Decontamination by Irradiation for RMs and Components

Supporting specific requirements for finished product

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Overview

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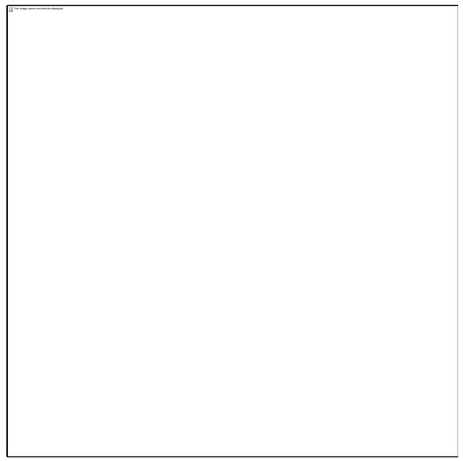
- Use of irradiation for decontamination across sectors
- Advantages, Challenges and Opportunities
- Consumer Products
- Medical Devices and Combination Products
- Supporting Aseptic Fill Processes

Use of irradiation for decontamination across sectors

Consumer Products

- Cosmetics and toiletries strive for microbiological controls that protect product integrity, and protect end users from infection.
- A longer shelf-life may be required for these personal care products.
- Likely to work with a large volume of material.



Use of irradiation for decontamination across sectors

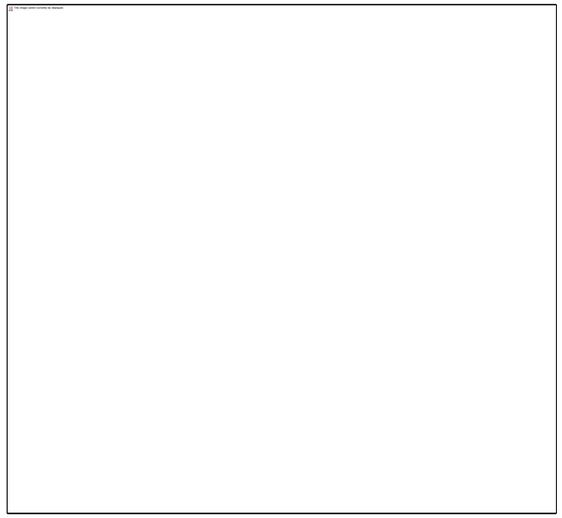
Sterile Medical Devices

- Sterility Assurance Level established based on risk.
- Controlled manufacturing and environments.
- Microbiological limits for raw materials and product/package components.

Use of irradiation for decontamination across sectors

Aseptic Processing/Pharmaceutical

- Strict Microbiological controls.
- Strict Environmental and Process Controls.
- Consistency required in Raw Material, Packaging and Product.



Advantages, Challenges and Opportunities

Why Irradiation?

- Significant parameter: Dose delivery
- Organism deactivation by irradiation is temperature independent
- Minimal residue: Effective on Natural Raw Materials, medical herbs & active ingredients
- Known effect on many materials used in packaging and manufacturing

Advantages, Challenges and Opportunities

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Things to think of:

- Difficulty with liquids/solutions.
- Sustainability of Gamma irradiation, and design constraints of e-beam or X-ray.
- Variability in microbiological quality.

Advantages, Challenges and Opportunities

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Things to think of:

- Maximum dose that the material will tolerate.
  - Changes to physical and chemical properties – color, odor, physical integrity.
  - Configurations of Raw Materials and components are often unfavorable to dose uniformity.
  - Tolerance of the material to the process after decontamination.
  - Total dose, additive of decontamination and terminal processing.
- Variability in microbiological quality.
  - Lack of good controls in sources of Raw Materials and components

Advantages, Challenges and Opportunities

Advantages, Challenges and Opportunities

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Potential Benefits:

- Use of materials that otherwise would not be available: Natural products, heat/RH sensitive products.
- Reduction of manufacturing process and product risk.
  - Contamination avoidance in controlled environments and equipment.
  - Elimination of variability which could cause micro non-conformities.
- Capability increase for products and processes to meet stricter criteria.
  - Development of products that otherwise may not be able to meet a defined SAL or other micro requirement
  - Competitive advantage

Establishment of an Irradiation Dose

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What are the finished product and process requirements?

- Specific Microbiological Limits?
- Absence of resistant or objectionable organisms?
- “Ultra-low” bioburden?
- Sterile label claim?
- Need for components to be sterile during processing?

Establishment of an Irradiation Dose

Example 1: Consumer finished product with micro requirement of <100cfu/g, and absence of objectionable microorganisms

Product consists of non-woven product moistened with cosmetic or OTC drug formulation.

History of variability has resulted in micro non-conformances (presence of gram negative objectionable organisms).

Investigation determined that the non-woven raw material was the source of the objectionable organisms, with spikes up to 10^3cfu/g of material.

Irradiation was implemented for non-woven material.

Dose Specification: 6-18kGy, which is effective for elimination of the targeted contaminants.

Establishment of an Irradiation Dose

Example 2: Combination Biologic Medical Device with 10^{-6} SAL, achieved with control of pre-sterile bioburden of <10cfu/device (“Ultra-low bioburden”).

In this case, components and raw materials can not contribute any viable microorganisms to the product or process.

Controls were implemented by applying dose establishment methodology to the delivery device and product-contacting packaging. This ensured that finished device bioburden was not impacted by packaging components or the delivery device.

Dose Specification: 25-38kGy.

Other applications: Elimination of radiation-resistant organisms in packaging and components

Establishment of an Irradiation Dose

Example 3: Aseptically filled product labeled Sterile.

In this case, packaging components must be introduced to the manufacturing environment free of viable microorganisms.

Product-contacting packaging (bottles, tips, caps) maintain an irradiation processing program with quarterly dose audits.

Irradiation dose: 25kGy.

Is formal validation required in this case?

Further Activities

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- Material qualification to determine the influence of radiation on materials – Find out the maximum acceptable dose.
  - Consider impact of decontamination and terminal irradiation.
- Process development and qualification for material or product
- Document Quality standards for irradiated materials – processing specifications, established configuration, assess transportation and storage conditions
- Quality Control for the process
- Supply Chain - Analysis of capacity and logistics
- Regulatory impact

Innovation Opportunities

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Use of natural products, botanicals, active ingredients

Research exists indicate 5kGy irradiation dose for full microbiological decontamination of traditional Chinese medicines with original bioburden of $5.0x10^5$cfu/g. Chemical constituents, biological activity and toxicity of the medicines tested showed no obvious change when irradiated.

For powder forms, effective decontamination occurs with 3kGy of dose.

Reference: STUDY ON THE IRRADIATION DECONTAMINATION OF TRADITIONAL CHINESE MEDICINES; WANG B., SHI S., LI B., WANG G. National Institute for the Control of Pharmaceutical and Biological Products, Temple of Heaven, Beijing, People's Republic of China

Innovation Opportunities

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In-line/on-site irradiation using e-beam

- Implementation of e-beam decontamination in manufacturing equipment
  - Wipes
  - Packaging
- Components and packaging materials for aseptic processing

Combination products

- Drugs or biologics with low dose or temperature tolerances
- Potential for terminal processing on-site
  - Streamlining of release testing required by drug regulation

Innovation Opportunities

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Control of inputs to product and process to limit bioburden

- Makes possible “Ultra-low” bioburden manufacturing
- Use of combined BI/Bioburden method in conjunction with other Sterilization modalities

Acknowledgement/Reference

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INTERNATIONAL ATOMIC ENERGY AGENCY

Coordinated Research Project

Radiation sterilization and decontamination of pharmaceuticals and pharmaceutical raw materials

2005

Discussions, Questions, and Answers

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