Standardization of Moist Heat Sterilization / Sterilizers

Expert’s Congress
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Sterilizers are used in:
- Manufacturing of Medicinal Products
- Manufacturing of Medical Devices
- Manufacturing of APIs
- Manufacturing of Components
- Bioengineering / Biotechnology
- Laboratories
- Hospitals / Surgeries
- (Food Industry)

- Including the equipment used
**Standardization of Moist Heat Sterilizers**

**Standards could regulate:**
- The performance of the process (SAL 10-6)
- The process and process parameter (121°C; 15 min)
- Service (Steam Quality)
- Validation of the process
- Qualification of the equipment
- Dimensions / Engineering standards (material, surface quality)
- Metrology / Calibration / Control / Process documentation
- Maintenance
- Safety (HSE)

**Medicinal Products ⇔ Medical Devices**
- Pharmacopeia (USP, EP)
  - SAL, test organism, D-Value, temperature, time
- GMP-Guidelines
  - General requirements for Qualification / Validation
- Guide to inspection / guidance for industry / Aide memoire
- Additional, non binding requirements
  - PDA Technical Monograph No. 1
Standardization of Moist Heat Sterilizers

Requirements for Medicinal Products (EP, USP)

- Standard process: 15 min, 121°C
- Sterility Assurance Level (SAL Value) $10^{-6}$; microbial survivor probability $10^{-6}$
- Validated process
- Biological test organisms / Bio Indicator (BI) Geobacillus stearothermophilus
  - $D$-Value 1.5 min
- Qualified equipment

Requirements for Medicinal Products (USP)

- ... the process equipment has the capability of operating within the required parameters.
- ... critical equipment and instrumentation are capable of operating within the prescribed parameters for the process equipment.
- ... perform replicate cycles representing the required operational range of the equipment and employing actual or simulated product.
- ... that the process have been carried out within the prescribed protocol limits.
- ... that the probability of microbial survival in the replicate process completed is not greater than the prescribed limits.
- ... monitor the validated process during routine operation.
Requirements for Medicinal Products (EP-GMP)

• All sterilization processes should be validated according to the EP requirements.
• … the suitability for the product and the efficacy in achieving the desired sterilizing conditions should be demonstrated.
• … by physical measurements and by biological indicators.
• … the validity of the process should be verified at scheduled intervals.
• … loading patterns should be established.
• … recorded on a time / temperature / pressure chart
• … precautions against contamination of the sterilized load during cooling.
• … steam of suitable quality; no additives at a level which could contaminate product or equipment

Standards for Sterilizers and Sterilization Processes

• Germany => DIN
• Europe => EN
• USA => ANSI / AAMI
• International => ISO

• PDA (Technical Monograph No. 1)
• HMSO (HTM 2010)
Standardization of Moist Heat Sterilizers

History: Standardization of Sterilizers

- In the 70th and 80th a lot of countries and organizations started with the standardization of sterilizers or sterilization processes.

- End of the 70th: User and manufacturer create the first Standards in Germany

- The industry grew together. For the worldwide economy, more international standards are required.

- Beginning of the 90th: EU mandate to create Standards for Medical Devices
- End of the 90th: Local and EU Standards growth to international Standards

In Europe, the Pharmacopeia and the GMP Guidelines are not valid for Medical Devices.

- The Medical Device industry got a mandate from the EU to create standards, e.g. for the sterilization of Medical devices.

- **DIN EN 556**
  - Sterilization of medical devices; Requirements for medical devices to be labelled „STERILE“

  Medicinal products, sterilized in its final pack and labeled Sterile

  must be sterilized with an SAL of at least $1 \times 10^{-6}$
Standards for Moist Heat Sterilization (Sterilizers)

  Sterilization of Health Care Products, requirements for validation and routine control, industrial moist heat sterilization.

  Sterilization of Health Care Products; moist heat sterilization.
  Development, validation and routine control of a sterilization process for medical devices.

Sterilization of Health Care Products, requirements for validation and routine control, industrial moist heat sterilization.

- It covers all moist heat processes, including saturated steam and air-steam mixtures, and applies to all industrial manufacturers and all others who perform contract moist heat sterilization.
Although moist heat sterilization in non industrial health care facilities is not specially covered in the International Standard, the principles outlined may be useful to the user of moist heat sterilization in these facilities.
ISO 11134 (2003) Content

1. Scope
2. Normative references
3. Definitions
4. General
5. Equipment (only general)
6. Sterilisation process development
7. Sterilization process validation
8. Routine moist heat sterilization

- Annex A Guidance for Validation and routine control of industrial moist heat sterilization
- Annex B Sterilization cycles

DIN EN ISO 17665 (2006)
Sterilization of Health Care Products - moist heat -
(Supersedes DIN 58946-6 and DIN EN 554)

Scope

- This part of ISO 17665 specifies requirements for the development, validation and routine control of a moist heat sterilization process for medical devices.
- NOTE: Although the scope of this part of ISO 17665 is limited to medical devices, it specifies requirements and provides guidance that may be applicable to other health care products.
DIN EN ISO 17665, Content

Moist heat sterilization processes covered by this part of ISO 17665 include but are not limited to:

- a) saturated steam venting systems;
- b) saturated steam active air removal systems;
- c) air steam mixtures;
- d) water spray;
- e) water immersion

DIN EN ISO 17665, Content

1. Scope
2. Normative references
3. Terms and definitions
4. Quality management system elements
5. Sterilizing agent characterization
6. Process and equipment characterization
7. Product definition
8. Process definition
9. Validation
10. Routine monitoring and control
11. Product release from sterilization
12. Maintaining process effectiveness
DIN EN ISO 17665. Content

- Annex A  Guidance
- Annex B  (informative) Process definition based on inactivation of the microbial population in its natural state (bio burden-based method)
- Annex C  (informative) Process definition based on the inactivation of a reference micro-organism and a knowledge of bio burden on product items to be sterilized (combined bio burden/biological indicator based method)
- Annex D  (informative) Conservative process definition based on inactivation of reference micro-organisms (overkill method)
- Annex E  (informative) Operating cycles

Standards for Moist Heat Sterilizers (Sterilization)

- DIN EN 285
  Steam Sterilizers, Large Sterilizers

- DIN EN 13060
  Small Steam Sterilizers

- DIN 58959
  Steam sterilizers for pharmaceutical products
  (German language only)
Standardization of Moist Heat Sterilizers

DIN EN 285
Steam Sterilizers, Large Sterilizers

- Scope
This European Standard specifies requirements and the relevant test for large steam sterilizers primarily used in health care for the sterilization of medical devices and their accessories contained in one or more sterilization modules. The test load described in this European Standard are selected to represent the majority of loads (i.e. wrapped goods consisting of metal, rubber and porous material) for the evaluation of general purpose steam sterilizer for medical devices. However, specific loads (e.g. heavy metal objects or long and/or narrow lumen) will require the use of other test loads.

Standardization of Moist Heat Sterilizers

DIN EN 285, Content

- 1. Scope
- 2. Normative references
- 3. Terms and definitions
- 4. Mechanical components (standardization of some components e.g. for test instruments)
- 5. Process components (steam source, Air filters)
- 6. Instrumentation, indicating and recording devices
- 7. Control systems
- 8. Performance requirements (steam penetration, microbial lethality, physical parameters, air detection, dryness)
- 9. Sound power
- 10. Rate of pressure change
- 11. Safety
- 12. Marking
- 13. Service and local environment (steam, non condensable gases, superheat, water, compressed air, drains etc.)
Standardization of Moist Heat Sterilizers

DIN EN 285, Content

• 14. Testing (test program, calibration)
• 15. Microbiological test (rubber load)
• 16. Thermometric tests (Cotton sheet test kit)
• 17. Bowie and Dick test
• 18. Air leakage test
• 19. Air detector test
• 20. Load dryness tests
• 21. Sound power test
• 22. Steam quality tests (non condensable gases, dryness, superheat)
• 23. Dynamic sterilizer chamber pressure test (risk / damage for the packaging)
• 24. Test apparatus, equipment and material
• 25. Documentation to be supplied by the manufacturer
• 26. Information to be supplied by the manufacturer

Standardization of Moist Heat Sterilizers

DIN EN 285, Content

• Annex A Environmental aspects
• Annex B Stream supply (contaminants)
• Annex C Recommended material
• Annex D Temperature and Time Tolerances
• Annex E Guidance for installation and operational qualification
• Annex F Criteria for identifying sterilizers as the same type
DIN 58950 Steam Sterilizers for Pharmaceutical Products

- Part 1 Terminology
- Part 2 Apparatus requirements
- Part 3 Tests
- Part 6 Operation
- Part 7 Requirements on services and installation

DIN 58950, Part 1 Terminology

- Definitions
- Fo-calculation
- Sterilization Programmes
DIN 58950, Part 2 Apparatus requirements

• Variation according load, program and quality standards
• Standard dimension for chamber and equipment
• Performance requirements
• Material, surface quality, insulation
• Pressure and safety requirements
• Process logic control system
• Documentation
• Annex A-C: Tables with standard dimensions

DIN 58950, Part 3 Tests

• Test methods (e.g. Qualification, Calibration, Safety tests, etc.)
• Test location (FAT, SAT)
• Tests (number)
• Tools and utilities for testing
• General Checklist
• Annex A-J: Detailed checklists for the tests
DIN 58950, Part 6 Operation

- ...
- 4 What is the right program for the load
- 5 Documentation, training, ready to use
- 6 Daily use and maintenance (log-book)
- 7 Change management
- 8 Qualification and Re-qualification
- 9 End of use / retirement / de-comisioning

DIN 58950, Part 7 Requirements on services and installation

- ...
- 4 Services
- 5 Requirements for the different services
  - Steam, water, compressed air, condensate, waste water, power, etc.
- 6 Requirements for building and installation

- Annex A: Checklist for service
### More Standards

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<td>EN 868</td>
<td>Packaging materials and systems for medical devices which are to be sterilized</td>
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<td>ISO 11737</td>
<td>Sterilization of medical devices — Microbiological methods</td>
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<td>ISO 11138</td>
<td>Sterilization of Health Care Products; Biological indicators</td>
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<td>ISO 11139</td>
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<td>ISO 11607</td>
<td>Packaging for terminally sterilized medical devices</td>
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<td>ISO 14161</td>
<td>Sterilization of health care products — Biological indicators</td>
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<tr>
<td>DIN EN ISO 14937</td>
<td>Sterilization of health care products — General requirements for characterization of a sterilizing agent and the development, validation and routine control of a sterilization process for medical devices</td>
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<td>ISO 13683</td>
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