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Performance qualification of Industrial steam Sterilizer(Autoclave)

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Abstract

Steam sterilization used to sterilize items that can withstand moisture and high temperature. An autoclave or steam sterilizer is used to sterilize surgical equipment, laboratory instruments, pharmaceutical items, and other materials. Steam Sterilizer or autoclave Validation / periodic Qualification is mandatory for all machines used for biological sterilization, in the biomedical and pharmaceutical industries. The purpose of the periodic requalification is to verify the performance of the equipment with respect to time. Autoclaving is the most effective and most efficient means of sterilization. All autoclaves operate on a time/temperature relationship. These two variables are extremely important and need to establish through validation. Periodic requalification required to challenge the pre-established time/ temperature relationship during the equipment life cycle. Periodic qualification divided into two parts. First part is physical verification and critical operational control checks. Second part is performance evaluation. First step is to assure the equipment is in state of control. Second step deals with the output. Heat penetration study performed with pre-established worst load items. Study mapped with external temperature sensors for mapping the thermal effect on the load articles during sterilization. Biological indicators also used to challenge the microorganism challenge efficiency.

Keywords : Steam sterilizer, periodic qualification, Biological indicators, pharmaceutical items, performance evaluation

Introduction

The invention of the autoclave sterilizer is attributed to Charles Chamberland, in 1879. Around that time, researchers started to understand the advantages of sterile surgery, and doctors needed a more reliable sterilization method than open flaming. The autoclave's benefits were soon evident, and it became an essential part of every clinic and hospital. An autoclave or steam sterilizer is used to sterilize surgical equipment, laboratory instruments, pharmaceutical items, and other materials. It can sterilize solids, liquids, hollows, and instruments of various shapes and sizes. Autoclaves vary in size, shape and functionality. A very basic autoclave is similar to a pressure cooker; both use the power of steam to kill bacteria, spores and germs resistant to boiling water and powerful detergents

Validation procedure

Temperature Monitoring Equipment

A pre-calibrated external multi-channel Data logger, capable of displaying and recording temperature with a sensitivity of 0.1°C, shall be used for recording the temperature readings at different locations within the Hinged door Bung processor cum steam

sterilizer and the calibration protocol of Data logger. The details of Data Logger shall be provided in the protocol for make, capacity, number & type of channels shall be described in the Protocol.

The data logger shall have flexible temperature probes / RTDs (temperature sensors), which shall be capable of sensing temperature with a sensitivity of 0.1°C. also have an in-built real-time clock, to record temperature at predetermined time intervals. 16 temperature probes / sensors shall be placed at different locations inside the Hinged door Bung processor cum steam sterilizer to record temperature readings at critical places, during the validation activity.

Calibration of Associated Components

All the in-built instruments, which measure the critical parameters such as temperature, vacuum or pressure, shall becalibrated.

Steam Quality Checks

Collect the Pure Steam Sample from the sampling points which is provided to Bung processor & Send it to QC & Microbiology laboratory for testing as per Pure steam Specification. Record the observations in Annexure - 1

Calibration of External Data Logger Probes

The external data-logger probes, used for the temperature measurements, shall be calibrated, prior to the Hinged door Bung processor cum steam sterilizer Validation and the protocol of these calibrations shall be attached in Attachment-
03. A deviation of not more than 0.5oC, from the set temperature. The data obtained during the calibration of 16 data-logger probes / sensors, shall be reviewed and all the probes / sensors should be within the specified range.

Gasket integrity Check

The door gaskets of Hinged door Bung processor cum steam sterilizer shall be checked visually, for any physical damages and gasket fitment. No damage should be there in both the gaskets and should fit properly. Record the observations in Annexure - 02.

Validation Test Procedure

The Hinged door Bung processor cum steam sterilizer will be validated (As per the methods outlined in this Protocol) the equipment for desired performance and its ability to sterilize different components and / or loads at the set parameters and set loading patterns, repeatedly and consistently.

Validation Methodology1.Vacuum Leak Test Objective:

To ensure that the rate of vacuum drop is within the acceptable limits when the Hinged Door Bung processor cum steam sterilizer is subjected to the vacuum of more than/equal to -0.700 Bar on gauge (equivalent to 100m Bar absolute pressure).

Procedure:

During chamber vacuum leak test, the Hinged Door Bung processor cum steam sterilizer chamber shall be subjectedas shown in table:

Parameter	Set Values
Vacuum Level	-0.700 Bar
Vacuum stabilize delay	05 Min
Vacuum Hold time	10 min
Process End Pressure	-0.090 Bar
Acceptance Leakage	0.013 Bar
Print Interval	60 Second

The set parameters and the observed parameter values during the Vacuum Leak Test cycles shall be recorded inAnnexure – 03.

Acceptance criteria:

For vacuum leak test, vacuum decay should not be more than 0.013 bar during the vacuum hold phase.

2. Bowie-Dick TestObjective:

To ensure that the Vacuum pulsing applied before the Sterilization Hold period is sufficient to remove the entrapped air or non-condensable gases so as to facilitate rapid and uniform steam penetration into all parts of the load and maintaining these conditions for the specified temperature holding time (17 minutes at 121.0°C to 124.0 °C). If air is present in the chamber, it will collect within the pack as a bubble. The indicator in the region of the bubble will be of different color as compared to the color on the remaining part of the test paper, because of a lower temperature, lower moisture level or both. In this condition the cycle parameters shall be reviewed and the normal sterilization cycles

Sr. No.	Test	No of Run
1.	Vacuum Leak Test With Probe	1 Runs
2.	Bowie –Dick Test	1 Runs
3.	Empty Chamber Heat Distribution Studies	1 Runs
4.	Loaded Chamber Heat Penetration Studies	1 Runs for each load
6.	Standard Process	1 Run

shall be modified accordingly.

Procedure:

Place one Bowie-Dick Test Pack in the centre of the Hinged door Bung processor cum steam sterilizer, supported approximately 100 to 200 mm above the Hinged door Bung processor cum steam sterilizer base. Select cycle on the control panel and operate the Hinged door Bung processor cum steam sterilizer.

Set Parameters for Bowie Dick Test are as follows:

Pre Vacuum level	0.700Bar	Ster. Stop Temp.	120.9 °C
Pre Vacuum hold time	03 Min	Ster. Reset Temp.	120.5 °C
Pre heat pressure	0.500Bar	Overshoot Temp.	124.0 °C
Pre Pulses Number	2 Nos.	Exhaust End processor	0.080Bar
Sterilization temperature	121.5 °C	Control band	0.3 °C
Post vacuum Hold time	05 Min	Jacket alarm time	02 Min.
Post vacuum Break	0.080Bar	Heat up Alarm Time	10 Min.
Ster. Hold Time	17 Min.	Post vacuum level	0.600Bar
Post pulse number	02 No.	Print interval time	60 Sec

Table 1.

The printout taken during the Bowie-Dick test cycle and the Bowie-Dick Test Indicator should be preserved as perthe Annexure - 04.

Remarks: The Bowie-Dick cycle should be normally preceded by a warm-up cycle, as the effectiveness of air removal may depend on all parts of the sterilizer being at working temperature.

Acceptance criteria:

The Bowie-Dick Test Indicator should have uniform Color change.

3. Empty chamber (Heat Distribution Study) testingObjective:

Objective of this test is to ensure that:

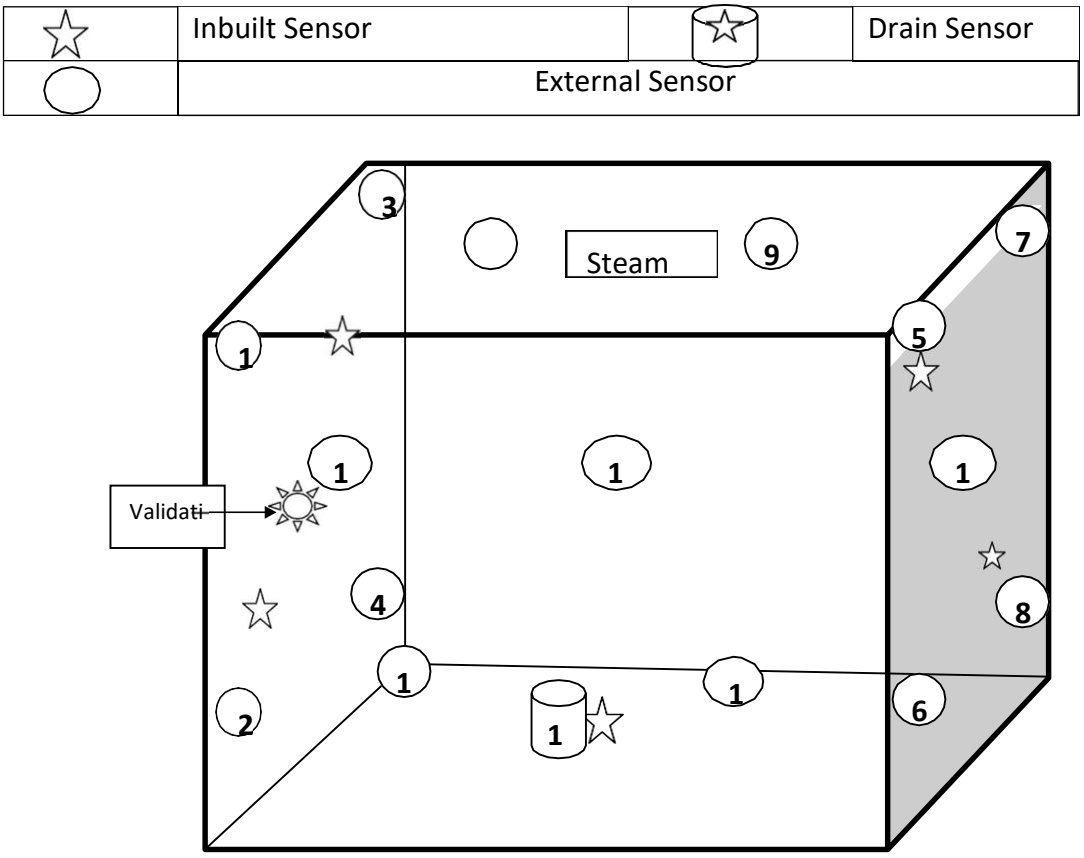
The sterilizer is capable of attaining desired sterilization temperatures during the sterilization hold period.

Temperature spread within the range of 121.0°C to 124°C during sterilization cycle (30 Min) will demonstrate theuniform heat distribution within the chamber.

Any location(s) where the temperature indicator is placed, not achieving minimum sterilization temperature of121.0°C throughout the sterilization temperature hold will be considered as cold spot (slow to heat).

Procedure:

Record the set parameters for the sterilization cycle to be operated during the test for empty chamber heat distribution study, in the Annexure - 05.Insert minimum 16 temperature mapping probes into chamber through the port of the sterilizer, out of which keep one probe in drain point. Seal the port with the help of silicone sealant so that steam leakage cannot take place .Suspend the probes in the chamber in different positions such that the probes do not touch any solid surface. The location of each probe should be illustrated in a diagram with probe numbers (Refer Diagram-01). Attach the probes connecting cable to the data logger which can scan and print the date, time and temperature ofprobes



Set Parameters for Empty Chamber Heat Distribution Studies (HPHV Process) are as follows:

Pre Vacuum level	0.700Bar
Pre Vacuum hold time	03 Min
Pre heat pressure	0.500Bar
Pre Pulses Number	1 Nos.
Sterilization temperature	121.5 °C
Post vacuum Hold time	10 Min
Post vacuum Break	0.080Bar
Ster. Hold Time	30 Min.
Post pulse number	03 No.

Ster. Stop Temp.	120.9 °C
Ster. Reset Temp.	120.5 °C
Overshoot Temp.	124.0 °C
Exhaust End processor	0.080Bar
Control band	0.2 °C
Jacket alarm time	02 Min.
Heat up Alarm Time	10 Min.
Post vacuum level	0.700Bar
Print interval time	60 Sec

Table 2

Operate the autoclave and also start the data logger to record the actual temperatures within the chamber with respectto time. Compile the complete data generated during the Validation test for complete evaluation of the system.

Acceptance Criteria:

During empty chamber heat distribution studies, the Hinged door Bung processor cum steam sterilizer should be capable of attaining a temperature of 121.0ºC to 124.0ºC during the sterilization hold period of 30 minutes with steam pressure of approximately 1.1 to 1.4 Kg/cm². Temperature spread should be uniform in the Hinged door Bung processor cum steam sterilizer within the range of 121.0ºC to 124ºC during 30 minutes of entire sterilization hold period from all chamber thermocouple readings.

4. Loaded Chamber Heat Penetration Studies Objective

Objective of this test is to ensure that:

The heat is sufficiently penetrating into the innermost portions of the load subjected for sterilization to achieve a temperature of 121.0°C - 124°C during the sterilization hold period (30 Min.) with steam pressure of not less than 1.1 Kg/cm². If sterilization temperature (121.0°C) is not achieved throughout the cycle, load configuration or size of the load has to be reviewed and cycles to be repeated. The equilibration time between the drain probe and coldest part of the load for achieving sterilization temperature should not exceed the (time limit 30 Seconds*) against each load.

NOTE: The Time limit is tentative and shall be established after evaluation of validation trials for each load. Temperature spread within the range of 121.0°C to 124°C during sterilization hold period (30 Min) will indicate that uniform heating process which is achieved in the empty chamber heat distribution study is not affected by load.

Procedure:

The following loads shall be considered in Loaded Chamber Heat Penetration Study

LOAD PATTERN	Load Size	No of Run Cycles	Load Description
Loaded Chamber Heat Penetration Study of Garments.(HPHV Cycle)	Minimum	1	05 Head gear, 05 Gown with leggie,05 Pair of botties & 02 lint free duster, Sterile paper 15.
	Maximum	1	30 Head gear, 30 Gown with leggie, 30 Pair of botties & 20 lint free duster, Sterile Pen 1, Sterile paper100, Tyvek paper 10,
Loaded Chamber Heat Penetration of Miscellaneousload (HPHV Cycle)	Minimum	1	SS Container 01, mop withhandle 01, lint free duster 01, microplate Stands 05.
	Maximum	1	SS Container 06, mop withhandle 04, lint free duster 10, microplate Stands 49.
Loaded Chamber Heat Penetration of Filling and Sealing Machine Parts (HPHVCycle)	Minimum	1	Filling pump Piston 06, manifold 01, Filling needles 08, Nitrogen needles 14, Buffer tank 01, Silicon tube for nitrogen 12 mtr , silicon tube for product filling 12+2 mtr, Nitrogen filter 01, SS container 04, SS mug 04, SS clamps 10, Forceps 08, Gasket 10, nozzles 10. SS Scissors 02, Pressure vessel 10 ltr 01
	Maximum		Filling pums 08, Manifold 03, filling needles 08, Nitrogen needles 12,buffer tank (Pressure vessl) 01,

		1	silicon tubing for product filling 18, silicon tubing for nitrogen 16, nitrogen filter 01, SS clams 10, forceps 08, gaskets 10, nozzles 10, SS scissors 02, pressure vessel 100 ltr 01,
Loaded Chamber Heat Penetration of 20 mm Rubber Stopper (HPHV Cycle)	Minimum	1	5000 Nos
	Maximum	1	60000 nos
Loaded Chamber Heat Penetration of Flip of aluminum seal (HPHV Cycle)	Minimum	1	5000 Nos
	Maximum	1	60000 nos
Loaded chamber heat penetrationstudy Stainless Steel Tray	Minimum	1	10 tray
	Maximum	1	104 tray
Loaded Chamber Heat Penetration of Disinfectant & fogging Load (HPHV Cycle)	Minimum	1	Largene container 01, membrane holder or capsule filter 01, Silicon tubing's 10 mtr, TC clamp and gaskets 02, SS mug 01, SS scissors 01, SS pressure vessel 01, Sample Bottle 03, Dipstick 01, IPA spray bottle 03.
	Maximum	1	Largene container 04, membrane holder or capsule filter 04, Silicon tubing's 10 mtr, TC clamp and gaskets 05, SS mug 02, SS scissors 01, SS pressure vessel 02, Sample Bottle 10, Dipstick 01, IPA spray bottle 15.

NOTE: If New Load introduce or modification done in exiting Load pattern then need to take 3 cycle for each Modified or Newly introduced load.

Insert minimum 16 Temperature Mapping probes into the chamber through the port of the sterilizer, out of which keep one probe in drain point. Seal the port with silicone sealant (if required) so that steam leakage cannot take place. Place the probes inside the loaded components which are supposed to be most difficult points for steam penetration. Place 16 biological indicators along with temperature mapping probe inside the loaded articles. BIs are not required to be placed outside the loaded articles. After completion of Cycle incubate the B.I at 55 to 60◦C for 7days or as per Vendor COA. Suspend the probes in the chamber in different positions such that the probes do not touch any solid surface. The location of each probe and BIs should be illustrated with in a probe. Attach the probes connecting cable to the data logger which can scan and print the date, time and temperature of probes. Operate the Hinged door Bung processor cum steam sterilizer and also start the data logger to record the actual Temperatures within the chamber with respect to time. Runs the cycle for each load to demonstrate cycle and sterilizer reproducibility.

Set Parameters for Loaded Chamber Heat Penetration Studies same ass Heat Distribution Studies shown in Table 2

Acceptance Criteria:

The Hinged door Bung processor cum steam sterilizer should be capable of attaining a temperature of 121.0ºC during the sterilization hold period of 30 minutes with steam pressure of approximately 1.1 kg/Cm² (1.1 kg/cm2 to 1.4 kg/cm2). Temperature spread should be uniform in the chamber within the range of 121.0ºC to 124ºC during sterilization cycle. The measured temperatures including active chamber discharge should be within 20C of each other The measured temperatures including active chamber discharge should not fluctuate by more than 10 C The recorded chamber pressure should not be less than 1.03 bars Each autoclaved Biological indicator should give the 'NEGATIVE' test during the incubation. ***Fo*** value calculated from the temperature data obtained from individual temperature mapping probe should indicate more 6 log reduction of bio-burden or should be more than the calculated value of Biological Indicator as below with a D value of Not Less Than 1 min.

$$Fo = D_{121} \times (\text{Log } N_o - \text{Log } B)$$

Where,

D121 : D Value of the Biological Indicator used in the study time at 121°C to reduce most resistantmicroorganisms, found in product or environment by 90% .

No: Spore population in each biological indicator strip.B : Sterility Assurance Level. i.e. 1x10-6 (SAL).

Test for Rubber Stoppers Objective:

To ensure the sterilization of rubber stopper during rubber stopper sterilization cycles.

This Procedure shall be applicable for each load and each run of washing of rubber stoppers.

Test Procedure: -

After completion of Sterilization cycle send the sample to Microbiology laboratory for Testing purpose.

Sterility Test: - Perform the sterility test by direct inoculation method. In which aseptically add 5 No of rubber stopper in SCDM & 5 No of Rubber stopper in FTM then Incubate SCDM at 20-25ºC & FTM at 30-35 ºC for 14Days. Observe the result up to 14 days on daily basis.

Liquid bourn Particle count: - Take clean, Dry glass beaker in which add 100 ml Particle free water, then add 10 no of rubber stopper, Shake for some time, then out of 100 ml collect 25 ml in other cleaned glass Beaker & performLBPC as per SOP NO SOP/MIC/059.

BET Test: - Perform BET Test as per WFI Specification.Estimation of F0 Value

Basis of Calculations:

Testing Parameters	**Acceptance Criteria**
Moisture Content	Free from Moisture Contain
Sterility	Growth should not be observed
Liquid bourn particle count	10 µm ≤ 6000 particles per container 25 µm ≤600 particles per container
BET	Less than 0.25 EU / ML

The actual observations obtained during the Empty chamber heat distribution / Heat penetration studies at different temperature sensing locations should be subjected for calculation of ***F0*** values. The calculations are doneby using the following formula

$$F0 = dt \sum 10^{(T-121)/Z} \quad \text{..... (a)}$$

$$F0 = dt \sum (\text{Sum of lethal rates})$$

Where,

dt = The time interval between successive temperature measurements (1 min.).

T = The observed temperature at that particular time (As per the actual temperatures recorded).

Z = The change in the heat resistance of Bacillus Stearothermophilus spores as temperature is changed(10°C).

Acceptance Criteria:

Validation Parameter	**Acceptance Criteria**
Vacuum Leak Test	Vacuum decay should not be more than 0.013 bar during the vacuum hold phase.
Bowie-Dick Test	The Bowie-Dick Test indicator should show a uniform colour change.
Heat distribution	There should be uniform distribution of heat in the sterilizer chamber during the sterilization hold period (30 Min.) and the temperature at each temperature mapping probe should be within the range of 121.0°C to 124°C at the onset of sterilization hold period (30 Min) .

Heat penetration	There should be uniform penetration of heat in the load subjected for sterilization during the sterilization hold period (30 Min.) and the temperature at each temperature mapping probe should be within the range of 121.0°C to 124°C at the onset and during the sterilization hold period (30 Min).
Biological challenge studies	In Case of Ampoules: Colour should not be Changed from Purple to Yellow orTurbid. In Case of Streep's: No Growth Should be observed
F0 Value	The Calculated minimum F_0 value (by equation a) should be more thansterilization Hold period.
Moisture Content	Free from moisture Content
Sterility	Growth should not be observed
Liquid bourn particlecount	10 µm ≤ 6000 particles per container 25 µm ≤600 particles per container
BET	Less than 0.25 EU / ML

Re-validation criteria

1. Replacement of existing instrument / component with a new one, which can have a direct impact on theperformance of the machine.
2. If the machine is found to be malfunctioning during Re-Validation studies.
3. Once in a Year

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