Validation of hydrogene peroxide Sterilizers following ISO 14937

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Fields of activities:

Validation of the cleaning processes

Validation of disinfection processes

Validation of sterilization processes

Validation of instrument behaviour with respect to

- **Steam sterilization**
- **Ethylenoxide sterilization**
- **Formaldehyde sterilization**
- **Hydrogene peroxide sterilization**

Research in the field of prions

Testing of new instruments designs

Testing of cleaning agents

Testing of disinfection agents

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ISO 14937:2009

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

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ISO 14937:2009

Requirements:

1. Selection of the test organism
2. Definition of the D-Value of the organism
3. Biological Indicators following ISO 11138
4. Chemical Indicators following ISO 11140
5. Pass-Fail criteria

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Selection of the test organism

- Geobacillus stearothermophillus is well ATCC 7953 is well accepted to test hydrogene peroxide sterilization processes.
- A minimum of 10^6 cfu per indicator should be used, when the sterilizer is running in half cycle mode.
- All microorganisms have to be killed in half cycle mode

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Definition of the D-Value of the test organism

- In microbiology, **D-value** refers to **decimal reduction time** and is the time required at a given temperature to kill 90% of the exposed microorganisms. The term is used in assessing microbial thermal resistance and thermal death time analysis.
- Thus after a colony is reduced by 1 D, only 10% of the original organisms remain, i.e., the population number has been reduced by one decimal place in the counting scheme. Generally, each lot of a sterilization-resistant organism is given a unique D-value. When referring to D-values it is proper to give the temperature as a subscript of the "D". For example, given a hypothetical organism which is reduced by 90% after exposure to temperatures of 300° F for 20 minutes, the D-value would be written as D_{300F} = 20 minutes. D-value determination is often carried out to measure a disinfectant's efficiency to reduce the number of microbes present in a given environment.[1]
- (Wikipedia)

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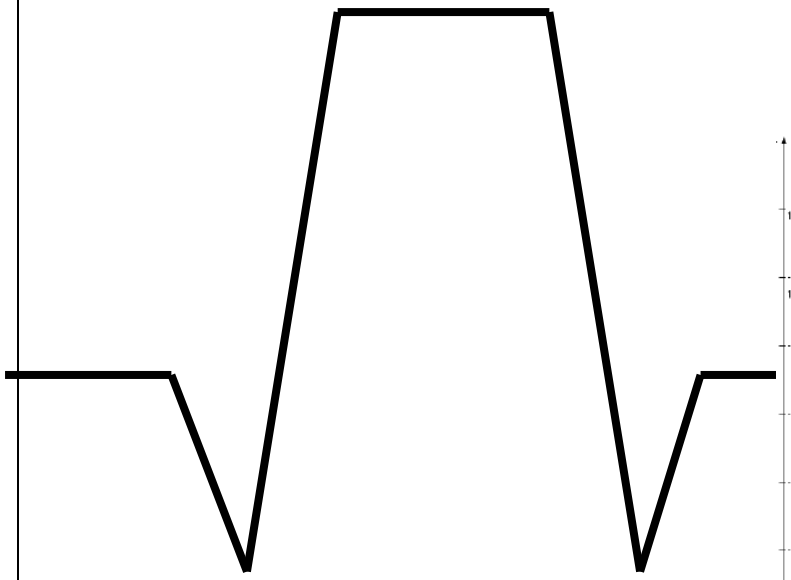
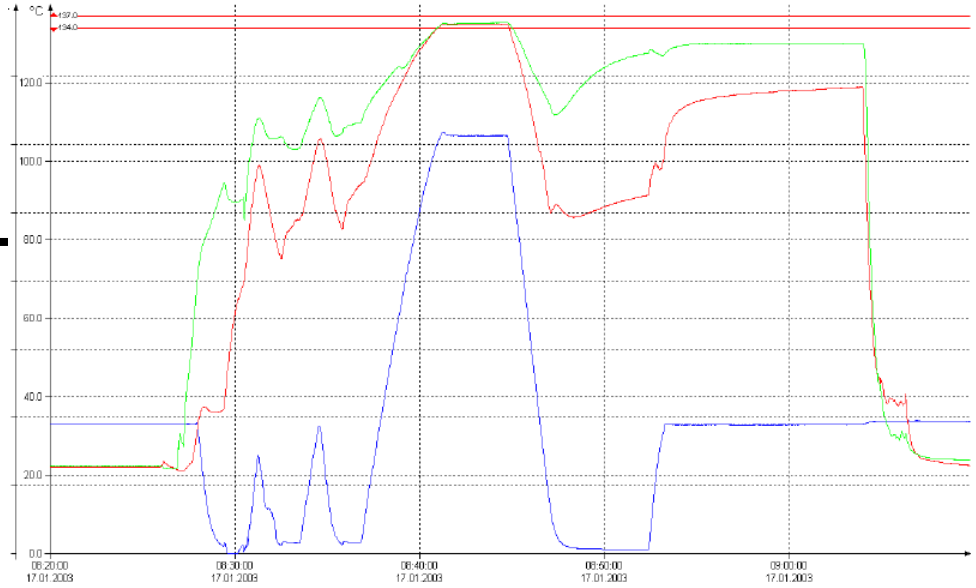
Definition of the D-Value

Cycle in a resistometer for steam

ISO 18472



Cycle in a steam sterilizer



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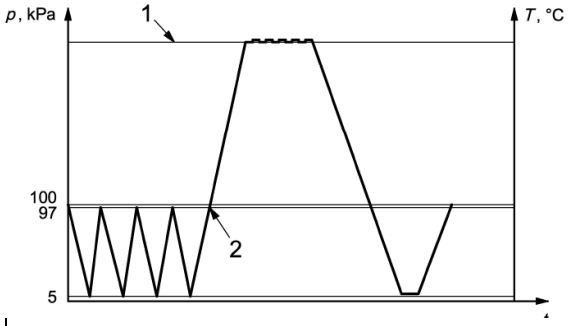
Definition of the D-Value

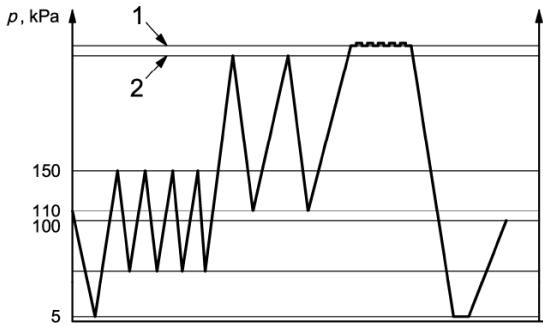
The cycles in a steam sterilizer are well established.

Different types of cycles are known:

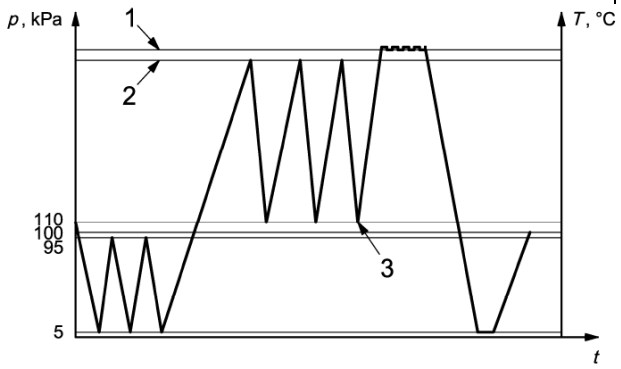
Subatmospheric



Transatmospheric



Super atmospheric



The preparation time is not defined.

Only the plateau phase is defined by time, temperature and pressure

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Definition of the D-Value

Sterilization cycles in a plasma sterilizer:

Each manufacturer has designed his own cycle.

Some manufacturer have the same cycle for all models and adapt the amount of H_2O_2 to the size of the chamber.

Some manufacturer has an individual cycle for each model

We found cycles with

One injection phase

Two injection phases

Four injection phases

The individual design of the sterilization phase has to be regarded when setting up a resistometer for H_2O_2 sterilization.

We found in reports D-values between 0.56 min and 6 min.

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Biological Indicators following ISO 11138

- Depending of the carrier material biological indicators failed
- Also the same indicators but from different lots showed different behavior

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Chemical Indicators following ISO 11140

- Most of the chemical indicators had already a complete color change after the half cycle

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Pass-Fail criteria

- Temperature
- Humidity
- Insufficient vacuum
- Low amount of hydrogene peroxide
- Load
- Combination of failures

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Pass-Fail criteria

Temperature

- Temperature was set on a lower level (2°C beneath the warning level given by the manufacturer)
- Acceptance criteria:
- BI has to pass in half cycle mode
- If the BI fails in halfcycle mode the CI has to fail in full cycle mode
- CI has to fail in half cycle mode

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Pass-Fail criteria

Humidity

Depending on the possible load for the sterilizer a wet fabrics was placed inside the chamber. The amount of water was increased until the sterilizer was going into failure mode.

The BI‘s and CI‘s of the cycle were evaluated using the same criteria as mentioned before.

Pass-Fail criteria

Insufficient vacuum

Vacuum was set on a higher level (above the warning level given by the manufacturer)

The BI‘s and CI‘s of the cycle were evaluated using the same criteria as mentioned before.

Pass-Fail criteria

Low amount of hydrogene peroxide

- Cycles were run with a lower portion of hydrogen peroxide
- Also Hydrogen peroxide at the end of the shelf live was used

The BI‘s and CI‘s of the cycle were evaluated using the same criteria as mentioned before.

Pass-Fail criteria

Combination of failures

Simulated failures all together have been run with empty and full chamber

The BI‘s and CI‘s of the cycle were evaluated using the same criteria as mentioned before.

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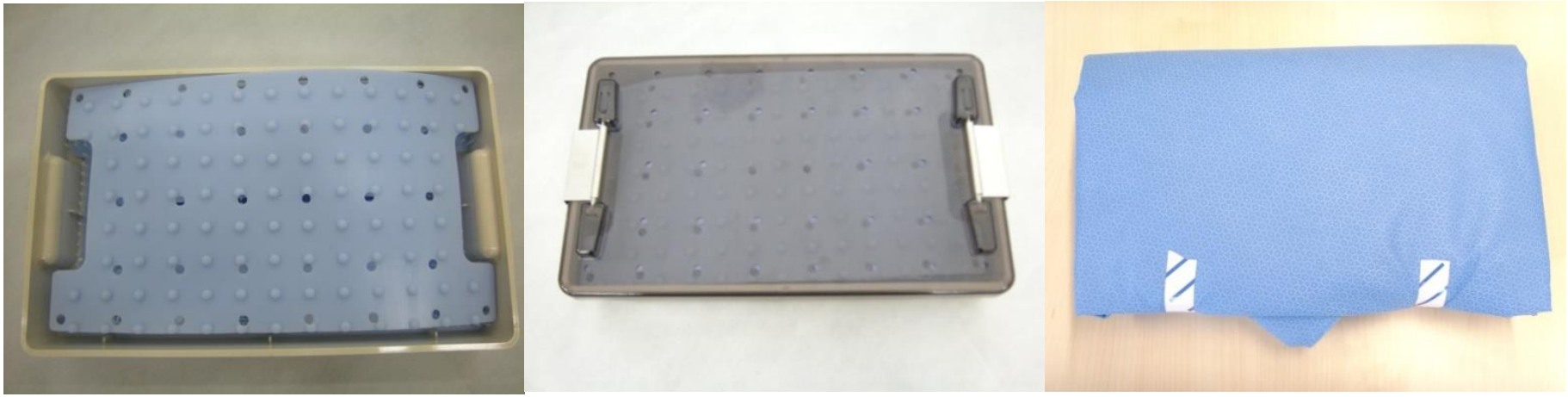
Pass-Fail criteria

Load

The sterilizers have been loaded with silicone mats and/or other materials.

The size of the load was depending on the results of the BI‘s. Sterilization has been performed in half cycle mode.



Example for challenge pack

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Sterilizer tested since 2000

Manufacturer	1				2			3	4
Sterilizer	1	2	3	4	5	6	7	8	9
Comparable Cycle of the different sterilizer models					x	x	x		
Plasma phase	x	x	x	x	x	x	x	x	
Pre-heating	x	x			x	x	x	x	x
Concentration of H_2O_2			x	x				x	
Parametric control with calculated concentration of H_2O_2	x	x			x	x	x	x	x
Parametric control including measurement of H_2O_2			x	x					

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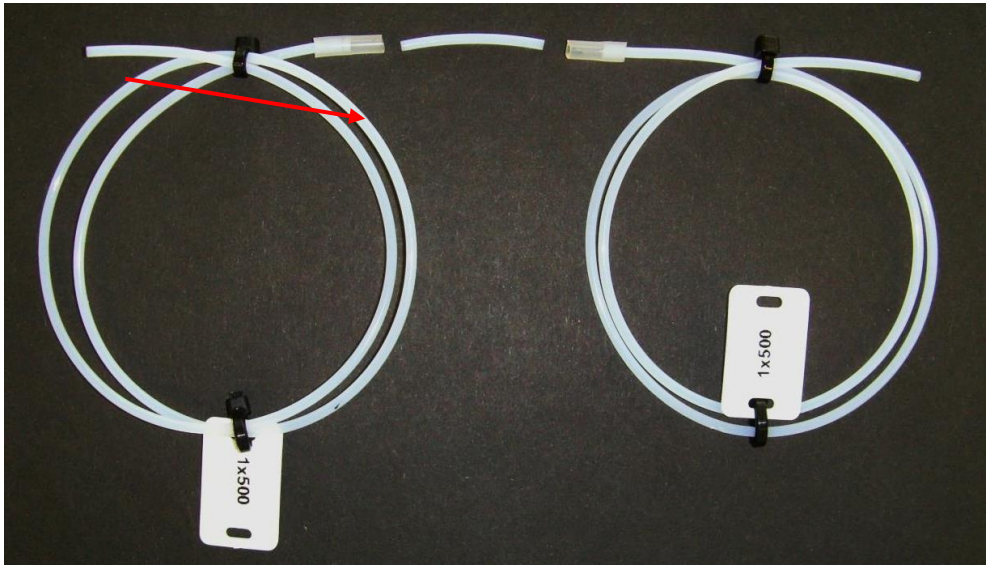
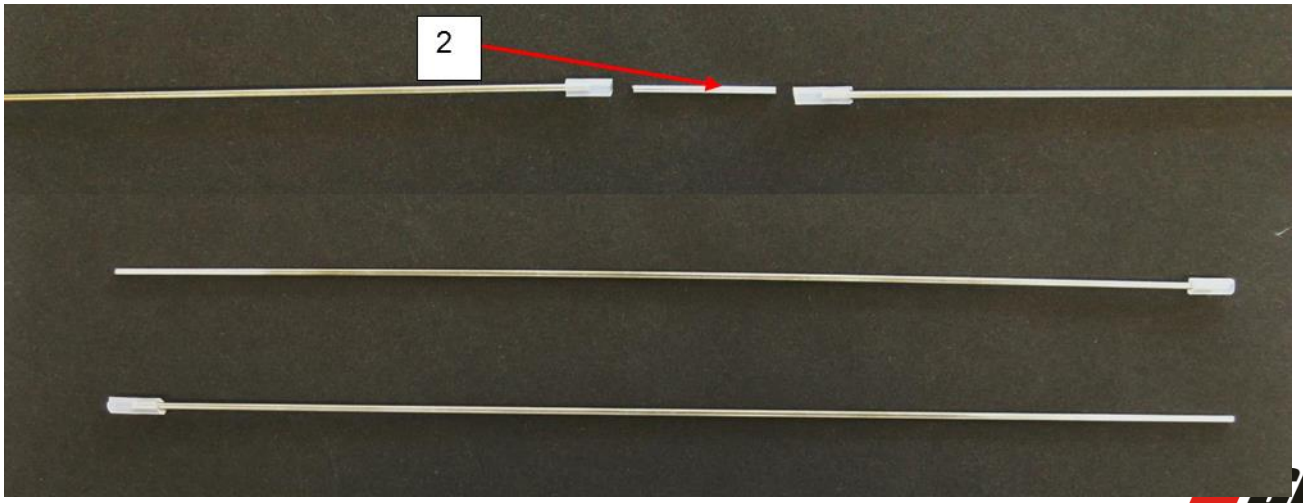
Bioindicators used for the tests





Testing of the spore suspension

Sample No.	Inoculated location	CFU / plate[1)]	Incubation ofthe TSB eluate[2)]	Identification[3)]	CFU /Inoculated location[4)]
54%-1	1	0	+	*G. stearotherm.*	0
54%-2	1	7	+	*G. stearotherm.*	<10
54%-3	1	20	+	*G. stearotherm.*	>20
27%-1	1	>300	+	*G. stearotherm.*	>300
27%-2	1	>300	+	*G. stearotherm.*	>300
27%-3	1	>300	+	*G. stearotherm.*	>300
13.5%-1	1	Lawn growth	+	*G. stearotherm.*	>1000
13.5%-2	1	Lawn growth	+	*G. stearotherm.*	>1000
13.5%-3	1	Lawn growth	+	*G. stearotherm.*	>1000

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Influence of the temperature

Position	Beschreibung	Temperatur (warm/kalt)	Beladung [kg]	Halbzyklus	Vollzyklus	Fläche unter der Kurve [mg-s/l]
1	4 Bioindikatoren (2x Stahl Lumen, 2x PTFE-Lumen)	-	-	x		8892,7
2	3 Blaue Silikonmatten	kalt	-		x	1:6829,8 2: 8025,8
3	**eloxierter Container**	**warm**	**4,5**	x		**8649,4**
4	**eloxierter Container**	**kalt**	**4,5**	x		**2938,4**
5	**nicht eloxierter Container**	**warm**	**4,5**	x		**8794,5**
6	**nicht eloxierter Container**	**kalt**	**4,5**	x		**2473,2**
7	**nicht eloxierter Container**	**kalt**	**6**	x		**2408,4**
8	16 Bleche "1-neu" (Lauf 1)	kalt	-		x	1: 6093,7 2: 8801,0
9	16 Bleche "1-neu" (Lauf 2)	kalt	-		x	1: 6357,5 2: 8847,0
10	16 Bleche "1-neu" (Lauf 3)	kalt	-		x	1: 6443,9 2: 8822,5

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Conclusion

- The use of ISO 14937 as a guidance for the IQ, OQ, PQ process for H_2O_2 sterilizer has limitations as not all requirements can be fulfilled (resistometer etc. is missing)
- Indicator has to be designed for each specific cycle
- The load of the sterilizer has to be defined in details. Deviations in material weight and surface area of the load may lead to a reduction of the safety of the process
- PCD‘s should simulate not only the geometry but also the material of the instruments

- Specific standards for H_2O_2 sterilizers and the accessories are needed

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Thank you very much

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