PERFORMANCE QUALIFICATION PROTOCOL/REPORT

AUTOCLAVE OF STERILE AREA

DOCUMENT NO. :
VERSION No. :
DATE OF ISSUE :

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Protocol Approval

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CONTENTS

1. DOCUMENT DESCRIPTION

Document No.

Version No.

Date of Issue

Description

2. PURPOSE

To authenticate and document that the performance of the Autoclave (Steam sterilizer) of Sterile Production area (Cephalosporin Block) of XX Pharmaceutical Limited (PPL) is satisfactory in all critical aspects related to the operational requirements during sterilization of porous, solid and liquid loads. This protocol describes the performance qualification procedures of the Autoclave manufactured by Zirbus, Germany.

3. SCOPE

This Performance Qualification (PQ) is to be performed against agreed acceptance criteria on different types of loads which will be sterilized by the Autoclave (Steam Sterilizer) installed in the Sterile Production area of Cephalosporin Block of XX Pharmaceutical Limited.

4. RESPONSIBILITIES

Preparation of the protocol	Validation (Engineering) Department with the assistance of Microbiology, Engineering and Maintenance department.
Executing the protocol	Validation (Engineering) Department along with respective departmental person and engineers or other suitably qualified staff allocated from the site or contracted specialists as appropriate.
Microbiological Challenge Test	Microbiology department
Data documentation and preparation of the report	Validation (Engineering) department.

Verifying of the report	Concerned departmental person.
Providing documentation on the equipment	Related departments i.e. Engineering, Production, Microbiology, Validation or other appropriate departments and manufacturer.

5. REVISION HISTROY

Document No.	Version No.	Date of issue	Reason
	01		New protocol

6. SYSTEM AND PROCESS DESCRIPTION

6.1 Equipment Information

Manufacturer	:	ZIRBUS, Germany
Capacity	:	702 Ltr.
Model	:	HST 6×6×12
Serial no.	:	3609

6.2 The Equipment under test

The autoclave under validation study is a double door horizontal autoclave; chamber is made of SS 316L. The product is fed into the chamber via a loading port and drawn off after the sterilization cycle via the discharging port in a clean room of Grade B.

A chamber leak test is performed to ensure that there is no leakage. It is very important to remove the air from the chamber. A water ring vacuum pump is used to remove the air from the chamber.

For porous loads pre vacuum is important to remove the air pockets from the pores of the loads. To remove residual air vacuum pulse followed by steam pulse is used. After completion of vacuum and steam pulse the chamber is heated up with pure steam to the set sterilization temperature. There are two temperature sensors of which one is set inside the chamber and another is set in the drain port of the chamber. When the solid cycle is run, the drain temperature sensor controls the cycle. On the other hand, when the liquid cycle is run, the product temperature sensor controls the cycle.

6.3 Checking Parameters

The PQ of autoclave will be carried out to evaluate the following conditions to confirm the sterilization conditions:

i) Chamber Leak Test (LT).
ii) Bowie-Dick (BD) test.
iii) Heat Penetration (HP) studies.
iv) Microbiological Challenge (MC) test using Biological Indicators (BI).

6.4 The system/ equipment to be used as Standard for testing

Performance of the autoclave will be judged based on thermal and biological studies which are mentioned below:

- Equipment Name: Anville Data Logger, Series 825 NATO.
  Software: TQ Soft version 6.0
- Requirement for challenge test: -Bowie-Dick test pack
  -Biological Indicator

a) After completion of the cycles, all individual cycle records are summarized and compared with the autoclave printouts to verify the cycle consistency and performance.

b) For Biological studies, Biological Indicators will be placed along with probes and will be studied for microbiological challenge test.

6.5 Pre requirement For Validation:

6.5.1 Calibration of thermocouples of the data logger/Validator before and after validation with proper identification.
6.5.2 Valid calibration record of Data Logger/Validator.
6.5.3 Data logger reading intervals set at 30 seconds (maximum).
6.5.4 Successful calibration of the Pressure and Temperature sensors of autoclave.
6.5.5 Successful completion of IQ and OQ of Autoclave.
6.5.6 Tubes of *Geobacillus Stearothermophilus* spores will be used as biological indicators. They should be labeled and placed at the front, middle and back of the autoclave chamber.

6.6 Study Procedure:

6.6.1 **Chamber Leak (CL) Test:** Thermocouples and reference pressure transducer are introduced into the chamber via the validation port. Then, the port and doors are sealed properly. There is a cycle, named as "*Vacuum air test*" cycle for leak test which is programmed in the PLC of the machine.

During leak test, chamber pressure is reduced to a 70 mbar pressure and then this pressure is compensated and hold for 5 and 10 minutes respectively. The test is declared passed if the pressure rise is within 13 mbar within the holding time.

If there is any leakage of steam for disintegration of gasket or any other reason, the autoclave might fail to achieve vacuum and leak test will be failed.

The results of above test will be recorded in the Appendix – 03 and will be accepted if met the acceptance criteria.

6.6.2 Bowie-Dick (BD) test: The Bowie-Dick (BD) test is done to detect air pockets and to evaluate that the vacuum retains as well as steam penetrates sufficiently for sterilization. This is because, air removal from the pores of the loads is essential for proper sterilization and to remove this air pre-vacuum pulse is important.

For conducting this test, Bowie-Dick test paper kits will be exposed for 10 minutes at a temperature of 121.1^{O}C inside the chamber. If the color of the centered sheet turns completely into black, it ensures proper vacuum of the chamber as well as proper steam penetration into the load and the test will pass.

Any intermediate color change of centered sheets except black (e. g. grey, brown or blue) indicates the presence of residual air in the chamber. So, the test will fail. It may occur due to the failure of retaining required vacuum of the chamber and the insufficient steam penetration. In that case, increase the pre-vacuum pulse number or sterilization time which will ensure proper removal of air as well as the steam penetration respectively. This must be recorded in the report. The successful bowie-dick test's pre-vacuum pulse numbers and sterilization time must be followed in the porous loads' cycle.

The results of above test should be recorded in the Appendix – 04 and will be accepted if met the acceptance criteria.

6.6.3 **Heat Penetration (HP) Study:** The equipment must be run three times at fully loaded condition for each load pattern where twelve sensors are exposed to monitor the temperature within the loads as well as in the chamber. Care must be taken to avoid contact between the thermocouples and the metal surface of the chamber.

Evenly distribute the thermocouples as it is shown in the Appendix – 2. In case of liquid load place the thermocouple no. 02, 03, 07 inside the container of the liquid. The Results of this test will be recorded in the Appendix-05 (Number of this appendix will be increased as per number of cycles) and will be accepted if met the acceptance criteria.

6.6.4 **Microbiological Challenge (MC) test**: This test will be performed with HP study. The temperature probes are distributed at different positions within the chamber and loads as per specified load pattern. Biological Indicators are placed beside the thermocouples as per BI placement diagram (Appendix – 01).

It is to be noted that the Microbiological challenge test will be conducted for the heat penetration study cycles. Furthermore, the lethality value (F_0) must be calculated by the TQ software and minimum lethality value must be recorded in Appendix 06. The results of above test should be recorded in the designated form (Appendix – 06). (Number of this Appendix will be increased as per number of cycles).

7. ACCEPTANCE CRITERIA

7.1 **Chamber Leak test:**

This test is deemed to be passed if the pressure rise of the chamber is within 13 mbar.

7.2 **For Bowie-Dick test:**

This test is passed if the color of the Bowie-Dick test kit turned uniformly to black having no intermediate color change throughout the entire pattern (e.g. gray, blue or violet) which ensures full vacuum and complete steam penetration.

7.3 **For Heat Penetration (HP) study:**

i) Throughout the sterilization period; all temperatures measured in the chamber has to be within a 4°C band from the set point i.e. 121°C (–1°C/+3°C).

ii) During sterilization period; the difference in temperature between the coolest spot and the mean chamber temperature during sterilization hold period shall be within ±2°C.

7.4 **For Biological Indicator Test:**

i) Biological indicators must have an initial viable spore count of 10^6 or greater of the selected microorganism.

ii) Biological Indicator must not show any growth after autoclaving and subsequent incubation.

iii) Positive control biological indicators must show “growth” of *Geobacillus Stearothermophilus*.

iv) The lethality (F_0 value) must be equal or greater than 12 minutes.

8. DEVIATION AND FAILURE INVESTIGATION SUMMARY

In the column below, record any deviations or failures that occurred during the PQ exercise.

Deviation/ Failure No.	Description and Assessment of Impact on Validation	Initial	Date
1			

2			
3			
4			

9. REFERENCE DOCUMENTS

Sl. No.	Title of the Document	Document No.
01.	SOP for validation of Moist Heat Sterilizer by Biological Indicator.	SOP/ C-MICRO/018/02
02.	USP general chapter <1222> Terminal Sterilized Pharmaceutical Products-Parametric release	N/A
03.	FDA Guidance for Industry (for the Submission Documentation for Sterilization Process Validation in Applications for Human and Veterinary Drug Products); November 1994	N/A
04.	Practical Guide to Autoclave Validation by Raymond G. Lewis, PE © ISPE 2002	N/A

10. LIST OF APPENDIX

Appendix 01: Thermocouple and Biological Indicator Placement Diagram for fully loaded heat penetration Studies.

Appendix 02: Detail Record of Loaded item.

Appendix 03: Summary report of Chamber Leak test result.

Appendix 04: Summary report of Bowie Dick Test.

Appendix 05: Summary report of fully Loaded Heat Penetration Study.

Appendix 06: Biological Indicator Challenge test summary.

Appendix 07: Calibration Status Check of reference instruments and data logger / Validator.

11. DOCUMENTATION REQUIREMENTS

Attached data are listed in the table below:

Sl. No.	Attachment No.	Name of the Attachments	Remarks

Attached document verified by:

Name.....Designation.....Signature.....Date.....

12. REPORT SUMMARY

The report summary of performance qualification of Autoclave of Sterile Production area of Cephalosporin Block is as follows:

Sl. No.	Checking parameter	Acceptance Criteria Met		Deviation	
		Yes	No	Yes	No
1	Chamber Leak Test				
2	Bowie Dick Test				
3	Heat Penetration study				

4	Microbiological Challenge test				
Comments:					

Performed by:

Name ……. Designation ……. Signature ……... Date ……..

Verified by:

Name ……. Designation ……. Signature ……... Date ……..

13. CONCLUSION

The performance qualification of the Autoclave of Sterile area of Cephalosporin Block **Complies / Does Not Comply** with the acceptance criteria taken above and the results obtained are attached with the protocol.

The autoclave of Sterile Production area of Cephalosporin Block **is / is not** qualifying the Performance Qualification test as per this Protocol. Hence, the Autoclave **can be / cannot be** used for production operation.

Performed by:

Name ……. Designation …… Signature ……... Date ……..

Verified by:

Name ……. Designation …… Signature ……... Date ……..

14. VERIFICATION OF COMPLETION

Department	Name	Designation	Signature	Date

15. REPORT APPROVAL

Name	Designation	Signature & Date
Milton Alvarado	Manager, Engineering	
Laurie Ramirez	Manager, Plant	
Joanna Warner	Manager, Quality Assurance	

16. ABBREVIATIONS

Sl. No.	Abbreviated Form	Full Extended Form
1.	HP	Heat Penetration
2.	BI	Biological Indicator
3.	LT	Leak test
4.	TC	Thermocouple
5.	USP	United States Pharmacopeia
6.	FDA	Food and Drug Administration

APPENDIX – 01

Thermocouple and Biological Indicator Placement Diagram of Fully Loaded (Porous and Non Porous) Heat Penetration Study

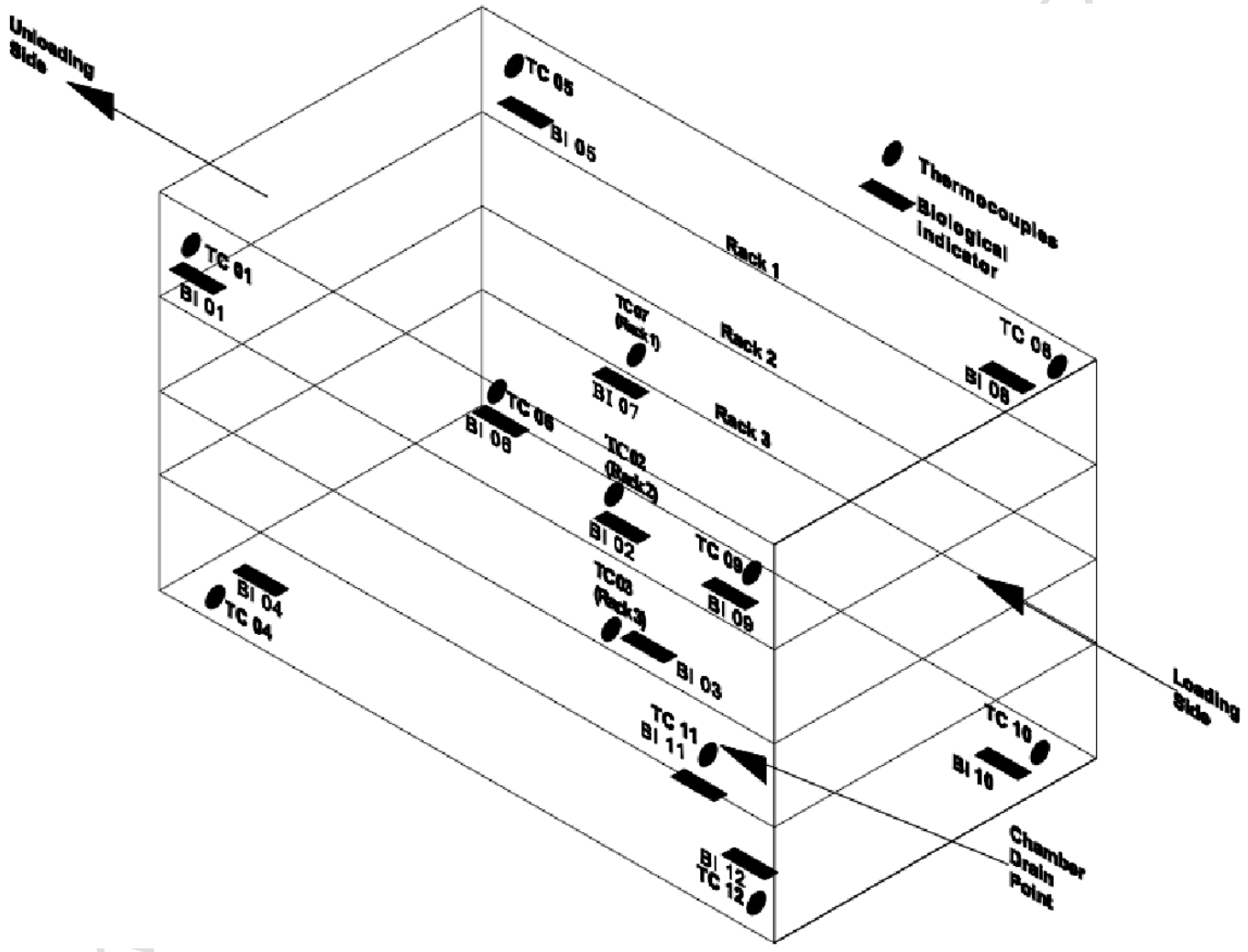

Figure: Position of Thermocouples and Biological Indicators for fully loaded heat penetration studies.

Thermocouple No.	Thermocouple Position	Thermocouple No.	Thermocouple Position
TC 01	Top left corner (Unloading side)	TC 07	Inside the load of Rack 1
TC 02	Inside the load of Rack 2	TC 08	Top right corner (loading side)
TC 03	Inside the load of Rack 3	TC 09	Top left corner (loading side)

TC 04	Bottom left corner (Unloading side)	TC 10	Bottom right corner (loading side)
TC 05	Top right corner (Unloading side)	TC 11	Chamber drain point
TC 06	Bottom right corner (Unloading side)	TC 12	Bottom left corner (loading side)

Appendix – 02

RECORD OF LOADED ITEMS

Sl. No.	Cycle Name	Type of Load

Comments:

	Name	Designation	Signature and Date
Performed By			
Checked By			

Appendix – 03

Summary Report of Chamber Leak Test Result

Equipment name			
Required vacuum pressure (abs.)		Date:	
Events	Data logger report	Autoclave Report	Remarks
Cycle Started at			
Initial compensated Pressure (abs. mbar)			
Final compensation (abs. mbar)			
Initial vacuum pressure P1 (abs. mbar)			
Pressure Holding Started at			
Hold Time			
Pressure Holding Ended at			
Final vacuum pressure P2 (abs. mbar)			
Pressure rise (P2 – P1)			

Acceptance criteria	Results
The rise of Pressure has to be less than 13 mbar in 10 minutes.	☐ Pass ☐ Fail

Data Reference: For summary report of Chamber Leak Test see Attachment No. …….

Comments:

	Name	Designation	Signature and Date
Performed By			
Checked By			

Appendix – 04

Summary Report of Bowie Dick Test

Holding time:	Holding temperature:	Date of study:
Bowie-Dick test paper (*after performance*):		

Test	Acceptance Criteria	Result

Bowie-Dick (BD) test	Color of indicator graphic of Bowie-Dick kits turned uniformly into black having no intermediate color change (e.g. gray, blue or violet) which ensures full vacuum and complete steam penetration.	€ Satisfied € Not satisfied
Comments:		

	Name	Designation	Signature and Date
Performed By			
Checked By			

Appendix – 05

Summary report of Heat Penetration Study No. ☐

(Number of this APPENDIX will be increased as per number of cycles)

EQUIPMENT NAME :	Run No. :	Load Description:
Cycle Parameter……..°C / ……....min	Date of Study:	Load Status :

Summary Report for Heat Penetration

Acceptance Criteria	**Remarks**	
Throughout the sterilization period; all temperatures measured in the chamber has to be within a 3°C band from the set point i.e. 121°C (–1°C/+3°C).	Pass	Fail

Summary Report for Cold spot and minimum lethality

Acceptance criteria: During holding period; the difference in temperature between the coolest spot and the mean chamber temperature during sterilization hold period shall be within ±2°C.

Report Source		Thermocouple ID	Temp.	Time	Chamber Mean Temp.	Temp. Difference from mean	Remarks	
							Pass	Fail
Data logger Report	Min. Temp.							
	Max. Temp.							
Autoclave Report	Min. Temp.							

	Max. Temp.							
Autoclave Report				Chamber cold spot temperature:				
Please see the attached report in Attachment no. _____								

Comments:

	Name	Designation	Signature and Date
Performed By			
Checked By			

Appendix – 06

Summary Report of Biological Indicator Challenge Test

(Number of this APPENDIX will be increased as per number of cycles)

EQUIPMENT NAME :	Date of Study:
No. of BI exposed:	Cycle Parameter:
Incubation condition:	

RUN NO. ____		RUN NO. ____	RUN NO. ____
BI#	INCUBATION RESULT	INCUBATION RESULT	INCUBATION RESULT
01.			
02.			
03.			
04.			
05.			
06.			
07.			

08.						
09.						
10.						
11.						
12.						
BI Positive Control		BI Positive Control		BI Positive Control		
BI Negative Control		BI Negative Control		BI Negative Control		
Minimum accumulated F_O:		*Minimum accumulated F_O:*		*Minimum accumulated F_O:*		

Acceptance Criteria	**Results**	
Biological indicators must have an initial viable spore count of 10^6 or greater of the selected microorganism.	*PASS*	*FAIL*
Control biological indicators must show “growth” of the selected microorganism.	*PASS*	*FAIL*
All recovered processed biological indicators must show “no growth” of the treated organisms.	*PASS*	*FAIL*
F_o value for BI is more than 12 minutes.	*PASS*	*FAIL*

Data Reference: For Details See The Attachment No. ……..

Comments:

	Name	Designation	Signature and Date
Performed By			
Checked By			

Appendix – 07

Calibration Status Check of Reference Instruments and Data logger / Validator

Name of the Instrument/(Parts)	Instrument ID	Calibration Date	Calibration Due Date	Remarks
Reference Temperature probe				
Data Logger / Validator				
Thermocouples of Data Logger / Validator				

Data Logger's Pressure transducer				
Autoclave's pressure transducer				
Autoclave's temperature sensors				
Comments:				

	Name	Designation	Signature and Date
Performed By			
Checked By			