Risk Assessment for

HPHV Steam Sterilizer (Autoclave)

Equipment ID:……

PHARMA DEVILS

QUALITY ASSURANCE DEPARTMENT

RISK ASSESSMENT FOR STEAM HEAT STERILIZER

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1.0 APPROVAL SIGNATURE

This document is prepared by the Validation team of the .....for the project "Integrated Sterile Bulk and Formulations Facility" of ....., under the authority of Unit Head & QA Head. Hence this document before being effective shall be approved by the Unit Head & QA Head.

PREPARED BY		
NAME/FUNCTIONAL AREA	**DESIGNATION**	**SIGNATURE/DATE**
Validation & QA		
CHECKED BY		
NAME/FUNCTIONAL AREA	**DESIGNATION**	**SIGNATURE/DATE**
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2.0 INTRODUCTION

According to the definition, given in Annex 15, 20 of the EU-GMP-Guide and ICH Q9, a risk assessment is a method to assess and characterize the critical parameters in the functionality of an equipment or process. Therefore, risk assessment is a key element in the qualification and validation approach.

In the project context, risk analyses are performed as basic GMP/EHS-Risk assessment, which shall help to identify important GMP/EHS-requirements.

3.0 AIM OF THE RISK ANALYSIS

At the very basic stage of design the risk assessment is to verify that all features are taken into consideration to avoid the risk of failure of critical GMP and EHS parameter in the equipment.

During study all GMP and EHS parameters will be identified and assessed for the risk if not considered in the design or requirements.

The Risk assessment report is produced to provide the documented evidence that design concepts or requirement are complete in considering all GMP and EHS risks.

4.0 REFERENCE DOCUMENTS

S.No.	Document Title	Document Number
1.	Validation master plan	
2.	Project validation plan	

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5.0 SYSTEM DESCRIPTION

This risk analysis is conducted for a HPHV Steam heat Sterilizer (Autoclave) for production consisting of the following main components:

- Sterilization chamber
- Connections for clean media piping
- Vacuum system
- Heating and cooling system
- Control System
- Instrumentation/equipment for process control, monitoring and recording

The unit shall be used for sterilization of Equipments, Garments and other components used in aseptic area.

The sterilization processes would be facilitated by use of pure Steam.

Most of the possible risk concerning the handling/operation of the Steam heat sterilizer has been considered in this RAD.

6.0 PARTICIPANTS

Name	Function	Signature

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7.0 RISK MANAGEMENT PROCESS

A typical Risk management process consists of following steps:

- Risk Assessment:
  - Risk Identification
  - Risk Analysis
  - Risk Evaluation
- Risk Control
  - Risk Reduction
  - Risk Acceptance
- Result of Risk management processes
- Risk Review
- **Risk Assessment:**

  It consists of the identification of hazards and the analysis and evaluation of risks associated with exposure to those hazards.

  Risk identification is a systematic use of information to identify hazards referring to the risk question or problem description.

  Risk analysis is the estimation of the risk associated with the identified hazards. It is the qualitative or quantitative process of linking the likelihood of occurrence and severity of harm.

  Risk evaluation compares the identified and analyzed risk against given risk criteria. Risk evaluation considers the strength of evidence for all three of the fundamental questions.

  The output of a risk assessment is either a quantitative estimate of risk or a qualitative description of range of risk. In case of qualitative description the risk is expressed using descriptors such as “high”, “medium” or “low”.

- **Risk control:**

  It includes decision making to reduce and/ or accept risks. The purpose of risk control is to reduce the risk to an acceptable level. The amount of effort used of risk control should be proportional to the significance of the risk.

  Risk reduction focuses on processes for mitigation or avoidance of quality risk when it exceeds a specified (acceptable) level. Risk reduction might include actions taken to mitigate the severity and probability of harm.

  Risk acceptance is a decision to accept risk. Risk acceptance can be a formal decision to accept the residual risk or it can be a passive decision in which residual risks are not specified.

- The output/ result of the quality risk management process should be appropriately communicated and documented.

- Risk management should be an ongoing part of the quality management process. A mechanism to review or monitor events should be implemented.

  The output/results of the risk management process should be reviewed to take into account new knowledge and experience.

This document applies the risk management principles to identify the risks associated with the design, construction and operational features of any equipment, which is going to be procured and installed in the facility.

7.1 IDENTIFYING GMP RISK

Identification of Risk associated with the equipment, is generally based on prior experience and the concerns of the participants of risk assessment document.

The risks identified are categorized as “GMP risk” or “Non-GMP risk”.

GMP is defined as “the practices which ensures that products are consistently produced and controlled to the quality standards appropriate to their intended use and as required by the marketing authorization.”

Thus, GMP covers all aspects of the manufacturing process: defined manufacturing process; validated critical manufacturing steps; suitable premises, storage, transport; qualified and trained production and quality control personnel; adequate laboratory facilities; approved written procedures and instructions; records to show all steps of defined procedures have been taken; full traceability of a product through batch records and distribution records; and systems for recall and investigation of complaints. Thus those risks which might have a direct or indirect impact on the quality of the product are classified as “GMP risk”. Also, those risks which might result in regulatory guidelines non-compliance are also classified as “GMP risk”. For example: The MOC of the product contact part has a direct impact on the quality of the product. Thus, it is classified as GMP risk.

The “Non GMP” risks include risks related to EHS, operational and other non-critical hazards.

Following types of risks are mainly identified during risk assessment process:

- Risk related to product contact materials for equipment and containers (eg. Selection of SS grade, gaskets, lubricants etc.)
- Risks related to appropriate utilities and their control (e.g. Steam, gases, power source, compressed air etc.)
- Risks related to calibration/ preventive maintenance
- Risks related to protection the environment and health & safety of personnel.
- Risks related to cleaning & sterilization
- Risks related to control system of the equipment
- Risks related to product loss

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7.2 RISK ANALYSIS & EVALUATION

The risk analysis is performed using a qualitative basis of approach.

Qualitative analysis uses word form or descriptive scales to describe the magnitude of potential consequences/ impact and the likelihood that those consequences will occur.

The qualitative measures of likelihood includes descriptors like “Unlikely”, “Possible” and “Likely”, whereas the qualitative measures of consequence/ impact includes descriptors like “Minor”, “Moderate” and “Major”.

Qualitative measures of likelihood

Level	Descriptor	Example detail description
1	Unlikely	May occur at some time
2	Possible	Might occur at some time
3	Likely	Will probably occur in most circumstances

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Qualitative measures of consequence/ impact

Level	Descriptor	Example detail description
1	Minor	• No impact on the product quality or outcome of the equipment. • Features required for easing equipment operation.
2	Moderate	• No direct impact on product quality/ outcome of equipment. However may indirectly affect the product quality. • Minor effect on personnel health • Used in the initial stage of operation, however it may affect the final output but those are not used for final release of output. • Effect on environment such as clean room.
3	Major	• Features having direct impact on product quality/ outcome of equipment like contact parts MOC, Surface finish, Control system, Process air quality etc. • Failure could lead to regulatory non-compliance. • Loss/ damage to equipment or its critical sub-components • Critical instruments not calibrated or not of desired range or accuracy. • Proper supporting documentation not provided. • Major effect on personnel health

Based on the above parameters of likelihood and consequence a qualitative risk analysis matrix is prepared to identify the overall Level of Risk, as mentioned in table below.

Qualitative risk analysis matrix – level of risk

Likelihood	Consequences/ Impact		
	1 – Minor	2 – Moderate	3 – Major
1 (Unlikely)	Low	Low	Medium
2 (Possible)	Low	Medium	High
3 (Likely)	Medium	High	High

The final Risk level shall thus be described using descriptors such as “Low”, “Medium” & “High”, where each descriptor implies the following meaning:

Low Risk can be accepted or ignored. These do not affect the final quality of the equipment/ system and it can be managed by routine procedures and are unlikely to need specific application of resources.

Medium Risk required ongoing monitoring and review, to ensure level of risk does not increase. Otherwise manage by routine procedures.

High Action plans must be developed, with clear assignments of individual responsibilities and timeframes.

8.0 PROCESS FOR RISK ANALYSIS

In the following section a table is produced for the risk analysis. The significance or instruction for each column is described in the following paragraph.

Column 1:	**Serial number** of Risk analysis item.
Column 2:	**Process step/Component**: Identify the process step or component associated with the risk.
Column 3:	**Risks**: Identify the type of risk associated with the process or component.
Column 4:	Verify that whether risk have **GMP impact.**
Column 5:	**Justification**: Provide justification for declaring both yes/no for GMP Impact in column 3.
Column 6:	For the risk **other than of GMP impact,** write what is the type of risks e.g. EHS, Operational.
Column 7:	**Justification**: Provide justification for considering any risk.
Column 8:	**Risk level** Determine the Risk level as High, Medium or low based on the impact.
Column 9:	**Risk Control:** It is further divided into following three sections.
Column 9a:	**Mitigation Method**: Write the risk mitigation strategy as considered in design.
Column 9b:	**Residual risk level**: After the risk mitigation what is the residual risk level, whether it is acceptable, low or Medium
Column 9c:	**Test Point**: Write the test point where the risk mitigation strategy will be verified.

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S. No	Process steps/ component	Risk	GMP Risk Yes/No	Justification	Other Risk type	Justification	Risk Level	Risk Control		
								Mitigation Method	Residual risk level	Verification
A.	**General Design of Equipment/ Components**									
1.	Size	Equipment is not of suitable size	No	NA	Operational	Due to smaller size no. of loads will increase	Low	Equipment shall be suitable Internal and external sizes.	Acceptable	IQ
2.	Cleaning	Improper cleaning of chamber	Yes	Chance of contamination	No	NA	High	Finishing of chamber shall be smooth and easily cleanable	Acceptable	IQ
3.	Labelling	Labelling of components inappropriate	Yes	Prerequisite for qualification	No	NA	High	Unique identity no. / Flow direction must be on components / media, operator panel, etc. (e.g. according to P&ID).	Acceptable	IQ
B.	**Chamber**									
4.	Gasket for Sterilization chamber	Gasket MOC not compatible	Yes	Product to be sterilized will be active with MOC	No	NA	High	MOC should be of food grade (Silicon/PTFE). Gasket should be temp resistant up to 200 ºC.	Acceptable	IQ

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S. No	Process steps/ component	Risk	GMP Risk Yes/No	Justification	Other Risk type	Justification	Risk Level	Risk Control		
								Mitigation Method	Residual risk level	Verification
5.	Sterilization chamber	Chamber cannot be drained completely / not fully self draining	Yes	Accumulation of condensate in parts of equipments, sterilization out of control ,Risk of contamination, Complete drainage not possible.	No	NA	High	▪ Appropriate design of chamber. ▪ Drain to be located at the deepest points. ▪ Temperature measurement at drain.	Acceptable	IQ
6.	Sterilization chamber	Leakage in Chamber	Yes	Sterilization process out of specification may led to contamination	No	NA	High	Vacuum leak test cycle should be considered in design	Acceptable	OQ
7.	Validation port	No/insufficient validation ports	Yes	Qualification activity may not be performed properly	No	NA	Medium	User friendly Validation port shall be provided for multi point temp. Mapping.	Acceptable	IQ
8.	Weld joints of Sterilization chamber	Weld quality not adequate	Yes	Cleaning problems, may lead to contamination.	No	NA	High	Welds to be grinded and polished.	Acceptable	IQ

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S. No	Process steps/ component	Risk	GMP Risk Yes/No	Justification	Other Risk type	Justification	Risk Level	Risk Control		
								Mitigation Method	Residual risk level	Verification
9.	Sterilization Chamber inclusive doors and connected parts / equipment in direct contact with chamber, piping	Material not suitable	Yes	Interaction with media possible	No	NA	High	Metal materials: Stainless steel AISI 316 or better material Non metallic/ Elastomer parts must have a food grade quality.	Acceptable	IQ
10.	Sterilization Chamber Pressure	Inadequate chamber Pressure	Yes	Inefficient sterilization	No	NA	High	Pressure transmitter along with the signal distributor is provided to monitor & record the chamber pressure regularly.	Acceptable	IQ
11.	Jacket for Sterilization Chamber	Increased Heat consumption	No	No direct impact on Process	Operational/EHS	Heat consumption increased. Heat transmission to the	Medium	Dimple construction jacket should be provided to increase Heat transfer efficiency & structural	Acceptable	IQ

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S. No	Process steps/ component	Risk	GMP Risk Yes/No	Justification	Other Risk type	Justification	Risk Level	Risk Control		
								Mitigation Method	Residual risk level	Verification
						environment may increase the room temperature		strength. MOC:SS304		
12.	Sterilization Chamber inclusive doors and connected parts / equipment in direct contact with chamber, piping.	Surface finishing insufficient	Yes	Micro-organisms may accumulate on metallic surfaces	No	NA	High	• Surface roughness, Ra ≤ 0.8 µm, proven by certificates for metal parts; exception for pipe welds: Ra ≤ 1.2 µm • Crevice free smooth, rounded corners & smooth surface. • Surfaces must be plain with rounded corners and without gaps. • Pipeline	Acceptable	IQ

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S. No	Process steps/ component	Risk	GMP Risk Yes/No	Justification	Other Risk type	Justification	Risk Level	Risk Control		
								Mitigation Method	Residual risk level	Verification
								internals should be mill finished.		
13.	Loading Trolley	No Trolley provided.	Yes	The loading /Un-loading Trolley is a basic GMP requirement manual loading shall not have any GMP impact.	Operational	Loading /Unloading trolley facilitate the operation	Medium	Loading/Un-loading trolley for smooth and easy loading shall be provided. Loading trolley should be on same plane with the floor of chamber MOC:SS304	Acceptable	IQ
14.	Loading Trolley	Trolley Can move during loading of the article on the carriage.	No	The loading trolley movement is having no GMP impact	Operational & Safety	This may cause production loss and can lead to accident.	Medium	Trolley shall be provided with locking system with the wheel. & trolley shall be moved in compliance with SOP	Acceptable	IQ & OQ
15.	Chamber carriage	Chamber carriage not available.	Yes	The proper loading of articles is requirement for uniform	Operational	Loading the article inside the chamber and keeping the materials	High	Loading Carriage shall be provided for loading the articles in	Acceptable	IQ

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S. No	Process steps/ component	Risk	GMP Risk Yes/No	Justification	Other Risk type	Justification	Risk Level	Risk Control		
								Mitigation Method	Residual risk level	Verification
				temperature distribution and penetration.		manually on the chamber floor will be difficult for the operator		uniform manner for sterilization.		
C.	**Doors**									
16.	Doors seal	Door sealing damage	Yes	Sterilization out of validated procedure.	No	NA	High	• Failure has to be alarmed. • Preventive maintenance of the sealing. • Regular visual check of the sealing.	Acceptable	OQ/ SOP
17.	Doors position indicator	Door position indicator failure/damage	Yes	Sterilization out of validated procedure. Contamination of clean room possible by opening both doors.	No	NA	High	Regular checks define standard operating procedure "Calibration and maintenance". Provide door Interlocking to prevents opening of both doors and start of	Acceptable	OQ/ SOP

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S. No	Process steps/ component	Risk	GMP Risk Yes/No	Justification	Other Risk type	Justification	Risk Level	Risk Control		
								Mitigation Method	Residual risk level	Verification
								sterilization.		
18.	Doors safety device	Door-safety device fails	No	No influence	EHS	Operating personnel may be at risk.	Medium	Door-safety device failure alarms shall be available Door safety device checked before operation.	Acceptable	OQ/ SOP
19.	Doors interlock	Door interlock does not work	Yes	Contamination of room class A/B.	No	NA	High	Verification of interlock during qualification. Should define in SOP 'Operation of the autoclave'. The provision should be made to start the sterilization process only when the door is interlocked.	Acceptable	OQ/ SOP
20.	Door opening	Door open with the high pressure	Yes	Door open with the pressure may led to Product to move with the	EHS	Personnel may be at Risk. Environment temperature	High	Gasket release valve should be provided & made open before the door is to be	Acceptable	IQ/OQ

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S. No	Process steps/ component	Risk	GMP Risk Yes/No	Justification	Other Risk type	Justification	Risk Level	Risk Control		
								Mitigation Method	Residual risk level	Verification
				pressure flow.		may get increased.		opened.		
21.	Door opening in case of incomplete sterilization /abort	Door at clean side not locked in case of failed sterilization process/ abort	Yes	un sterilised components may transfer to Grade A/B.	No	NA	High	Door at unloading side(Grade A/B) should not open (locked) in case of sterilization process not completed/ abort / Vacuum leak test /bowie-dick cycle Should define in SOP 'Operation of the autoclave'.	Acceptable	OQ/ SOP
D. Piping										
22.	Valves for clean utilities	Inadequate joints	Yes	Contamination possible	No	NA	High	Hygienic sanitizable valves shall be part of equipment	Acceptable	IQ
23.	Piping for Clean utility	Inclination of piping too low	Yes	Risk of contamination / microbial growth in piping possible due to stagnant of water	No	NA	High	Clean utilities piping should be inclined to the chamber (>1 %). Direct connection between pipe and	Acceptable	IQ

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S. No	Process steps/ component	Risk	GMP Risk Yes/No	Justification	Other Risk type	Justification	Risk Level	Risk Control		
								Mitigation Method	Residual risk level	Verification
								drain should be avoided		
24.	Piping for Clean utility	pipelines having dead legs, air pockets	Yes	contamination / microbial growth	No	NA	High	Dead legs, air pockets, should be minimised (preferred <3d)	Acceptable	IQ
25.	Welding of pipes	Welding Quality not adequate (piping)	Yes	Internal surface finish quality out of specification	No	NA	High	Orbital welding shall be considered	Acceptable	IQ
26.	MOC of clean utility piping	Material not suitable	Yes	Material not resistant – interaction with media possible	No	NA	High	Metal materials: Stainless steel AISI 316 or better; material certificates Non metallic/elastomer parts must have a food grade quality.	Acceptable	IQ
27.	Vacuum break Filters	No filter for fresh air inlet	Yes	Load present in chamber may be contaminated.	No	NA	Medium	Sterile grade filter shall be considered with necessary connections.	Acceptable	IQ/PQ

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S. No	Process steps/ component	Risk	GMP Risk Yes/No	Justification	Other Risk type	Justification	Risk Level	Risk Control		
								Mitigation Method	Residual risk level	Verification
28.	Filter	Affected by High temperature during the process	Yes	Filter Efficiency decrease, Leading to further contamination of product under process.	No	NA	High	• High temp. Resistant filters should be used. • Provision shall be made in SOP .	Acceptable	IQ/SOP
29.	Filter	No SIP/Sterilization of Filter possible	Yes	Contamination of equipment or product possible	No	NA	High	SIP/Sterilization of filter have to made possible	Acceptable	OQ
30.	Filter	Traceability of filter not possible	Yes	Pre-Requistie for Qualification.	No	NA	High	• Should be implement in control system (entry of serial no. Of filter in batch record)	Acceptable	OQ/SOP
31.	Filter	Wrong cartage material for sterile filters	**Yes**	Damage/blockage of filter possible	No	NA	High	• Types of filter cartridge should be defined. • Filter certificates have to be available.	Acceptable	IQ
32.	Filter	Integrity not tested	**Yes**	Inefficient filter accuracy leading to inefficient sterilization process.	No	NA	High	• Certification regarding the integrity testing of the filters should be provided.	Acceptable	OQ

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S. No	Process steps/ component	Risk	GMP Risk Yes/No	Justification	Other Risk type	Justification	Risk Level	Risk Control		
								Mitigation Method	Residual risk level	Verification
33.	Filter	Non Resistant to excess pressure of the supply utilities	Yes	Damaged filter leads to inefficient sterilization process	No	NA	High	• High pressure resistant filters shall be used.	Acceptable	IQ
34.	Load patterns	Undefined / wrong Loading patterns	Yes	May lead to improper sterilization	No	NA	High	Loading patterns has to be defined and validated loading patterns should be defined in SOP	Acceptable	PQ/ SOP
35.	Heating time	Long Heating time	Yes	Cycle-time increases, negative influence on heat sensitive media possible	No	NA	Medium	Heat up time shall be optimize with Proper process designing	Acceptable	OQ/ PQ
36.	Sterilization temperature	High Temperature during sterilization process	Yes	Negative influence on heat sensitive components	No	NA	Medium	Alarm provision for temperature overshoot shall be provided	Acceptable	OQ

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S. No	Process steps/ component	Risk	GMP Risk Yes/No	Justification	Other Risk type	Justification	Risk Level	Risk Control		
								Mitigation Method	Residual risk level	Verification
37.	Sterilization temperature	Low Temperature during sterilization process	Yes	Sterilization process out of validated range	No	NA	Medium	If chamber temperature falls below specified level & the timer should stops counting. If chamber temperature falls further below specified level the timer should reset. Alarm provision for low temperature shall be provide.	Acceptable	OQ
38.	Sterilization hold time	Sterilization hold time too short	Yes	Components remain un-sterilized	No	NA	High	Appropriate sterilization cycles shall be design. Sterilization cycles should be validated.	Acceptable	OQ/ PQ
39.	Temperature control	Incorrect temperature	Yes	Sterilization out of validated	No	NA	Medium	Temperature	Acceptable	OQ/ SOP

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S. No	Process steps/ component	Risk	GMP Risk Yes/No	Justification	Other Risk type	Justification	Risk Level	Risk Control		
								Mitigation Method	Residual risk level	Verification
	system	measurement (control system)		procedure (monitoring by independent sensors)				sensors should be calibrated. SOP “calibration and preventive maintenance”. Independent temperature measurement (one for control one for monitoring)		
40.	Sterilization process end	Product will remain under the High temp. & High pressure influenced environment, even after the sterilization process is over.	Yes	Excess exposure will influence articles negatively.	No	NA	Medium	Gasket release valve should get open automatically after the process ends. Alarm should be provided to assure that the sterilization cycle had completed.	Acceptable	OQ
41.	Sterilization time measurement	Time measurement works incorrect	Yes	Sterilization process insufficient	No	NA	High	Periodic check of time measurement.	Acceptable	OQ/ SOP

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S. No	Process steps/ component	Risk	GMP Risk Yes/No	Justification	Other Risk type	Justification	Risk Level	Risk Control		
								Mitigation Method	Residual risk level	Verification
								SOP “calibration and preventive maintenance”		
42.	Sterilization	Cold spots due to incomplete displacement of air	Yes	Sterilization process insufficient	No	NA	High	Pre-sterilization vacuum cycle. Temperature mapping of empty chamber, identification of “cold spot” during OQ. “Mobile” temperature sensors within chamber for local temperature measurement at cold spot during sterilization cycle.	Acceptable	OQ/ PQ
43.	Drying with vacuum and post sterilization heating	No/Inadequate vacuum	Yes	Improper Moisture removal	No	NA	Medium	Vacuum Pressure measurement with alarm provision. SOP “calibration	Acceptable	OQ/ SOP

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S. No	Process steps/ component	Risk	GMP Risk Yes/No	Justification	Other Risk type	Justification	Risk Level	Risk Control		
								Mitigation Method	Residual risk level	Verification
								and preventive maintenance" (vacuum pump)		
44.	Drying with vacuum and post sterilization heating	Incorrect pressure measurement (control system)	Yes	Sterilization out of validated procedure (monitoring by independent sensors)	No	NA	High	Pressure transmitter should be calibrated. SOP "calibration and preventive maintenance"	Acceptable	IQ/ SOP
45.	Drying with vacuum and post sterilization heating	Failure of fractionated post-vacuum process	Yes	Sterilization out of validated procedure	No	NA	High	Cycle shall be design for porous load and validated	Acceptable	OQ/ PQ
46.	Drying with vacuum and post sterilization heating	Vacuum pump fail	Yes	Drying out of Validated procedure.	No	NA	High	•Pressure measurement with alarm provision •SOP "Calibration and preventive maintenance" (vacuum pump)	Acceptable	OQ/SOP

E. Utilities

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S. No	Process steps/ component	Risk	GMP Risk Yes/No	Justification	Other Risk type	Justification	Risk Level	Risk Control		
								Mitigation Method	Residual risk level	Verification
47.	Pure steam quality	Steam quality not adequate / Steam pressure conditions not adequate	Yes	Inadequate sterilization	No	NA	High	Qualification of steam generation. • Pressure gauge/ pressure switch to be provided at pure steam inlet line for monitoring and controlling of steam pressure, along with alarm provision. • Sampling valve shall be provide at inlet of steam for sampling. • Sampling valve shall be provide in condensate drain line for sampling of condensate.	Acceptable	IQ/ OQ
48.	Soft Water for vacuum pump	Inefficient vacuum	Yes	Inefficient sterilization & drying	No	NA	High	Soft water should be supplied at the particular	Acceptable	IQ/OQ

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S. No	Process steps/ component	Risk	GMP Risk Yes/No	Justification	Other Risk type	Justification	Risk Level	Risk Control		
								Mitigation Method	Residual risk level	Verification
								predefined temp. At pump inlet. Pressure switch should be provisioned at pump inlet to monitor soft water pressure along with alarm provision.		
49.	Compressed air	Insufficient pressure	Yes	Equipment operation will be disturbed	No	NA	High	Pressure gauge/ Pressure switch should be provisioned at compressed air inlet to monitor & control compressed air pressure along with alarm provision.	Acceptable	IQ/ OQ
F.	**Maintenance**									
50.	Maintenance	Malfunctions due to worn parts	Yes	Basic GMP requirement	No	NA	High	Machine shall be easy to maintain. Preventive	Acceptable	IQ/SOP

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								Mitigation Method	Residual risk level	Verification
								maintenance procedure should be available.		
G.	**Safety**									
51.	Moving & electrical parts	Moving & electrical parts are not covered.	No	Does not have any impact on quality of the product	EHS	Operator safety	Medium	All moving & electrical parts are to be covered properly	Acceptable	IQ
52.	Utility	Failure of utility supply is not indicated	Yes	Process parameters may get disturbed	EHS	High pressure may cause accident	High	Various utilities like compressed air supply, Pure steam, plant steam, sealing water should be interlocked and indicated by alarm.	Acceptable	OQ
53.	Emergency stop	Instantaneous stopping of the equipment not possible	No	Does not have any impact on quality of the media/plates /articles	EHS	Emergency stop function is required for equipment, personnel and product protection	High	Emergency stop with alarm to be installed on accessible areas.	Acceptable	IQ/ OQ
54.	Noise level	More noise is produced by the equipment	No	Does not have any impact on quality of the	EHS	High noise may cause deafness and	Medium	Noise level shall be below 80db at a distance of 1 m	Acceptable	OQ

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								Mitigation Method	Residual risk level	Verification
		during the operation		product		anxiety		from the equipment.		
55.	Heating	Excess heating & Excess pressure	No	NA	EHS	Environmental & operator safety hazards.	Medium	Temp. & Pressure limit for the resistance of the equipment should be defined & feeded. Elevated temp. & pressure should be alarmed leading to the opening of the safety valve.	Acceptable	IQ/OQ
56.	Autoclave wall	Leakage in wall in which autoclave is integrated, between clean room grade D and grade A/B area	Yes	Pressure concept prevents contamination of clean room (overpressure in clean room)	No	NA	High	Bio seal barrier panel shall be installed between sterile room side and non sterile side.	Acceptable	IQ
57.	Pipeline	Steam leakage from the pipeline	Yes	Disturb room temperature and relative humidity	No	NA	High	Regular preventative Maintenance	Acceptable	SOP

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								Mitigation Method	Residual risk level	Verification
H.	**Sensors**									
58.	Sensors	Sensors not suitable	Yes	Improper measurements	No	NA	High	Sensors must have a suitable measuring range. Operational range of sensor > instrument working range. Sensors must have appropriate accuracy.	Acceptable	IQ
59.	Sensors	Sensors not calibrated	Yes	Non calibrated sensors may lead to false machine functions	No	NA	High	It should be possible to calibrate sensors (3-point calibration, full loop calibration)	Acceptable	IQ
60.	Sensors	Damage of sensor during operation	Yes	Wrong / no measurements	No	NA	High	Constructional solution: e.g. mechanical protection of sensors, position of sensor	Acceptable	IQ

RISK ASSESSMENT FOR STEAM HEAT STERILIZER

S. No	Process steps/ component	Risk	GMP Risk Yes/No	Justification	Other Risk type	Justification	Risk Level	Risk Control		
								Mitigation Method	Residual risk level	Verification
61.	Measurement sensors	Not accessible	Yes	Basic requirement	No	NA	High	Sensor plug-in termination for validation (compatibility of sensor manufacturing and validation equipment). Re-calibration of sensors should be possible.	Acceptable	OQ
62.	GMP relevant measurement sensors	Sensors cannot be dismounted	Yes	Defective sensors must be dismounted for exchange and calibration	No	NA	High	Mounting of sensors must give the possibility for dismounting and replacement Constructional solution: easy access for calibration activities shall be given	Acceptable	IQ
63.	Temperature	Temperature sensor not	Yes	Must be appropriate, basic GMP	No	NA	High	Range: 0 – 200°C Accuracy: 0.1 °C	Acceptable	IQ

RISK ASSESSMENT FOR STEAM HEAT STERILIZER

S. No	Process steps/ component	Risk	GMP Risk Yes/No	Justification	Other Risk type	Justification	Risk Level	Risk Control		
								Mitigation Method	Residual risk level	Verification
		suitable		requirement						
64.	Temperature	Wrong sensor is control sensor	Yes	Must be appropriate, basic GMP requirement	No	NA	High	Control sensor must be appropriate	Acceptable	OQ
65.	Pressure	Pressure sensor not suitable	Yes	Must be appropriate, basic GMP requirement	No	NA	High	Range: (-)1 – 3bar Accuracy: 0,1 bar Specification: relative or absolute values	Acceptable	IQ
I.	**Control & Monitoring System**									
66.	Human - machine Interface	Process / process status not visible for operating personnel	Yes	Operating personnel must have the process status for control	No	NA	High	Machine shall be provided with adequate display and clean room suitable key board for operation Operator panel on both sides of autoclave (A/B and C).	Acceptable	IQ
67.	HMI	Recorder failure	Yes	Basis GMP requirement	No	NA	High	▪ Data backup for process data must	Acceptable	OQ

RISK ASSESSMENT FOR STEAM HEAT STERILIZER

S. No	Process steps/ component	Risk	GMP Risk Yes/No	Justification	Other Risk type	Justification	Risk Level	Risk Control		
								Mitigation Method	Residual risk level	Verification
	Recorder			(incomplete / no documentation)				be foreseen. Diagnostic function test to be a part of qualification activity.		
68.	Printer	Print outs not fade proof	Yes	Basis GMP requirement (documentation cannot be stored for required time period)	No	NA	High	Print outs of alarm printer and recorders (Batch record) have to be fade proof / archive proof.	Acceptable	OQ
69.	HMI language	Display language not identified.	Yes	Pre-requisite for the GMP compliant operation	No	NA	High	The language on the display of MMI should be English language only.	Acceptable	OQ
70.	Printer	Printer not suitable for clean room	Yes	Basic requirement	No	NA	Medium	Printer to be housed with casing of panel	Acceptable	IQ
71.	HMI	Monitoring/recording and documentation of GMP relevant	Yes	Basic GMP requirement	No	NA	High	It should be possible to monitor/record GMP relevant	Acceptable	OQ

RISK ASSESSMENT FOR STEAM HEAT STERILIZER

S. No	Process steps/ component	Risk	GMP Risk Yes/No	Justification	Other Risk type	Justification	Risk Level	Risk Control		
								Mitigation Method	Residual risk level	Verification
		data not possible						data. Batch records / print outs to be defined		
72.	HMI	GMP relevant alarms missing / limits not defined	Yes	Basic GMP requirement	No	NA	High	Limits have to be defined and alarmed (+,-), inclusive malfunction of sensor (e.g. cable breakage) Alarm list has to be defined.	Acceptable	OQ
73.	PLC/ Control System	Controlling of critical process parameters not possible	Yes	Basic GMP requirement	No	NA	High	PLC should be able to control critical process parameters like heating, sterilization, drying etc.	Acceptable	OQ
74.	PLC / Control system	Malfunction	Yes	Correct function basic requirement for GMP-compliant operation	No	NA	High	Supplier analysis (quality management system for software and	Acceptable	OQ

RISK ASSESSMENT FOR STEAM HEAT STERILIZER

S. No	Process steps/ component	Risk	GMP Risk Yes/No	Justification	Other Risk type	Justification	Risk Level	Risk Control		
								Mitigation Method	Residual risk level	Verification
								control system hardware development) Test implementation in qualification activities. Verification of Input/ output signals.		
75.	PLC / Control system	Incorrect recording or printing of GMP-relevant data	Yes	Basic GMP requirement	No	NA	High	Test of correct data processing	Acceptable	OQ
76.	PLC / Control system	Breakdown of sensor	Yes	GMP-relevant data not available, process out of specification	No	NA	High	Broken sensor should be identified in the system.	Acceptable	OQ
77.	PLC / Control system	Status parameters not clear	Yes	Process for the particular product at particular stage can't be regulated easily.	No	NA	High	Status parameters should remain displayed at each process stage. The flow of the process shall be	Acceptable	OQ

RISK ASSESSMENT FOR STEAM HEAT STERILIZER

S. No	Process steps/ component	Risk	GMP Risk Yes/No	Justification	Other Risk type	Justification	Risk Level	Risk Control		
								Mitigation Method	Residual risk level	Verification
								provided with the help of arrows. Alarm should also be visualized along with the fault displayed.		
78.	Accessibility to PLC	Parameter settings not identified universally	Yes	Basic GMP requirement	No	NA	High	Parameters settings should be in numeric only.	Acceptable	OQ
79.	Control system	No PLC with different recipe	No	NA	Operational	The machine operates in same manner, even when the different task is required.	Medium	PLC should be equipped with different cycles as per different requirements- Garment & component cycle. Standard cycle. The machine operates in same manner, even when the different task is required. Vacuum Leak test	Acceptable	OQ

RISK ASSESSMENT FOR STEAM HEAT STERILIZER

S. No	Process steps/ component	Risk	GMP Risk Yes/No	Justification	Other Risk type	Justification	Risk Level	Risk Control		
								Mitigation Method	Residual risk level	Verification
								cycle. Bowie & Dick test cycle.		
80.	PLC / Control system	Time measurement works incorrect	Yes	Process insufficient	No	NA	High	▪ PLC Clock verification ▪ SOP "calibration and maintenance" ▪ Time synchronisation of system	Acceptable	OQ
81.	PLC / Control system	Power failure / emergency stop	Yes	Process out of specification	No	NA	High	▪ Operator settings unchanged and restored after emergency stop / power failure; ▪ Alarm message; ▪ Machine must not start automatically without operator intervention after incident ▪ SOP for 'Maintenance and operation of Tablet	Acceptable	OQ

RISK ASSESSMENT FOR STEAM HEAT STERILIZER

S. No	Process steps/ component	Risk	GMP Risk Yes/No	Justification	Other Risk type	Justification	Risk Level	Risk Control		
								Mitigation Method	Residual risk level	Verification
								compression machine'.		
J.	**Documentation**									
82.	User	Faulty operation & maintenance	Yes	SOPs are basic GMP-requirement	No	NA	High	All end-users have to be trained on SOPs Training of SOPs has to be documented Training on the job of end users by vendor Training on operation, setting parameters, trouble shooting & maintenance related activities.	Acceptable	OQ/ SOP
83.	User	Operation SOP does not contain proper information and user may operate system	Yes	User may make a wrong decision.	No	NA	High	System operation SOP must be reviewed with all aspects and approved. Vendor shall provide execution	Acceptable	OQ

RISK ASSESSMENT FOR STEAM HEAT STERILIZER

S. No	Process steps/ component	Risk	GMP Risk Yes/No	Justification	Other Risk type	Justification	Risk Level	Risk Control		
								Mitigation Method	Residual risk level	Verification
								support to the user to complete all stages of the qualification report.		
84.	Vendor	Technical documentation from vendor not adequate	Yes	Adequate technical documentation is basic GMP requirement	No	NA	High	Vendor doc. (English) shall comprise: • DQ,IQ & OQ • Material certificates & surface finish reports • O &M manual • Calibration certificates • Software backup • Parts list (sufficient details - part no., supplier, type etc.) • Drawings (P&ID, GA, Power wiring etc.). • Certificates of bought out	Acceptable	IQ

RISK ASSESSMENT FOR STEAM HEAT STERILIZER

S. No	Process steps/ component	Risk	GMP Risk Yes/No	Justification	Other Risk type	Justification	Risk Level	Risk Control		
								Mitigation Method	Residual risk level	Verification
								components. • Filter certificates • Hydro test certificates of pressure parts.		

9.0 SUMMARY AND CONCLUSION

- The Risk analysis is performed to establish the design parameters of the equipment so as to meet the desired performance of the equipment i.e. HPHV Steam Sterilizer (Autoclave).
- The critical risks pertaining to GMP and other than GMP were analyzed with justification and mitigation procedures.
- For each recognized GMP-risk and other than GMP risks necessary measures are defined. Organizational measures, like SOPs, are also possible measures for special GMP-risks. The availability of these SOPs will be checked during the performance of the OQ.
- The risks where conceptual procedures shall be employed, standard operating procedures (SOPs), Preventive maintenance schedules, Certificates and related documents indicated as mitigation procedures shall be ensured at respective test points.

*"It is concluded that the **Risk Assessment** performed for the equipment will prevent the risk of failures of critical parameters during design, commissioning, installation, operation and performance of the equipment".*

10.0 ABBREVIATIONS

Acronym	Definition
EU-GMP	European Good Manufacturing Practices
RAD	Risk Assessment Document
ICH	International Conference of Harmonization
QC	Quality Control
SHS	Steam Heat Sterilizer
GMP	Good Manufacturing Practice
EHS	Environment Health and Safety
VMP	Validation Master Plan
PVP	Project Validation Plan
SS	Stainless Steel
MOC	Material of Construction
P&ID	Piping And Instrumentation Diagram
IQ	Installation Qualification
DQ	Design Qualification
OQ	Operational Qualification
PQ	Performance Qualification
SOP	Standard Operating Procedure
PTFE	Polytetrafluoroethylene
AISI	American Iron and Steel Institute
HPHV	High Pressure High Vacuum
PW	Purified Water

HMI	Human Machine Interface
MMI	Man Machine Interface
PLC	Programmable Logic Controller
db	Decibel
FDS	Functional design specifications
GA	General Attachments
O&M	Operational and Maintenance Manual