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Advanced Sterilization

E-Beam | X-Ray Irradiation and Its Use on Healthcare Products

Before electron beam (E-Beam) | X-Ray irradiation can be used as a method of sterilization, a validation process must be done to establish the sterility assurance level. This process then sets the sterility standard for future testing of a product. The validation process guidelines on health care products per ISO 11137 have three sections: Requirements for development, validation, and routine control of a drug product. Establishing the sterilization dose. Guidance on dosimetric aspects. What follows is an overview of the standards established by industry regulations for E-Beam | X-Ray irradiation.

Setting The Maximum Acceptable Dose

Before E-Beam | X-Ray processing is utilized, the possible effects it might have on the drug product and its sterile barrier packaging must be evaluated. During a drug product's development and design phase, companies must determine what effect radiation exposure might have. Especially on drug product packaging that includes polymers, or clear glass as compared to amber glass, results could consist of oxidation, discoloration, or even disruption at a molecular level that could change the drug products' packaging including physical, chemical, or mechanical aspects. Studies should assess whether or not the drug product and its packaging can withstand the maximum acceptable E-Beam | X-Ray dose in both accelerated and real-time aging.

Setting the maximum acceptable dose starts by irradiating the representative sample drug products at the expected maximum dose and evaluating for radiation-caused changes such as potency degradation of the drug product or packaging material color changes.

Determining the Minimum Sterilization Dose

Establishing the minimum radiation dose necessary to achieve sterility assurance starts with accessing the naturally occurring bioburden of a drug product. There are many methods for determining the minimum dose, as outlined in ISO 11137 and ISO/TS 13004.

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The process starts with a microbiology lab. They can quantify the kind and number of microorganisms in colony-forming units, known as CFUs, through ISO11737-1, a validated bioburden determination. The tables within ISO 11137 and ISO/TS 13004 will help guide the proper verification dose based on the testing method and results. The sterility assurance level (SAL) will then be determined. For illustration purposes, a VDmax25 verification dose might be a SAL of 10-1, while the sterilization dose of 25kGy is a SAL of 10-6.

Notes to consider:

Verification doses are typically low and must be delivered within a narrow dose window.

The highest radiation dose on the product samples is not to exceed the verification dose by more than 10%.

The mean of the drug product sample dose may not be less than 90% of the verification dose. If this happens, the verification dose test may be repeated if appropriate sterility levels are not achieved.

The verified dose will then be applied to the correct number of drug product samples. Calibrated dosimeters will measure the dose.

Upon completion of the irradiation processing, samples with the verification dose delivered will be returned to the lab to initiate the sterility test (ISO11737-2). From there, sterility assurance levels can be confirmed.

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E-Beam Irradiation Process

The electron beam (E-Beam) irradiation process uses high-energy electrons for terminal sterilization of drug products.

What is E-Beam Irradiation?

In the electron beam process, a product is struck with high-energy electrons, resulting in a blanket of these electrons moving through the target drug product. The electrons, which are produced by normal electrical current, are accelerated to near the speed of light by means of the LINAC. The electrons are focused to scan a defined size and sweeping motion, creating a veil of electrons. The product is carried on conveyors through the scan at a tightly managed and measured speed. The process takes place behind a radiation shield, typically a large concrete structure, which prevents radiation from leaving the bunker. The accelerated electrons collide with any viable microorganisms to inactivate and kill.

What is E-Beam Irradiation Used For?

Beam irradiation can effectively treat a wide variety of materials with varying densities, configurations, and orientations. Some examples of types of drug product primary packaging to be processed include:

- Blister Packs
- Small Volume Vials (2ml-10ml) for Human and Vet use
- Pre-filled Syringes
- Eye Droppers

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E-Beam Irradiation Process

What are the Benefits of E-Beam Irradiation Processing?

E-Beam Irradiation is safe, reliable and highly effective at treating a wide variety of drug products with varying densities. The combination of shorter exposure time and improved Dose Uniformity Ratios (DUR) make E-Beam irradiation a viable processing option for a variety of drug products. The only constraint to E- Beam is its penetration capability; therefore, depending on the configuration of the drug product, X-Ray is the better modality and technology solution for denser pack-outs.

Benefits of E-Beam include:

- Least potential for deleterious effects to drug products
- Fast and Efficient Targeted Processing that Facilitates Scale from Carton to Full Cases of Drug Product
- Flexibility - Ability to Mix Different Drug Products with Different Densities in the Same Irradiation Cycle
- Ability to Process Tight Dose Specifications through Improved DUR

Standards

E-Beam sterilization is supported by the internationally recognized consensus standard, ISO 11137, which describes the approach to validating a dose to achieve a defined sterility assurance level (SAL). Both the FDA and USP recognize use of this standard for advanced terminal sterilization validations and ongoing sterilization processing.

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X-Ray Irradiation Process

The X-Ray irradiation process utilizes photon radiation for terminal sterilization of drug products. The X-Ray process is compatible with most packaging materials and provides excellent penetration on dense products.

What is X-Ray Irradiation?

X-Ray starts as an electron beam where electrons are generated and accelerated to gain energy. Electrons are generated in equipment with an energy of 5 to 7.5 MeV (million electron volts) and at a higher power in the hundreds of kW (kilowatts). The electrons are then focused on a specific metal target of high atomic number. The X-Ray radiation is generated through a process called Bremsstrahlung to create electromagnetic energy (photons) with an energy in the same range as gamma radiation.

What is X-Ray Irradiation Used For?

X-Ray irradiation can effectively treat a wide variety of materials with varying densities, configurations, and orientations. Some examples of types of drug product primary packaging to be processed include:

- Bulk Drug Raw Materials
- Mini IV Bags
- Large Volume Vials (30ml+) for Human and Vet Use

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X-Ray Irradiation Process

What are the Benefits of X-Ray Irradiation Processing?

X-Ray irradiation is safe, reliable and highly effective at treating a wide variety of drug products with varying densities. The combination of shorter exposure time and improved Dose Uniformity Ratios (DUR) make X-Ray irradiation a viable processing option for a variety of drug products. Similar to electron beam, X- Ray processing is powered by electricity.

Benefits of X-Ray include:

- Improved Penetration Ability
- Fast and Efficient Targeted Processing that Facilitates Scale from Carton to Full Cases of Product
- Flexibility - Ability to Mix Different Drug Products with Different Densities in the Same Irradiation Cycle
- Ability to Process Tight Dose Specifications through Improved DUR
- Incremental Lap-Based Dose Delivery

Standards

X-Ray sterilization is supported by the internationally recognized consensus standard, ISO 11137, which describes the approach to validating a dose to achieve a defined sterility assurance level (SAL). Both the FDA and USP recognize use of this standard for advanced terminal sterilization validations and ongoing sterilization processing.