Risk Assessment Document Paste Kettle (15 Ltr.) Equipment ID:

Revision index

Revision	Date	Reason for revision
00		First issue

FAILURE MODE EFFECT ANALYSIS FOR PASTE KETTLE

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1.0 Approval

This document is prepared by …….Plans for the project "OSD Formulation facility" at ……..under the authority of their Project Manager. Hence, this document before being effective shall be approved by the QA team of ……

PREPARED BY		
NAME	**DESIGNATION**	**SIGNATURE /DATE**

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NAME	**DESIGNATION**	**SIGNATURE /DATE**

APPROVED BY		
NAME	**DESIGNATION**	**SIGNATURE /DATE**

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2.0 Introduction:

According to the definition, given in Annex 15, 20 to 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 Assessment is performed as basic GMP/EHS-Risk Assessment, which shall help to identify important GMP/EHS-requirements.

3.0 Aim of the 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.

4.0 Reference Documents:

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

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5.0 Equipment Description:

Paste kettle is used for the preparation of paste (binder).which is used for preparation of granules

There is a stirrer inside the bowl. Stirrer revolves on a horizontal plane to vigorously mix the binder with solvent to make paste.

The machine is so designed that the components are easily dismantled, Kettle tilting easily through gear box attachment The machine mainly consists of bowl made up of SS316 within the bowl the stirrer is situated. The electric heater is for providing desired temperature for kettle.

In this GMP risk Assessment all critical components of the Paste kettle, based on the technical details, are listed and rated according to their influence of the product quality, EHs and operational requirements.

6.0 Participants:

Name (Block letters)	Function	Signature

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 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.

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 (eg. 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

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

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.

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Level	Descriptor	Example detail description
		• 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	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.

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8.0 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 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 there is **GMP risk.**
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 risk,** write what is the other 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:	**Verification**: 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
Charging										
1.	Transfer of material	Transfer of material into kettle is difficult	Yes	Spillage due to complicated manual transfer, area contamination	No	NA	Medium	Suitable method of material transfer will be considered to avoid spillage as per SOP.	Acceptable	IQ/OQ
Process										
2.	Paste preparation	Paste not properly soluble at room temperature.	Yes	Paste cannot be prepared properly due to insufficient temperature	No	NA	High	Electrical heater should be provisioned in the design in order to ensure efficient heating.	Acceptable	IQ
3.	Paste preparation	Temperature could not be monitored.	Yes	Paste preparation requires specified temperature conditions.	No	NA	High	A temperature sensor and controller should be provided to maintain the oil chamber temperature.	Acceptable	IQ
4.	Shaft	Oil sealing is poor	Yes	It will contaminate the product	No	NA	High	Oil sealing shall be effective, robust and detectable so as to ensure the same	Acceptable	IQ
5.	Mixing bowl	Bowl is not leak proof	Yes	Material may spill out result in yield loss, area contamination	EHS	Operator protection	Medium	Mixing bowl shall be leak proof without any crevices.	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
6.	Lubrication system	Lubricants migrates into product through coupling	Yes	It will cause contamination	No	NA	High	Lubrication system must be leak proof. Lubricant must be of food grade	Acceptable	IQ
7.	Mixing	Formation of dead zones	Yes	It will lead to inconsistent mixing	No	NA	High	The equipment will be designed so as to cover processing material over entire periphery of the kettle bowl for proper mixing.	Acceptable	OQ
8.	Process control	Process parameters could not be monitored and controlled	Yes	Process requirement	No	NA	High	All the process related parameter shall be controlled by the control panel of the equipment	Acceptable	IQ/OQ
9.	Machine operation	Operator cannot operate the machine	Yes	Process parameters cannot be achieved	Productivity	Machine cannot be operated	High	Proper training to be provided to concern person for setting and operation of machine	Low	OQ
Discharge										
10.	Discharge	Paste cannot be transferred manually	Yes	Yield loss	No	NA	High	Suitable method shall be employed for effective discharge through kettle.	Acceptable	IQ/ OQ
Cleaning and Material of Construction:										

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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
11.	Cleaning	Cleaning improper	Yes	It will lead to cross contamination	No	NA	High	Proper cleaning shall be done, smooth surface and easy access of machine shall facilitate easy cleaning.	Acceptable	IQ/OQ
12.	Surface finish	Bowl surface material is not cleanable	Yes	Lead to contamination	No	NA	High	Surface should be smooth, with no crevices and weld with ground finish.	Acceptable	IQ
13.	MOC for contact parts	Product contact surface of the machine is not compatible with product and cleaning agent.	Yes	It will lead to product contamination due to corrosion	No	NA	High	MOC of the contact and critical surface shall be taken into consideration. All product contact metallic surfaces should be of SS 316 or better with internal mirror finish. There should not be any crevices. Weld and joints should be ground finish.	Acceptable	IQ
Safety										

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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
14.	Power	Power recovery is not warned	No	Does not have any impact on product quality	EHS	Staff protection	Medium	After power recovery equipment starts with human intervention only and process should start from the step it stopped.	Acceptable	OQ
15.	Noise level	More noise is produced by the equipment during the operation	No	Does not have any impact on product quality	EHS	High noise may cause deafness and anxiety	Medium	Noise level shall be below 80 db at a distance of 1 m from the equipment.	Acceptable	OQ
16.	Rotating & electrical part	Appropriate closure of the rotating part is not provided.	No	Does not have any impact on product quality	EHS	It may lead to accident	High	Appropriate closure of all the rotating & electrical parts.	Acceptable	IQ
17.	Oil Chamber	Oil chamber pressure could not be monitored	No	Does not have any impact on product quality	EHS	Pressure monitoring required for safety of operator	High	A pressure gauge should be installed to monitor the oil chamber pressure.	Acceptable	IQ
18.	Oil Chamber	Pressure build up in oil chamber	No	Does not have any impact on product quality	EHS	It may lead to an accident	High	A safety valve should be installed for the oil chamber safety.	Acceptable	IQ
Instrumentation and controlling										

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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
19.	Measuring instruments	Measuring instruments not suitable	Yes	Improper measurements	No	NA	High	Measuring instruments must have a suitable measuring range and accuracy.	Acceptable	IQ
20.	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
21.	Measuring instruments	Instruments not calibrated	Yes	Non calibrated instruments may lead to false machine functions	No	NA	High	Measuring instruments should be calibrated, traceable to national or international standards.	Acceptable	IQ
22.	Control panel	Controlling of process / equipment not possible	Yes	Controls all critical process	No	NA	High	Control panel/ relay shall be provided to control all process related parameter and to ensure effectiveness of process.	Acceptable	IQ / OQ
Documentation:										

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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
23.	Documentation	Critical surfaces are not tested for material of construction and test reports are not provided	Yes	Lack of documented evidence leads to question on the quality of MOC	No	NA	High	MOC description and certification of critical parts to be provided	Acceptable	IQ
24.	Documentation	Instruments are not provided with calibration certificate	Yes	Calibration cannot be assured due to lack of documented evidence	No	NA	High	Critical instrumentation shall be supported with calibration certificates.	Acceptable	IQ
25.	Documentation	Equipment is not provided with design and functional specification	Yes	Design qualification is not possible	No	NA	High	Design and functional specification should be supplied as per URS	Acceptable	IQ
26.	Documentation	Equipment is not provided with Operation & maintenance manual	Yes	Correct operation is not ensured and Qualification requirement	No	NA	High	O & M manual should be supplied per URS	Acceptable	IQ
27.	Standard Operating procedure	Standard operating procedures are not available.	Yes	Procedures critical operations cannot be carried out successfully resulting process failure.	Operational	Productivity will get decrease to unavailability of procedure.	High	SOPs for Operation, Cleaning and maintenance shall be prepared in line with operational and maintenance manual and finalized.	Acceptable	IQ / OQ

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9.0 Summary and Conclusion:

- The risk Assessment is performed to establish the design parameters of the equipment so as to meet the desired performance of the equipment i.e. Paste Kettle.
- 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 at the time of accomplishment of OQ of the machine.
- To control the risk, various mitigation methods shall be verified through SOPs ,operation & maintenance manuals, and calibration certificates at respective verification points
- Based on Risk Assessment, the URS shall be prepared.

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

10.0 Abbreviation:

Acronym	Definition
cGMP	Current Good Manufacturing Practice
db	Decibel
EU-GMP	European –Good Manufacturing Practice
GA	General Arrangement
GAMP	Good Automated Manufacturing Practices
GMP	Good Manufacturing Practices
HMI	Human Machine Interface
IQ	Installation Qualification
MOC	Material Of Construction
OQ	Operational Qualification
O & M	Operation and Maintenance Manual
PQ	Performance Qualification
SOP	Standard Operating Procedures
SS	Stainless steel
URS	User Requirement Specification