Risk Assessment Document

For

Pure Steam Generation System

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RISK ASSESSMENT FOR PURE STEAM GENERATION SYSTEM

1 Introduction

According to the definition, given in Annex 15 to the EU-GMP-Guide, 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 assessment for the equipment is performed as basic GMP/EHS-Risk Assessment, which shall help to identify important GMP/ EHS-requirements.

2 Aim of Risk Assessment

At the very basic stage of design the Risk Assessment is carried out 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, EHS and operational parameters will be identified and assessed for the risk, appropriate mitigation will be proposed and verification point will be identified and defined.

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

3 Reference Documents/ Drawings

S.No.	Document Title	Document Number
1.	Validation master plan	

4 Equipment/ System Description

This risk assessment is conducted for Pure Steam Generation System, which shall consist of the following main components:

Pure Steam Generation System:

Pure Steam Generation System produces Pyrogen free, sterile, Pure Steam. It operates on the Distillation as a Unit Process. Sterile steam generation engross with Liquid to Vapour phase change to produce very high purity steam. It removes the impurities at sterile temperature without using any filtration medium.

PSG works on “Falling Film Evaporator” principle. It is most reliable method to produce pure steam. It employs high temperature (Sterile state temperature), which assures constant production with high quality. As unit does not have moving parts, it demands very little maintenance.

Pure Steam is used for steam sterilization in Sterilizer, Lyophilizer, pipelines and vessels etc.

Pure Steam Distribution System:

The whole distribution system will be fabricated and installed as per cGMP. Distribution system is fabricated out of SS316L tubes and tube fittings (sanitary type). These will be laser welded bead removed type. The tubes will have an inside surface finish of Ra < 0.6µm.

The fabrication will be done by using orbital welding machine with a closed head in an inert atmosphere of argon gas to give crevice free welds with the concavity and convexity of the weld well within permissible limits.

The distribution system on the whole will be designed so as to give minimum load on the pure steam generation plant, which reflects a good engineered system taking care of the cost factors involving the initial set up cost as well as the maintenance and running cost. Sanitary steam traps will be installed in the system for each header line

Most of the possible risk concerning the handling/ operation of the Pure Steam Generation System has been considered in this RA document.

5 Participants

Name	Designation/ Department	Signature/ Date

6 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 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 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.

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  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 the proposed sterile formulation facility.
  The objectives of this risk assessment are to:
  • Review the design around a structured methodology
  • Identify the failure modes and associated risks
  • Check if the proposed control measures are adequate
  • Identify recommendations to obtain a more acceptable risk level if required

6.1 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 Hygiene level of the manufacturing areas 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 hygiene level of the manufacturing and supporting areas
- Risks related to appropriate utilities and their control (eg. power source, compressed air etc.)
- Risks related to calibration/ preventive maintenance
- Risks related to protection of the environment and health & safety of personnel.
- Risks related to cleaning & sterilization
- Risks related to unidirectional flow of the material
- Risks related to cross contamination of the products
- Risks related to entry and exit of personnel and material.
- Risks related to all the environment features of the manufacturing areas.
- Risks related to requirement of particular rooms for different activities.
- Risks related to environment health and safety of personnel.

6.2 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

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

Level	Descriptor	Example detail description
		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	Medium	High
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 managed by routine procedures.

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

7 Risk Assessment

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

Column 1 : **Serial number** of the Risk assessment 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** in terms of Yes/ No.
Column 5	:	**Justification:** Provide justification for declaring both Yes/ No for GMP impact in column 4.
Column 6	:	For the risk **other than of GMP impact**, write that what is/ are the type of risks e.g. EHS, operational, etc.
Column 7	:	**Justification:** Provide justification for considering the 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 the following three sections:
Column 9a	:	**Mitigation Method:** Write the risk mitigation strategy as considered in the 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 document:** Write the test point where the risk mitigation strategy will be verified.
Column 10	:	**Status of RA:** Mention the status of the Risk assessment point i.e. whether it is ‘Closed” or “Open”, after the execution/ approval of the Test document.

RISK ASSESSMENT FOR PURE STEAM GENERATION SYSTEM

S. No. (1)	Process steps/ component (2)	Risk (3)	GMP Risk Yes/ No (4)	Justification (5)	Other Risk type (6)	Justification (7)	Risk Level (8)	Risk Control (9)			Status of RA (10)
								Mitigation Method (9a)	Residual risk level (9b)	Test Document (9c)	
1.	Pure Steam generation system	High Conductivity of feed water	Yes	High conductivity of feed water (Purified water) may challenge the system performance.	No	NA	High	• Conductivity sensor should be installed in the purified water distribution loop to monitor the conductivity of purified water. • PW system shall be provided with dumping valve in the distribution header line in case conductivity goes high in distribution system. • Pure steam generation stop in case of high conductivity of feed water. • Alarm provision shall be provided.	Acceptable	IQ & OQ	
2.	Pure Steam generation system	Very high flow rate of feed water	Yes	Incomplete evaporation may lead to endotoxin contamination	No	NA	High	• Flow rate shall be optimized and controlled. Flow meter shall be installed at feed water inlet line OR alternatively proportionate control valve should be installed on the feed water inlet line so as to control the flow of feed water with respect to plant steam pressure. • Continuous draining of extra feed water from distillation column • Level switch control on distillation column • Alarm provision in case of high level of condensate in column.	Acceptable	IQ & OQ	
3.	Pure Steam generation system	Low flow rate of feed water	No	Does not impact the quality of Pure Steam	Operation	Pure Steam generation will be less	High	• Pressure switch to be installed on feed water inlet line along with alarm provision. • Generation system should stop if flow of feed water is lesser than set value.	Acceptable	IQ & OQ	
4.	Pure Steam generation system	Higher Pure Steam conductivity	Yes	Performance failure	No	NA	High	• Test for system performance and all dependent parameters. • Conductivity sensor shall be provided on pure steam outlet. • Alarm provision. • Continuous high conductivity should	Acceptable	IQ & OQ	

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								trip the system.			
5.	Pure Steam generation system	High pressure Pure Steam generated	No	No impact on pure steam quality	Safety	High pressure may cause pipeline to burst or may damage downstream equipments.	High	• Safety valve should be provided on Pure steam outlet line to drain off excess pressure. • Pressure transmitter and indicator should be provided for manual monitoring of pure steam pressure. • Alarm provision.	Acceptable	IQ & OQ	
6.	Pure Steam generation system	Low Pure Steam pressure	Yes	Downstream sterilization processes may be affected.	No	NA	High	• Pressure indicator & switch should be provided for monitoring of pure steam pressure. • Alarm provision shall be provided.	Acceptable	IQ & OQ	
7.	Pure Steam generation system	Lower Heat transfer area	No	No impact on quality	Operational	Lower heating Efficiency; loss of feed water	Medium	Provision of pre-heaters so as to pre-heat the feed water before entering the main column.	Acceptable	IQ	

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8.	Pure Steam generation System	Non-condensable gases in pure steam	Yes	May lead to contamination of article which uses pure steam for sterilization.	No	NA	High	• Non-condensable gas removal system should be provided in the generation system. • Water should not go through the final column unless required temperature conditions for non-condensable gas removal are met.	Acceptable	IQ & OQ	
9.	Pure Steam generation system	Low temperature of feed water after Non-condensable gas removal system	Yes	Non-condensable gases may not be completely removed from the feed water.	No	NA	High	• Low temperature feed water shall be auto-dumped. • Feed water pump should not start unless feed water set temperature is reached. • Alarm provision.	Acceptable	OQ	
10.	Pure Steam generation system	Leakage in plant steam lines	No	No impact on pure steam quality	Operational	Required quantity of plant steam may not be available for generation of pure steam.	High	Pressure tests must be performed to ensure plant steam distribution lines integrity.	Acceptable	IQ	
11.	Pure Steam generation system	Pressure Regulating System failure at plant steam inlet	No	Does not have impact on the quality of the product.	Operational & safety	May lead to operational or safety hazard	High	• Pressure indicator should be provided at plant steam inlet for manual monitoring. • SOP for Preventive maintenance.	Acceptable	IQ & SOP	
12.	Pure Steam generation point	No sampling point	Yes	Required to test the pure steam sample.	No	NA	High	Sampling point to be provided at pure steam outlet for collection of pure steam sample.	Acceptable	IQ	

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13.	Pure Steam generation System	Insufficient vaporisation in column	Yes	May lead to inefficient accumulation of excess feed water inside column.	No	NA	High	• Purging valve should be provided with the column and should open in case of rise in water level inside column. • Level controller should be installed in the column for monitoring of condensate level. • Alarm provision.	Acceptable	IQ & OQ	
14.	Pure Steam generation System	Water stagnation in pump	Yes	Will lead to microbial growth.	No	NA	High	Pump should be of self draining design.	Acceptable	IQ	
Pure Steam Distribution System											
15.	Pure Steam Distribution System	Pipelines are not pressure tested	Yes	Leakage may cause microbial contamination	Safety	High pressure & High temperature water leakage may cause health hazards.	High	All pipelines shall be pressure tested before being used.	Acceptable	IQ	
16.	Pure steam quality	Steam quality not adequate	Yes	Sterilization out of validated procedure	No	NA	High	Qualification of pure Steam quality.	Acceptable	OQ	

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17.	Pure steam distribution system	Accumulation of condensate in distribution lines	Yes	Required Pure steam pressure and temperature might not be achieved at downstream user points.	No	NA	High	• All pipelines shall have drainable slope of > 1:100. • Steam Traps should be installed at required intervals so as to drain the condensate of the generation and distribution system.	Acceptable	IQ	
18.	Pure steam distribution system	Non insulated pipeline	Yes	Will lead to heat losses to environment. Some amount of pure steam may be converted to condensate.	Safety	High temperature pipeline may cause health hazards	High	• Insulation should be provided. • In clean area insulation should be non-shredding particle free or SS cladded.	Acceptable	IQ	
19.	Pure steam distribution system	No sampling point provided	Yes	Sampling point is required to check pure steam quality in loop and user points	No	NA	High	• Sampling points shall be provided at all user points. • Sampling cooler shall be provided at Pure steam generation point for pure steam sampling.	Acceptable	IQ	
Equipment Construction											
Internal Surface											
20.	Surface (Pure Steam Generation & distribution System)	Internal surface/ contact parts are not compatible with the pure steam.		May lead to the pure steam contamination	No	NA	High	• Metallic critical contact surfaces (piping) shall be constructed of 316L grade stainless steel or better, electro polished, orbitally welded. • Contact parts of all instruments, level sensors, valves, pumps etc, shall be of SS 316 or better. • Supporting structure and non contact parts In clean area shall be of SS 304 or better.	Acceptable	IQ	

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								• Diaphragm Valves: SS 316L, electro polished with PTFE facing. • Pure Steam distribution pipeline shall be of SS 316 or better. • Internal finish should be < 0.5 µm Ra			
21.	Polymeric materials (Pure Steam Generation & distribution System)	Polymeric materials are not compatible and are not replaceable		Shall lead to water contamination	No	NA	High	• Gaskets (shall be high temperature & pressure resistant) and O-rings coming in direct / indirect contact surfaces shall be made up of food grade polymeric materials only and shall be high temperature resistant. • The easy change of gaskets must be possible. • Vendor shall provide the certificate for food grade polymeric material.	Acceptable	IQ	
22.	Welding Joints (Pure Steam Generation & distribution System)	Weld joints not ground properly and are not passivated		Uneven and improperly ground weld joints will form a space for dust accumulation	No	Na	High	• All welds shall be ground finished to < 1.2 µm Ra and properly passivated and orbital welding should be done. • Welding to be done using high purity argon gas.	Acceptable	IQ	
23.	Finishing (Pure Steam Generation & distribution System)	Internal finish is not proper		May lead to improper cleaning of the surface which will lead to microbial growth hence product contamination	No	Na	High	▪ Surface roughness, Ra ≤ 0.6 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.	Acceptable	IQ	

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24.	Joints (Pure Steam Generation & distribution System)	Joints are leaking	Yes	Water contamination may affect the final water quality.	No	NA	High	• Suitable gaskets shall be provided for air tight connection which shall be replaceable. • Quick release Triclover joints are recommended.	Acceptable	IQ	
25.	Valves for clean media	No hygienic design	Yes	Contamination possible	No	NA	High	Appropriate hygienic design of valves.	Acceptable	IQ	
External Surface											
26.	Surface (Pure Steam Generation & distribution System)	Surface is not clean room suitable		May lead to the clean room contamination	No	NA	Medium	Supporting structures and frames shall be SS 304.	Acceptable	IQ	
27.	Finishing	External finish is not proper		May lead to the microbial growth	No	NA	Medium	External surface shall be free from sharp edges, corners, crevices etc., all metallic external surface shall be matt finished	Acceptable	IQ	
28.	Lubricant (if applicable)	Lubricant used is not food grade and is toxic in nature		Used lubricants coming in contact of the potential product contact surfaces may lead to the contamination of the product	No	NA	Medium	Lubricant shall not enter in processing zone of equipment. Any lubricant, if used in the equipment must be food grade and non-toxic. Vendor shall provide the certificate	Acceptable	IQ	
PLC/Control System											

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29.	Process automation	Process parameters are not controlled automatically.	Yes	Possibility of human error leads to a process which is not validated	No	Na	High	• The equipment shall control & detect failure mode automatically. • The System shall be PLC based and fully automatic.	Acceptable	IQ & OQ	
30.	Man-machine Interface	Process / process status not visible for operating personnel.	Yes	Operating personnel must have knowledge on the process status	No	NA	High	MMI shall be provided with adequate display and clean room suitable key board/Touch screen for operation.	Acceptable	IQ	
31.	Man-machine Interface	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.	Acceptable	OQ	
32.	Man-machine Interface	Recorder failure	Yes	Basis GMP requirement (incomplete / no documentation)	No	NA	High	• Data backup for process data must be foreseen (electronic recording, 21 CFR part 11 compliant). • Diagnostic function test to be a part of qualification activity.	Acceptable	IQ & OQ	
33.	Man-machine Interface	Monitoring/recording and documentation of GMP relevant data not possible	Yes	Basic GMP requirement	No	NA	High	• It should be possible to monitor/record GMP relevant data (e.g. recorder with compliance to GAMP 5 / 21 CFR, Part 11 etc.) • Batch records / print outs to be defined. • Printout facility should be available with fade proof prints.	Acceptable	OQ	
34.	Control system	Control system does not detect failures and generate alarms	Yes	Process optimization and validation is not possible	No	NA	High	Failure of set parameters gets indicated as alarms and machine stops.	Acceptable	OQ	

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35.	PLC / Control system	Power failure / emergency stop	Yes	Process out of specification	EHS	May lead to some accident	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 Pure Steam Generation System'.	Acceptable	OQ	
36.	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 provided with the help of arrows. • Alarm should also be visualized along with the fault displayed.	Acceptable	OQ	
37.	PLC / Control system	Malfunction	Yes	Correct function basic requirement for GMP-compliant operation	No	NA	High	• Supplier analysis (quality management system for software and control system hardware development) • Input/ Output test implementation in qualification activities • The system must contain all necessary protection devices to ensure that the equipment and article remain in safe condition.	Acceptable	OQ	
38.	Accessibility to PLC	Parameter settings not identified universally	Yes	Basic GMP requirement	No	NA	High	Parameters settings should be in numeric only.	Acceptable	OQ	

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39.	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 & SOP	
40.	PLC / Control system	No protection of PLC against manipulation & changes.	Yes	Basic GMP requirement.	No	NA	High	Minimum 3 level password protections should be provided. ➢ Level 1: for operator settable parameters. ➢ Level 2: for editing cycle parameters. ➢ Level 3: for admin/ Audit trial/ engineering level setting.	Acceptable	OQ	
Measuring Instruments											
41.	Measuring instruments	Measuring instruments not suitable	Yes	Improper measurements	No	NA	High	• Measuring instruments must have a suitable measuring range. • Operational range of measuring instruments > instrument working range. • They must have appropriate accuracy.	Acceptable	IQ	
42.	GMP relevant measuring instruments	Measuring instruments cannot be dismounted	Yes	Defective instruments must be dismounted for exchange and calibration	No	NA	High	• Mounting of instruments must give the possibility for dismounting and replacement • Constructional solution: easy access for calibration activities shall be given	Acceptable	IQ	

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43.	Measuring instruments	• Instruments not calibrated. • Re-calibration is not possible	Yes	Non calibrated instruments may lead to false machine functions	No	NA	High	• Measuring instruments should be calibrated, traceable to national or international standards. • Re-calibration of instruments should be possible.	Acceptable	IQ & OQ	
System Cleaning and											
44.	Cleaning	Difficult cleaning	Yes	Accumulation of particles, contamination of clean room possible	No	NA	High	• The design shall ensure adequate clean ability (smooth, SS316 or better surface). • Parts which are required for cleaning should be provided with quick fixing arrangement. • In Clean area all bolts, nuts on the exterior part of equipment will be with cap head or cap nut.	Acceptable	IQ	
45.	Pure Steam Distribution System	Distribution system pipelines are not passivated	Yes	Material left inside the pipelines may contaminate the pure steam quality.	No	NA	High	• Pipeline shall be passivated by the vendor before being used. • Passivation test reports to be provided. • SOP: Preventive Maintenance	Acceptable	IQ & SOP	
46.	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). • Labels affixed on the equipment should be heat resistant. • All labelling in English language and according to project standard.	Acceptable	IQ	
Maintenance											
47.	Maintenance	Malfunctions due to worn parts	Yes	Basic GMP requirement	No	NA	High	• Machine shall be easy to maintain. • Preventive maintenance procedure	Acceptable	IQ & SOP	

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								should be available • The unit must contain necessary protection devices to ensure that the equipment & the article remain in a safe condition.			
48.	Pure Steam distribution system	Failure of feed water pump	No	No impact on pure steam quality	Operational	Generation gets affected	Medium	• Provide stand by pump. • Alarm in case of pump overload.	Acceptable	IQ	
System Safety											
49.	Electrical system	Electrical systems are not verified for safety	No	It will not affect the final quality of water.	EHS	May lead to an accident	Medium	All electrical systems shall be tested for safety and shall be provided with safety markings e.g. C.E. marking.	Acceptable	IQ	
50.	Noise level	Noise level liberated by the system is high.	No	It will not affect the final quality of water.	EHS	Heavy noise will cause problems to the service persons	Medium	The noise liberated by the system shall not be more than 75 db from 1m from the system.	Acceptable	OQ	
51.	Emergency stop	Instantaneous stopping of the equipment not possible	No	Does not have any impact on quality of the product	EHS	Emergency stop function is required for equipment, personnel and product protection	High	Emergency stop with alarm to be installed on accessible areas on pure steam generation as well as distribution system.	Acceptable	IQ & OQ	

RISK ASSESSMENT FOR PURE STEAM GENERATION SYSTEM

S. No. (1)	Process steps/ component (2)	Risk (3)	GMP Risk Yes/ No (4)	Justification (5)	Other Risk type (6)	Justification (7)	Risk Level (8)	Risk Control (9)			Status of RA (10)
								Mitigation Method (9a)	Residual risk level (9b)	Test Document (9c)	
52.	Utility Failure	Compressed air is low		Improper function of pneumatic instruments leads to improper output.	Operational	May leads improper function of the system	High	• Compressed air pressure shall be indicative with alarm if low. • The total system shall be shut down if the compressed air is low.	Acceptable	IQ & OQ	
53.	Heating	Excess heating & Excess pressure	No	Does not have any impact on quality of the product.	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	
54.	Plant steam	High plant steam pressure	No	Does not impact the quality of Pure Steam	Safety & Operational	Environmental & operator safety hazards	High	• Pressure regulated valve and safety relief valve shall be installed. • Alarm provision.	Acceptable	IQ & OQ	
55.	Pipeline	Steam leakage from the plant steam or pure steam pipelines	Yes	Disturb room temperature and relative humidity	No	NA	High	Regular preventative Maintenance	Acceptable	SOP	
Documentation											
56.	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	Acceptable	OQ & SOP	

RISK ASSESSMENT FOR PURE STEAM GENERATION SYSTEM

S. No. (1)	Process steps/ component (2)	Risk (3)	GMP Risk Yes/ No (4)	Justification (5)	Other Risk type (6)	Justification (7)	Risk Level (8)	Risk Control (9)			Status of RA (10)
								Mitigation Method (9a)	Residual risk level (9b)	Test Document (9c)	
								vendor. • Training on operation, setting parameters, trouble shooting & maintenance related activities.			
57.	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.	Acceptable	OQ	
58.	User	Unauthorized person tries to start/stop the system	Yes	Untrained persons may damage the system or product quality may be affected	No	NA	High	• System should not start without password. • Key-switch should be provided for system power up. OR • Physical entry to equipment room is restricted.	Acceptable	IQ & OQ	
59.	Vendor Documentation	Technical documentation from vendor not adequate	Yes	Adequate technical documentation is basic GMP requirement for qualification and operation of the System	No	NA	Medium	Vendor documentation shall comprise: • Material certificates • Welding certificates along with welder qualification certificate. • Boroscopy reports • Slope Verification report • Pressure leak test report • Passivation report • Operating instruction • Maintenance instructions • Spare part lists • Drawings - P&I-diagrams - Electrical diagrams • Functional design specification • HMI functions with screen shot • List of failure indications	Acceptable	IQ	

RISK ASSESSMENT FOR PURE STEAM GENERATION SYSTEM

8 Summary & Conclusion

- The Risk Assessment was performed to establish the design parameters of the equipment so as to meet the desired performance of the equipment i.e. Pure Steam Generation System.
- The critical risks pertained 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".*

9 Abbreviations

EU-GMP	:	European – Good Manufacturing Practice
EHS	:	Environment Health Safety
PID	:	Proportional Integral Derivative
GMP	:	Good Manufacturing Practice
ICH	:	International committee for harmonization
PTFE	:	Polytetrafluoroethylene
RA	:	Risk Assessment
NMT	:	Not More Than
SOP	:	Standard Operating Procedure
SS	:	Stainless Steel
Ra	:	Roughness Average
P&ID	:	Process/ Piping & Instrumentation Diagram
PSG	:	Pure Steam Generator
PLC	:	Programmable Logic Controller
MMI	:	Man Machine Interface
CFR	:	Code of Federal Regulations
UPS	:	Uninterrupted Power Supply
CE	:	Conformité Européene
db	:	Decibel
IQ	:	Installation Qualification
OQ	:	Operational Qualification
PQ	:	Performance Qualification
O&M	:	Operation and Maintenance
GA	:	General Arrangement
USP	:	United States Pharmacopeia
IPSI	:	Integrated Project Services International, New Delhi

10 Revision History

Date	Revision	Reason for Revision
	00	New Document