Validation of radiation sterilization process

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Quality systems

- Quality management systems -Requirements

  EN ISO 9001:2000

  supersedes
  EN ISO 9001:1994
  EN ISO 9002:1994
  EN ISO 9003:1994

- Medical devices-Quality management systems-Requirements for regulatory purpose

  EN ISO 13485:2003

  supersedes
  EN ISO 13485:2002
  EN ISO 13488:2002

Why ISO 13 485 ?

- The standards for quality management systems recognize that, for certain processes used in manufacturing, the effectiveness of the process cannot be fully verified by subsequent inspection and testing of the product. Sterilization is an example of such a process. For this reason, sterilization processes are validated for use, the performance of sterilization process is monitored routinely and the equipment is maintained.

Particular requirements for sterile medical devices

- 7.5.1.3.The organization shall maintain records of the process parameters for the sterilization process which was used for each sterilization batch (see 4.2.4). Sterilization records shall be traceable to each production batch of medical devices (see 7.5.1.1.)
- 7.5.2.2 The organization shall establish documented procedures for validation of sterilization processes. Sterilization processes shall be validated prior to initial use.

  Records of validation of each sterilization process shall be maintained (see 4.2.4)

ISO 14937:2000

- Sterilization of health care products – General requirements for characterization of a sterilizing agent and the development, validation and routine control of a sterilization process

Validation

- The purpose of validation is to demonstrate that the sterilization process established in process definition can be delivered effectively and reproducibly to the sterilization load. Validation consists of a number of identified stages: installation qualification, operational qualification, and performance qualification.

Installation qualification (IQ)

- IQ is undertaken to demonstrate that the sterilization equipment and any ancillary items have been supplied and installed in accordance with their specification.

Operational qualification (OQ)

- OQ is carried out either with unloaded equipment or using appropriate test material to demonstrate the capability of the equipment to deliver the sterilization process that bas been defined.

Performance qualification (PQ)

- PQ is the stage of validation that uses product to demonstrate that equipment consistently operates in accordance with predetermined criteria and the process yields product that is sterile and meets specified requirements.

Management responsibility

- The development, validation and routine control of a sterilization process is likely to involve a number of separate parties, each of whom is responsible for certain elements.
- In order to illustrate the variety of possible allocations, three sample o scenarios are presented.

- Scenario 1 – Health care facility
- Scenario 2 –Medical device manufacturer using in-house facilities
- Scenario 3 – Medical device manufacturer using a sterilization subcontractor.

Medical device manufacturer using a sterilization subcontractor

- In this scenario, the user of the sterilization process is a manufacturer of single-use medical devices who is using sterilization subcontractor to deliver the sterilization process. Additionally, the medical device manufacturer is using a contract laboratory to undertake defined testing as part of the product release procedures. The parties involved are the medical device manufacturer, the sterilization subcontractor, and the contract laboratory.

The allocation of responsibilities might be as follows: (1/ 5)

- Quality management system elements
  - Each party has its own quality management system. The limits of responsibility of each party are laid down in formal contracts.
- Sterilizing agent characterization
  - The sterilization subcontractor has licensed the sterilization process from a separate organization who characterized and developed the sterilization process. The process developer has undertaken the sterilizing agent characterization and made the resultant data available to the sterilization subcontractor and the medical device manufacturer.

The allocation of responsibilities might be as follows: (2/ 5)

- Process/equipment characterization
  - The sterilization subcontractor has developed an equipment specification, including a control system for the equipment, which is capable of being programmed to deliver a predefined process. A sterilizer manufacturer has been contracted to manufacture and install the specified equipment.
- Product definition
  - The medical device manufacturer is responsible for specification of the product and its manufacture.

The allocation of responsibilities might be as follows: (3/ 5)

- Process definition
  - The medical device manufacturer defines a process for the particular medical device(s) to be sterilized. The medical device manufacturer undertakes the biological safety assessments and product compatibility studies. In this case, these studies are conducted using experimental sterilization equipment.
- Validation
  - The sterilization subcontractor undertakes installation qualification and operational qualification in accordance with documented procedures. The medical device manufacturer then undertakes performance qualification using the installed sterilization equipment conforming that the equipment is capable of delivering the defined sterilization process. The medical device manufacturer reviews and approves the validation exercise. A contract laboratory might perform microbiological testing in accordance with methods agreed with the medical device manufacturer.

The allocation of responsibilities might be as follows: (4/ 5)

- Routine control and monitoring
  - This is carried out by the sterilization subcontractor laboratory in accordance with documented procedures agreed with the medical device manufacturer.
- Product release from sterilization
  - This is carried out by medical device manufacturer in accordance with documented procedures, on the basis of records provided by the sterilization subcontractor and the contract laboratory.

The allocation of responsibilities might be as follows: (5/ 5)

- Maintaining process effectiveness
  - The sterilization subcontractor carries out equipment maintenance and calibration in accordance with documented procedures. The medical device manufacturer maintains the quality of product prior to sterilization and takes responsibility for requalification; the sterilization subcontractor carries out any necessary repetition of part or all of installation qualification or operational qualification.

EN ISO 11137 : 2006

- Sterilization of health care products - Radiation

Irradiator operator responsibilities

- Installation qualification
- Operational qualification
- Controlling the irradiation process
- Change control of the irradiator
- Certification of the radiation dose

Primary manufacturer responsibilities

- Establishing the sterilization dose
- Developing product families
- Establishing the maximum acceptable dose
- **Performance qualification**
- Controlling the manufacturing process including the specifications for products submitted to the irradiator operator, i.e., product density, orientation, dimensions
- Revision of specifications submitted to the irradiator operator
- Change control of the product to include a review of product-related variables that impact processing categories
- Product release

Installation Qualification

- Equipment documentation (describing the design and installation requirements; it should include drawings and details of all the construction materials, the dimensions and tolerances of the equipment, support services and power supplies)
- Any modification made to the irradiator installation

Records should include the following:

- For gamma irradiators, the activity of the source and description of the location of individual components of the source
- **For electron beam and X-ray irradiators, the characteristics of the beam (electron energy, average beam current, scan width and scan uniformity.**

Operational qualification

- Equipment calibration (including test instrumentation used for monitoring, controlling, indicating or recording)
- Irradiator dose mapping

Performance qualification

- Determination of product loading pattern
- Product dose mapping

Thank you for your attention