Steam Sterilization “What we need to know to comply with EN285-A Case Study”

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Predicate:

Steam sterilization is considered one of the method to ensure sterility. Steam Sterilization can be used for solutions and dry goods. This case study specifies the minimum documentation required to comply with EN 285. It must be recognized that the control of good manufacturing practices remain of utmost importance.

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Some questions (please chime in):

- This is a case study? What does this mean?
- Why do we have to comply with EN285?
- What document do we capture the requirements?
- What is the focus of this study? In-Process Materials specifically Solids

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Presentation Overview:

- Definitions
- Gap Analysis
- Recommended Tests
- IOPQ

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Definition:

- What does Steam sterilization mean? Steam Sterilization process uses water in its liquid and vaporous state to penetrate as steam.
- Distribution of moisture and temperature throughout the sterilization load is done by comparison of measurement results with cycle paraments shown by validation.
- What does sterilization process mean? Series of operations needed to achieve specified requirements for sterility.

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Definition:

- What does “Sterile” mean in Steam Sterilization? A combination of minimum process parameters to produce substantial overkill
- What is included in Sterilization process? Includes pre-treatment, exposure and post treatment. Sterilization process does not include any cleaning, disinfection or packing operation that precede sterilization.

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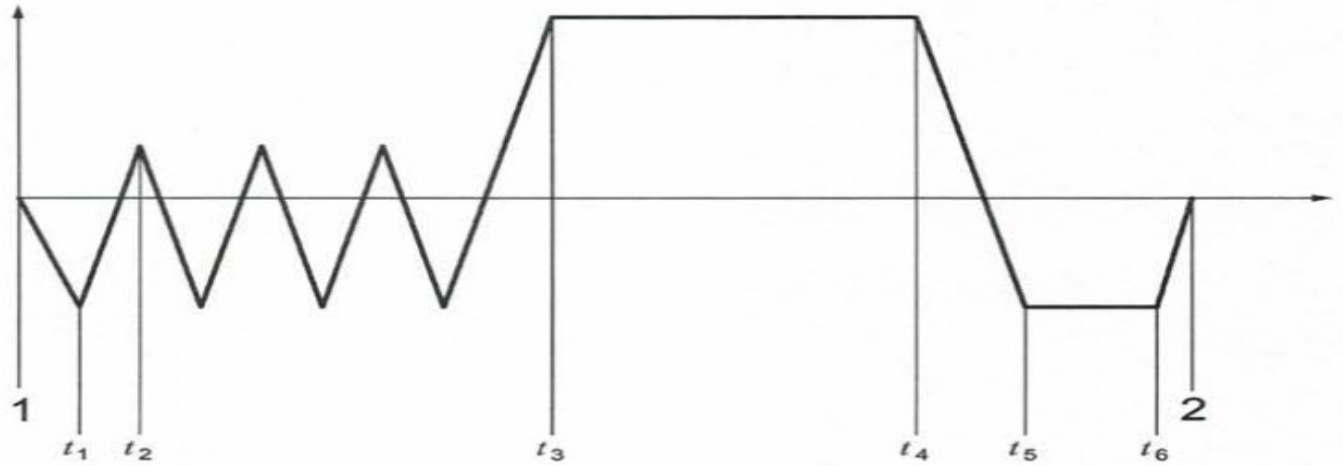

Key

1	start of the operating cycle	t_4	time at the end of the plateau period
t_1	time at the start of the first steam injection	t_5	time at the start of the drying period
t_2	time at the start of the second vacuum pulse	t_6	time at the end of the drying period
t_3	time at the start of the plateau period	2	end of the operating cycle

Figure 4 — Diagram of specimen operation cycle given as an example only

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Definition:

- What can effect the reproducibility of sterilization process?
  - Deviation of Cycle Parameters
  - Air retention in the load, Air Leak and Non-Condensable
  - Steam Overheat
  - Load orientation

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Definition:

- EN 285:15:
  - There are 25 sections plus 7 annexes
  - EN 285 specifies test procedure and criteria to confirm whether sterilizer is **safe** and **deliver** operating cycle and load configuration for sterilizing.
  - Steam Sterilizers-Large Sterilizers should follow European Standard.
  - EN 285:15 supersedes BS EN 285:2006.

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Definition:

- EN 285:15:
  - Approved by CEN
  - CEN is the European Committee for Standardization and it brings together the National Standardization Bodies of 34 European countries.

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Definition:

- Measuring chain: Series of elements of a measuring instrument or measuring system which constitute the path of the measurement signal form the input to the output.
- Risk Assessment: Overall process comprising a risk analysis and risk evaluation
- Risk Control: Process through which decisions are reached and protective measures are implemented for reducing risk to, or maintaining risks within, specified levels.

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Definition:

- Software Validation: confirmation, through the provision of objective evidence, that the requirements for a specific intended use or application have been fulfilled. This means data integrity.

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Gap Analysis

Section Numb

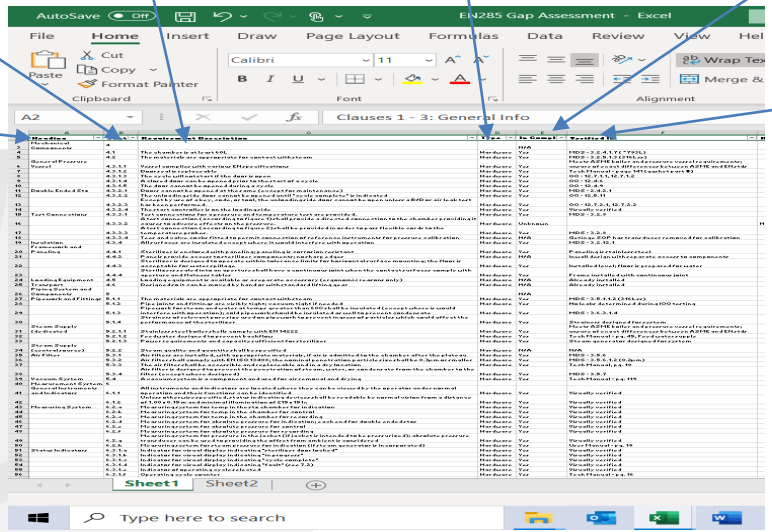
Section Name

Description

Type

Incompliance

Verified In



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Gap Analysis

Section Name	Section #	Requirement
Introduciton	Introducito n	An Air Detector is optional if there are other methods in place
Dimention, Material and Pressure Vessel	4.1	The chamber is at least 60L
	4.2	The materials are appropriate for contact with steam
	4.3.1.3	The cycle will not start if the door is open
	4.3.1.5	The door cannot be opened during a cycle
	4.3.2.2	The unloading side door cannot be opened until "cycle complete" is indicated
	4.3.2.4	The start controller is on the loading side
Piping and fitting	5.1.2	Pipe joints and fittings are visibly tight; vacuum tight if needed
	5.1.3	Pipework for steam and water at temps greater than 60C shall be insulated (except where is would interfere with operation); cold pipework should be insulated as well to prevent condensate
Measuring Chain and Recording	6.4.2	At least two independent temp measurement chains such that failure of an element in one chain will not cuase error or failure in the second chain
	6.4.2.c	Measurement error does not exceed 1% over 50 to 150C
	6.4.4	At least two independent pressure measurement chains ch that failure of an element in one chain will not cuase error or failure in the second chain
	6.4.4.g	Have a measurement error compensation that a measurement error caused by the ambient temp does not exceed 0.04K/K over the scale range 0KPa to 400KPa.
	6.5.1.1	The system shall be desinged to ensure integrity of raw data stored in sterilizer
	6.5.2.3	Printed and stored records shall be retrievable and readable when stored for a period of not less than 11 years; national regulations can apply

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Gap Analysis

Section Name	Section #	Requirement
Control System	7.1.6	Any controlled time deviation shall not exceed 1% of the specified value
	7.1.14	These is an automatic cycle for a leak test which displays the rate of pressure rise in kPa/min;
	7.2.7	If an air detector is installed, the system includes the ability to display measurements and adjust settings
	7.3.1	The software classification is established as part of a risk assessment.
	7.3.2	Software parts related to safety of patients, users, or any other persons shall be verified and validated.
Temperature Characteristics	8.2.1.2.1/8.2.1.3.1	In small and full load, the equilibration time shall not exceed 15s for stzs up to 800L usable space and 30s for larger stzs chamber
	8.2.1.2.4/8.2.1.3.4	The holding time shall not be less that 15 mins and 3 min for stz temps of 121C and 134C respectively
Risk Control	11.2.1	Risk assessment and risk control for sterilizer design and software should be performed following the method and requirements in ISO 14971
	11.2.2	Risk analysis should address the specific sterilizer design and features. Measures taken for risk reduction shall consider aspects as user knowledge, experience, training, ergonomics, and usability
Drains	13.8	The sterilizer shall be designed to operate with a drainage system resistant to water at 100C and be capable of passing the maximum flow rate of water, air and condensed steam (traps or air breaks added per national regulations)

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Gap Analysis

Section Name	Section #	Requirement
Steam Quality Test	21.1	Non-Condensable: the saturated steam containing up to 3.5 ml non-condensable gases collected from 100ml condensate. Repeat the test 3 times.
	21.2	Dryness: the saturated steam witht the dryness value not less than 0.95 where the dryness value deotes the mass of gas fraction in the mass of saturated steam. Basically, excessive moisture cause damp loads and too little moisture makes ultra superheat. Repeat the test 3 times.
	21.3	Superheat: When the steam expands to atmospheric pressure the superheat shall not exceed 25K. Repeat the test 3 times.
	21.4	Contaminants: Levels are in the presentation

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Gap Analysis

Table 4 — Suggested maximum values of contaminants in condensate from steam supply to the sterilizer chamber

Determinant	Condensate
Silicate	≤ 0,1 mg/l
Iron	≤ 0,1 mg/l
Cadmium[c]	≤ 0,005 mg/l
Lead[c]	≤ 0,05 mg/l
Rest of heavy metals except iron, cadmium, lead[b]	≤ 0,1 mg/l
Chloride	≤ 0,1 mg/l
Phosphate	≤ 0,1 mg/l
Conductivity (at 20 °C)[a]	≤ 4,3 µS/cm
pH (20 °C) value	5 to 7
Appearance	Colourless clean without sediment
Hardness (Σ Ions of alkaline earth)	≤ 0,02 mmol/l

[a] See European Pharmacopeia.

[b] If the condensate meets the requirements on conductivity, it is not necessary to perform heavy metal tests.

[c] The limiting values meet the requirements for potable water.

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Recommended Tests

Table 5 — Recommended test programme

Test	Requirement according to	Test method according to	Type test (see Annex E)	Works test
Thermometric tests				
– Small load	8.2.1.2	16.1	X	
– Full load	8.2.1.3	16.2	X	
Air removal and steam penetration				
– Bowie and Dick test	8.2.2	17	X	X
– Air leakage	8.2.3	18	X	X
– Air detector, small load [a]	8.2.4.2	19.2	X	X
– Air detector, full load [a]	8.2.4.3	19.3	X	
– Air detector function [a]	8.2.4.4	19.4	X	X
– Hollow load test	8.2.5	15	X	
Load dryness tests				
– Small load, textiles	8.3.1	20.1	X	
– Full load, textiles	8.3.2	20.2	X	
– Metal	8.3.3	20.3	X	
Sound power	9.1	9.1	X	
Rate of pressure change	10	22	X	
Steam quality tests				
– Non-condensable gases	13.3.1	21.1	X	
– Dryness value	13.3.2	21.2	X	
– Superheat	13.3.3	21.3	X	
X = denote a recommended test				
[a] If an air detector is fitted (see 8.2.4.1).				

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Recommended Tests

Table D.1 — Suggested tests

Test	Requirements according to clause	Test according to clause	Installation Qualification	Operational Qualification
Safety Tests and checks	11		XX	—
Steam quality tests				
- Non-condensable gases	13.3.1	21.1	X	X
- Dryness value	13.3.2	21.2	X	X
- Superheat	13.3.3	21.3	X	X
- Contaminants	Table 4	a	X	X
Thermometric tests				
- Small load	8.2.1.2	16.1	—	XX
- Full load	8.2.1.3	16.2	—	XX
Hollow load test [b]	8.2.5	15	—	XX
Bowie and Dick test	8.2.2	17	—	XX
Rate of pressure rise caused by air leakage	8.2.3	18	—	XX
Air detector[c]				
- Small load	8.2.4.2	19.2	—	XX
- Full load	8.2.4.3	19.3	—	XX
- Function	8.2.4.4	19.4	—	XX
Load dryness tests				
- Small load, textiles	8.3.1	20.1	—	X
- Full load, textiles	8.3.2	20.2	—	XX
- Metal	8.3.3	20.3	—	X
Rate of pressure change	10	22	—	X

XX tests which are suggested
X tests which can be considered
— tests which need not be performed during IQ and/or OQ

a Compliance tested in accordance with acknowledged analytical methods.
b This test is not intended to be used as a routine daily test.
c If an air detector is fitted (see 8.2.4.1).

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IOPQ:

- IQ: Typical verification of supporting documentation and filed verification
- OQ: Typical testing of control system and Empty chamber mapping
- PQ for dry goods using one cycle:
  - Engineering study:
    - Consulted with users (Manufacturing) and a list of all items were identified

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IOPQ:

- Engineering study:
  - Items were double bagged in autoclave pouches
  - Wireless temperature sensors we placed into each of the items
  - One conservative cycle by consideration of high loading capacity was selected. The cycle had five (5) pre-pulses and one (1) post-pulse (needed for drying).

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IOPQ:

- Engineering study:
  - After completion of all runs, a comparison of accumulated lethality (F0) during the hold time was performed.
  - Items with lower F0 was considered “worst-case”.
  - Total of eight (8) items were identified

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IOPQ:

- PQ:
  - Engineering study determined the load and the cycle
  - Challenged sterilizer in minimum and maximum load configuration.
  - Based on the number of racks in two shelves (4) , and number of items (8), a total of 32 items were distributed as maximum. One item was used as minimum.
  - Used Biological Indicators

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IOPQ:

- PQ:
  - Following two bullets from section 8.2.1 “Temperature characterization” were critical and used as acceptance criteria:
    - During the sterilization phase, temperature sensors shall not exceed the temperature measured at drain sensor (reference point) by more than 5°C for the first 60 second and 2°C for the remaining period.

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IOPQ:

- PQ:
  - Throughout the sterilization phase, temperature measured at drain sensor, all temperature sensors and the theoretical temperature of the saturated steam determined from the pressure sensor shall be within the sterilizer temperature band and not differ from on another by more than 2°C.

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IOPQ:

- PQ:
  - The other criteria were routine PQ acceptance criteria such calibration, F0, temperature within sterilization band,….

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