high-energy electrons. These electrons interact with microorganisms, causing damage to their DNA and rendering them unable to replicate or cause infection. The high-energy electrons penetrate the product, ensuring sterilization throughout.

Dose Uniformity Ratio: E-Beam irradiation systems can provide a more uniform dose distribution compared to gamma irradiation. The electron beam can be precisely controlled and focused, delivering a more consistent dose to the target material.

Temperature: Dependent upon design and power.

Processing unit: Boxes. Low-density configurations.

Irradiation exposure time: Minutes.

Induced radioactivity: Current scientific consensus indicates that electrons with energies below 10 MeV do not cause significant activation. The data show that typical pharmaceutical-related products irradiated with 10 MeV electrons to an absorbed dose exceeding 25 kGy are negligible from the standpoint of personnel safety and public health.

Regulatory: The International Standards Organization (ISO) has set out precise requirements in the ISO 11137 series for the development, validation, and routine control of a sterilization process for medical devices. In the US, E-Beam facilities typically have fewer regulatory requirements compared to Gamma irradiation facilities.

X-Ray

Radiation Source: X-Ray sterilization involves using ionizing radiation in the form of X-Rays generated by electrons striking a target material, such as tantalum or tungsten.

Mechanism of Action: X-Rays disrupt living cells by damaging their DNA and other cellular structures. This process leads to the death of microorganisms or renders them incapable of reproduction, achieving the desired sterility assurance level.

Dose Uniformity Ratio: X-Ray irradiation systems offer flexibility in dose distribution compared to gamma irradiation. The X-ray beams can be controlled and shaped, allowing a relatively uniform dose distribution.

Temperature: Dependent upon design and power.

Processing unit: Pallets or Boxes. High-density configurations.

Irradiation exposure time: Minutes.

Induced radioactivity: Current scientific consensus indicates that photons with energies below 7.5 MeV do not cause significant activation. The data show that typical pharmaceutical-related products irradiated with 7 MeV X-Rays to an absorbed dose exceeding 25 kGy are negligible from the standpoint of personnel safety and public health.

Regulatory: The International Standards Organization (ISO) has set out precise requirements in ISO 11137-1 series for the development, validation, and routine control of a sterilization process for medical devices. In the U.S., X-Ray facilities typically have fewer regulatory requirements compared to Gamma irradiation facilities.

Gamma

Radiation Source: Ionizing radiation in the form of Gamma rays from Cobalt-60.

Energy Source: The energy of photons emitted by Cobalt-60 is measured at 1.17 MeV and 1.33 MeV. These high-energy photons are emitted in all directions (isotropic). The photons from Cobalt-60 have high-penetrating capabilities through materials.

The radiation dose received by product: Within the irradiator, Cobalt-60 is arranged into known positions in a source rack (stored in a pool of water when not in use). The amount of radiation dose received by the product is a function of the irradiator's design, the source's activity, the product's density, and the time spent in each position around the source.

Mechanism of action: The high-energy photons (X-Rays and Gamma rays) emitted from the accelerator disrupt living cells by damaging the DNA and other cellular structures. These photons induce molecular changes, causing organisms to die or render organisms incapable of reproduction. This enables the reduction of the microbial load on the product to the desired sterility assurance level (SAL).

Directionality: Gamma rays irradiate in all directions. To accommodate this, the facility places rods around and above the product. Delivers dose from when products enter the irradiation chamber until they leave.

Dose uniformity ratio: Dose Uniformity Ratio (DUR) is a measure used in the context of irradiation. It quantifies the uniformity of the delivered radiation dose within the target product being irradiated. DUR is calculated by dividing the maximum dose received by the target by the minimum dose received. It is expressed as a ratio or a numerical value. Gamma irradiators typically utilize a cobalt-60 or cesium-137 radioactive source. Achieving a high degree of dose uniformity can be challenging due to the nature of the source and the geometric arrangements involved in the irradiation process. The DUR values in Gamma irradiation may be higher compared to E-Beam or X-Ray irradiation. In practical terms, a DUR value closer to 1 indicates a more uniform dose distribution, meaning that the radiation has been evenly distributed throughout the product. Conversely, a higher DUR value indicates a less uniform dose distribution, indicating that areas within the product may receive significantly higher or lower radiation doses. The DUR is an important parameter because it relates to the effectiveness of the sterilization process. Ideally, a uniform dose distribution is desirable to ensure consistent and reliable sterilization throughout the entire product delivering the highest dose uniformity ratio.

Temperature: Dependent upon irradiator design and cobalt activity.

Processing unit: Pallets or Boxes. High and low-density configurations.

Irradiation exposure time: Hours.

Induced radioactivity: Induced radioactivity is not possible when using Cobalt-60 irradiation as the photons emitted by the Cobalt-60 atoms are not energetic enough to induce radioactivity in any material.

Regulatory: The International Standards Organization (ISO) has set out precise requirements in the ISO 11137 series for the development, validation, and routine control of a sterilization process for healthcare products.

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Conclusion:

Both E-Beam and X-Ray sterilization methods provide viable alternatives to gamma irradiation for terminal sterilization. While each method has its advantages and considerations, adopting these alternative methods would reduce dependence on Cobalt-60 and enhance the supply chain's resilience for sterile drug products. It is crucial for the pharmaceutical industry to collaborate and implement these methods in a timely manner to ensure a secure and consistent supply of sterilized drug products worldwide.