International Standards for Radiation Sterilization of Medical Devices

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Sterilization of Medical Devices

- ***Medical Device Directive* 93/42/EEC**
- Has been implemented for CE marking in national legislation since 1998.
- A new Medical Device Directive was issued
  12 October 2007: 2007/47/EC
- It amends the old directive
- It must be implemented in national laws by end of 2008
- Manufactures must comply by March 2010

- Nothing is changed with respect to sterilization

Sterilization of Medical Devices

- ***Medical Device Directive* 93/42/EEC - 2007/47/EC**
- Essential requirements must be fulfilled in order for CE-marking of products
- Annex 1: Essential requirements
- 8.4**:**
  - **"Devices delivered in a sterile state must have been manufactured and sterilized by an appropriate, validated method."**
- How to comply with essential requirements?

- *Follow mandated standards*

The old standards

- **EN 552:1995** Sterilization of Medical devices – Validation and Process control of Sterilization by Irradiation.

  CEN/TC 204 Sterilization of Medical Devices

- **ISO 11137:1996** Sterilization of Health Care Products – Requirements for validation and routine control – Radiation sterilization.

  ISO/TC 198 Sterilization of Health Care Products

- **EN 556-1:2001** Sterilization of medical devices - Requirements for medical devices to be designated 'STERILE' - Part 1: Requirements for terminally sterilized medical devices

  CEN/TC 204 Sterilization of Medical Devices

The new standard

- **EN ISO 11137:2006 Sterilization of health care products – Radiation**
  - - has replaced the two old standards
  - When the standard is followed, compliance with EU Medical Device Directive is presumed
  - The standard is accepted as an American standard
  - The standard is accepted worldwide

EN 556-1:2001 Sterilization of medical devices - Requirements for medical devices to be designated 'STERILE' - Part 1: Requirements for terminally sterilized medical devices

EN 556-1

EN 556-1:2001 Sterilization of medical devices - Requirements for medical devices to be designated 'STERILE' - Part 1: Requirements for terminally sterilized medical devices

Requirement:

For a terminally sterilized medical device to be designated ”STERILE”, the theoretical probability of there being a viable micro-organism present on/in the device shall equal to or less than 1×10^{-6}.

Standards providing background for new EN ISO standard

- ISO 9001:2000, *Quality management systems – Requirements*
- ISO 13485 *Medical devices - Quality management systems - Requirements for regulatory purposes*
- ISO 14937 *Sterilization of medical devices - General requirements for characterization of a sterilizing agent and the development, validation and routine control of a sterilization process for medical devices*

Other standards that are incorporated into the new ISO EN standards

- ISO/TR 15843 Product families, dose audit frequency and dose audit sample sizes
- ISO/TR 15844 Radiation sterilization of one batch
- AAMI TIR 27 VD_{max}
  - substantiation of 25 kGy

EN ISO 11137:2006

- **Three Parts:**
  - Part 1: Requirements for the development, validation and routine control of a sterilization process for medical devices
  - Part 2: Establishing the sterilization dose
  - Part 3: Guidance on dosimetric aspects
- Covers gamma, electron beam and x-ray
- It is in principle limited to medical devices
  - - but can be used for other products

EN ISO 11137-1

Content

EN ISO 11137-1

Validation

Definitions 3.37:

documented procedure for obtaining, recording and interpreting the results required to establish that a process will consistently yield product complying with predetermined specifications.

EN ISO 11137-1

Validation

Definitions 3.37:

documented[6] procedure[5] for obtaining, recording and interpreting the results required to establish that a process[2] will consistently[4] yield product[1] complying with predetermined specifications[3].

EN ISO 11137-1

Validation

- Installation Qualification - IQ
  - Agreement supplier – customer
- Operational Qualification - OQ
  - show consistent operation
- Performance Qualification - PQ
  - specify how product shall be irradiated
- Routine Process Control
  - show that the process runs within specifications

EN ISO 11137-1 Requirements

- Documentation is in all steps based on ability to measure dose
- Sect. 4.3.4:
  - “Dosimetry used in the development, validation and routine control of the sterilization process shall have measurement traceability to national or international standards and shall have a known level of uncertainty.”

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ISO 11137-1 Requirements Revision issues 1

The use of Biological Indicators

- and Tests **for** Sterility are not required

Sterilizing agent characterization

- Radiation energy levels are not restricted.

  - but assessment is required for potentially induced radioactivity at energy levels higher than 5 MeV x-rays and 10 MeV electrons

ISO 11137-1 Requirements Revision issues 2

- Process and equipment characterization
- Product definition
  - Processing categories
    Grouping for processing
- Process definition
  - Establishing the maximum acceptable dose
  - Establishing the sterilization dose
    - detailed in 11137-2
  - Transference of established doses
    - between “similar” facilities: No additional testing

ISO 11137-1 Requirements Revision issues 3

- Product release
  - taking into account the uncertainty of the measurement system

- Maintaining process effectiveness
  - Frequency of bioburden determination
    - Quarterly (generally)
  - Frequency of sterilization dose audits
    - Quarterly → bi-annually → annually

ISO 11137-1 Requirements Revision issues 4

- Guidance
- Format of EN 552 followed with guidance for each section
- Annex A
  - Includes tables on recommended IQ / OQ actions for facilities

ISO 11137-2
Establishing the Sterilization Dose

Revision Issues 1

1. **Product Families**
   - definition and maintenance
   - grouping for bioburden, dose establishment and dose audits

2. **Designation of product to represent family**
   - master
   - equivalent
   - simulated

ISO 11137-2
Establishing the Sterilization Dose

Revision Issues 2

3. **Method 1**
   - change in table to reflect whole bioburden numbers
   - included table for bioburden 0.1 to 1.0 cfu
   - single batch procedure

4. **Method 2**
   - remains essentially unchanged

ISO 11137-2
Establishing the Sterilization Dose

Revision Issues 3

5. VD_{max}^{25} Substantiation of 25 kGy
   - method is based upon VD_{max}
   - bioburden ≤ 1,000 cfu/product
   - single batch procedure

6. VD_{max}^{15} Substantiation of 15 kGy
   - method is based upon VD_{max}
   - bioburden ≤ 1.5 cfu/product
   - single batch procedure

ISO 11137-2
Establishing the Sterilization Dose

Revision Issues 4

Dose audit

- audit procedures expanded and clarified
- dose augmentation expanded
  - allow processing to continue in case of dose audit failure

ISO 11137-3
Guidance on Dosimetric Aspects

- Specific guidance on dosimetry as used in parts 1 and 2
- Reference to ISO/ASTM standards on Dosimetry for Radiation Processing
- Annex A: Mathematical modelling
  - Point Kernel
  - Monte Carlo

ISO 11137-3
Guidance on Dosimetric Aspects

ISO/ASTM standards on Dosimetry for Radiation Processing

Presently 31 standards and guides

- Dosimetry systems
  - Alanine
  - Calorimeters
  - etc
- Dosimetry methods
  - Characterization of gamma plants
  - Characterization of electron accelerators
  - Dose mapping
  - etc

ISO 11137-3
Guidance on Dosimetric Aspects

Issues:

Dosimeter calibration

Guidance on practical use of dosimetry

Application of measurement uncertainties.

Use of statistical evaluation of PQ dose map data.

Present status

- ISO standards published April 2006
- EN standards parts 1 and 3 published April 2006
- Errors discovered in part 2
- Revised ISO 11137-2:2006
- EN ISO 11137-2:2007