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Standardization of Moist Heat Sterilization / Sterilizers

Expert‘s Congress
SBM Schoeller Bleckmann

Hubert Appolt

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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

Standards could regulate:

- The performance of the process (SAL 10-6)
- The process and process parameter (121℃; 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

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Requirements for Medicinal Products (EP, USP)

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

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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 mot greater than the prescribed limits.
- … monitor the validated process during routine operation.

Requirements for Medicinal Products (EP-GMP)

- All sterilization processes should be validated acc. 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)

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History: Standardization of Sterilizers

- In the 70th and 80th a lot of countries and organizations starts with the standardization of sterilizers or sterilization processes.
- End of the 70th : User and manufacturer create the first Standards in Germany
- The industry growth together. For the world wide 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

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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 it’s final pack and labeled

Sterile

must be sterilized with an SAL of at least $1x10^{-6}$

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Standards for Moist Heat Sterilization (Sterilizers)

- DIN EN ISO 11134 (2003)
  Sterilization of Health Care Products, requirements for validation and routine control, industrial moist heat sterilization.

- DIN EN ISO 17665 (2006)
  Sterilization of Health Care Products; moist heat sterilization.
  Development, validation and routine control of a sterilization process for medical devices.

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ISO 11134 (2003)

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.

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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

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DIN EN ISO 17665 (2006)

Sterilization of Health Care Products - moist heat - Part 1: Development, validation and routine control of a sterilization process for medical devices.
(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.

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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

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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)

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.

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.)

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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

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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

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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

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DIN 58950, Part 1 Terminology

- Definitions
- Fo-calculation
- Sterilization Programmes

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DIN 58950, Part 2 Apparatus requirements

- …..
- 4. Variations according load, program and quality standards
- 5. Standard dimension for chamber and equipment
- 6. Performance requirements
- 7 Material, surface quality, insulation
- 8 Pressure and safety requirements
- 9 Process logic control system
- 10 Documentation

- Annex A-C: Tables with standard dimensions

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DIN 58950, Part 3 Tests

- ….
- 4 Test methods (e.g. Qualification, Calibration, Safety tests, etc.)
- 5 Test location (FAT, SAT)
- 6 Tests (number)
- 7 Tools and utilities for testing
- 8 General Checklist

- Annex A-J: Detailed checklists for the tests

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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-bock)
- 7 Change management
- 8 Qualification and Re-qualification
- 9 End of use / retirement / de-comisioning

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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

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More Standards

EN 868	Packaging materials and systems for medical devices which are to be sterilized
ISO 11737	Sterilization of medical devices — Microbiological methods
ISO 11138	Sterilization of Health Care Products; Biological indicators
ISO 11139	Sterilization of Health Care Products; Vocabulary
ISO 11140	Sterilization of health care products — Chemical indicators
ISO 11607	Packaging for terminally sterilized medical devices
ISO 14161	Sterilization of health care products — Biological indicators

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More Standards

DIN EN ISO 14937	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
ISO 13683	Sterilization of Health Care Products; Requirements for validation and routine Control of moist heat sterilization in health care facilities
ISO 15882	Sterilization of health care products — Chemical indicators
ISO 17664	Sterilization of medical devices — Information to be provided by the manufacturer for the processing of re-sterilizable medical devices
ISO 18472	Sterilization of health care products — Biological and chemical indicators, Test equipment