QUALITY RISK ASSESSMENT & MITIGATION PLAN	
FAILURE MODE EFFECT ANALYSIS FOR VENDOR QUALIFICATION THROUGH QUESTIONNAIRE INSTEAD OF SITE AUDIT	
Reference Document No.	**Risk Assessment No.:**

QUALITY RISK ASSESSMENT & MITIGATION PLAN

(FAILURE MODE EFFECT ANALYSIS FOR VENDOR QUALIFICATION THROUGH QUESTIONNAIRE INSTEAD OF SITE AUDIT)

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Reference Document No.	Risk Assessment No.:

1. **OBJECTIVE:** To provide the documented evidence that there is low level of risk in case of "Vendor Qualification done through questionnaire instead of site audit".

2. **SCOPE:** The scope of this document is limited to Vendor Qualification at ……..facility.

3. **RESPONSIBILITY:**

Department	Responsibility
Quality Assurance	• Preparation, Review, and Compilation of FMEA • Post Approval of FMEA
CQA	• Review of FMEA

4. **REASON FOR RISK ANALYSIS:**
   To mitigate & monitor the risk associated with the Vendor Qualification through Questionnaire instead of Site audit.

5. **SITE OF STUDY:**

6. **RISK COMMUNICATION & TRAINING:**
   - The Risk analysis team shall be authorized by the Head-QA or his/her designee.
   - Quality Risk Management Team shall be cross functional team comprised of expert from different areas.
   - Training shall be imparted to the concerned team.

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7. RISK IDENTIFICATION, EVALUATION & MITIGATION:

INTRODUCTION: As per APIC guideline, manufacture of Medicinal Products and the Active Pharmaceutical Ingredients (API's) used as starting materials in the production of these products is subject to strict good manufacturing practice regulations that are designed to ensure their quality, safety and efficacy. This ensures that patients worldwide and at any time can have confidence in the quality, safety and efficacy of medicines.

In terms of defining the categories of materials, APIC guideline recommend that companies review the use of the material based on the ICH Q7 definition of Critical:- *"Critical describes a process step, process condition, test requirement, or other relevant parameter or item that must be controlled within predetermined criteria to ensure that the API meets its specification".*

Following are the criteria to be fulfilled for Vendor Qualification:

- Suppliers of all the materials should be approved using the Change Control procedure.
- cGMP & Regulatory compliances.
- Detail assessment of quality system required (Specifications/Manufacturing/Packaging/labelling details/MSDS/Logistic information/Certificates regarding Quality System, residual solvents, etc./BSE/TSE evaluation/Analytical test method).
- Raw material shall be evaluated as per specification.
- Plant trial prior to full production assessment required (Scale equipment, batch size, chemistry etc.).
- Safety/Health/Environmental.
- Quality Agreement shall be in place for all Suppliers.
- Any changes to the material specification, analytical methods or manufacturing process that may affect the quality of the material or downstream products should be informed in advance to evaluate the impact on final finished product.

Re-audit& Re-evaluation: The frequency of the re-audit should by dynamic and depending on the rating. In parallel with the re-audit, the supplier should be re-evaluated.

Evaluation through Questionnaire instead of Site audit for ……. (……..): Initial audit for …… was done in ……. and re-evaluation for ……. done through questionnaire in …… while for ……., no re-evaluation done, because as per SOP of Vendor Qualification.

- Re-evaluation to be done for those API vendors, of which minimum 5 API batches consignment are received.
- Any market complaint observed.
- Any Critical or 5 major observation found.
- Any critical change done in supplier site.
- Any critical change done in manufacturing process.
- Out of Specification observed.
- Re-audit shall be performed in case vendor site not acceptable poor performance (below 70% score).
- Periodic audit of API vendors (Domestic) audit shall be done 3 years ± 3 months, if the product is exported.

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RISK IDENTIFICATION	RISK EVALUATION	RISK MITIGATION
A per the APIC guideline, the re-audit plan should be as per the rating given during evaluation, that evaluation could be after initial audit or after re-audit. In case of repeated poor performance (below 70%) of the supplier during the re-evaluation procedure or repeated market complaints, the vendor should be discontinued for further supply.	As API's are the critical component of finish product, any compromise with the quality parameters may result into critical health issues.	• Vendor evaluation procedure in place, in case score obtained below 70% then re-audit shall be done. • Quality Agreement is in place. • Evaluation done for critical changes. • Annual performance review done for analytical data of existing API. • Nitrosamine/Mutagenic/Genotoxic/Impurities risk assessed and declaration taken from vendor. • Re-audit procedure is in place. • Evaluation procedure through questionnaire available. • Procedure for conducting virtual/Remote audit is in place.

8. RISK ASSESSMENT TOOL:

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

Column 1	Serial number of Risk Analysis item.
Column 2	Item/Function: Identify the process step or component associated with the risk.
Column 3	Potential Failure Mode: Identify the type of risk associated with the process or component.
Column 4	Effect of Potential Failure/Cause: Verify that whether risk have GMP impact.
Column 5	Potential Cause
Column 6	Risk Mitigation as a Current Control: Write the risk mitigation strategy as considered in design.
Column 7	References
Column 8/9/10/11	Severity/Occurrence/Detection/Risk level/Risk Acceptance: Risk Priority Number to be calculated by taking Severity, Occurrence & Detection of potential failure into consideration.
Column 12	Recommended action: Recommended actions should be given for controlling failure occurrence.
Column13/14/15/16	Severity/Occurrence/Detection/Risk level/Risk Acceptance: After recommendation implementations, Risk Priority Number to be calculated by taking Severity, Occurrence & Detection of potential failure into consideration.

Table 1: Instruction for each column given above

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Reference Document No.:	**Risk Assessment No.:**

Name of Facility/Equipment/Utility/System/Activity/Procedure/Unit Operation: Vendor Qualification done through Questionnaire instead of site audit	**Quality Risk Assessment Date:**

S.No.	Item/ Function	Potential Failure Mode (Failure Mode)	Potential Effect of Failure	Potential Cause/ Mechanism of Failure	Current Control	Reference document No.	S	O	D	Risk Priority Number (SxOxD)	Recommended Actions (if any)	Post Risk Evaluation			
												S	O	D	RPN SxOxD
1.	**Periodic audit not done**	• SOP not in place • SOP not appropriate • Schedule planner not available. • Required number of consignments not procured. • Qualified persons not available	Out of Specification observed	API of poor quality	• 100% testing of Starting material. • In case three consecutive OOS was observed, said vendor shall be hold for further supply. • No market complaint received. • Vendor questionnaire as per cGMP norms. • Quality agreement is in place. • In case any changes at RM manufacturer, same shall be informed to site. • No any critical observation. • Evaluation of each vendor on annual basis. • Annual rating above 70%. • No any critical change in equipment, process, method of analysis & facility observed. • Out of Specification not observed.	SOP No.: "Vendor Qualification" SOP No. "Handling of Out of Specification Results"	3	2	1	6	NA	NA	NA	NA	NA
			Critical changes not identified	As physical audit was not done											
			Impurities observed	API of poor quality											
			GMP practices not followed	As audit not performed hence updated regulatory norms not followed											
			Unqualified auditors	Improper planning											
			Planner unavailability	Schedule not prepared											
			Repeated market complaint	Low quality product manufactured											
			Critical failures observed	Audit not performed											

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Reference Document No.: | **Risk Assessment No.:**

S.No.	Item/ Function	Potential Failure Mode (Failure Mode)	Potential Effect of Failure	Potential Cause/ Mechanism of Failure	Current Control	Reference document No.	S	O	D	Risk Priority Number (SxOxD)	Recommended Actions (if any)	Post Risk Evaluation			
												S	O	D	RPN SxOxD
2.	**Audit through Questionnaire**	• Questionnaire not adequate • Critical parameters not included in questionnaire	Not effective as per physical audit	Physical verification not done		SOP No.: "Vendor Qualification"	2	3	1	6					
3.	**Questionnaire not appropriate**	• Questionnaire not the part of SOP. • Person prepared questionnaire not qualified. • Critical parameters not included in questionnaire.	Unqualified auditors Critical failures not identified GMP not complies Quality System verification not included Training program not included Updated list of instruments & equipment not available Preventive maintenance not included Calibration plan not available	Improper training Improper Checklist Auditor not qualified	• 100% testing of Starting material. • In case three consecutive OOS was observed, said vendor shall be hold for further supply. • No market complaint received. • Vendor questionnaire as per cGMP norms. • Quality agreement is in place. • In case any changes at RM manufacturer, same shall be informed to site. • No any critical observation. • Evaluation of each vendor on annual basis. • Annual rating above 70%. • No any critical change in equipment, process, method of analysis & facility observed. • Out of Specification not observed.	SOP No.: "Vendor Qualification" SOP No. "Handling of Out of Specification Results"	3	2	1	6	NA	NA	NA	NA	NA

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S.No.	Item/ Function	Potential Failure Mode (Failure Mode)	Potential Effect of Failure	Potential Cause/ Mechanism of Failure	Current Control	Reference document No.	S	O	D	Risk Priority Number (SxOxD)	Recommended Actions (if any)	Post Risk Evaluation			
												S	O	D	RPN SxOxD
			Equipment not qualified Periodic qualification not included												
			API not tested as per specification TSE/BSE certificates not available MSDS not available Process flow chart not provided Updated process flow chart not provided Environmental condition not maintained during manufacturing Environmental condition not maintained during storage	Improper checklist Auditor not qualified	• 100% testing of Starting material. • In case three consecutive OOS was observed, said vendor shall be hold for further supply. • No market complaint received. • Vendor questionnaire as per cGMP norms. • Quality agreement is in place. • In case any changes at RM manufacturer, same shall be informed to site. • No any critical observation. • Evaluation of each vendor on annual basis. • Annual rating above 70%. • No any critical change in equipment, process, method of analysis & facility observed. • Out of Specification not observed.	SOP No.: "Vendor Qualification"	3	2	1	6	NA	NA	NA	NA	NA

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Reference Document No.: | **Risk Assessment No.:**

S.No.	Item/ Function	Potential Failure Mode (Failure Mode)	Potential Effect of Failure	Potential Cause/ Mechanism of Failure	Current Control	Reference document No.	S	O	D	Risk Priority Number (SxOxD)	Recommended Actions (if any)	Post Risk Evaluation			
												S	O	D	RPN SxOxD
			Chance of intermixing												
			Proper segregation not available												
			Process Validation not available	Improper checklist Auditor not qualified	• 100% testing of Starting material. • In case three consecutive OOS was observed, said vendor shall be hold for further supply. • No market complaint received. • Vendor questionnaire as per cGMP norms. • Quality agreement is in place. • In case any changes at RM manufacturer, same shall be informed to site. • No any critical observation. • Evaluation of each vendor on annual basis. • Annual rating above 70%. • No any critical change in equipment, process, method of analysis & facility observed. • Out of Specification not observed.	SOP No.: "Vendor Qualification"	3	2	1	6	NA	NA	NA	NA	NA
			Hold time study not available												
			FIFO & FEFO not followed												
			Cleaning Validation not done												
			Man & Material movement not separate												
			Log books not updated												
			Operator & Supervisor not qualified												
			Disinfectant program not validated												

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S.No.	Item/ Function	Potential Failure Mode (Failure Mode)	Potential Effect of Failure	Potential Cause/ Mechanism of Failure	Current Control	Reference document No.	S	O	D	Risk Priority Number (SxOxD)	Recommended Actions (if any)	Post Risk Evaluation			
												S	O	D	RPN SxOxD
			Material COA not available												
			Material STP not available												
			Stability Studies not performed												
			Contract agreement expired												
4.	**Improper Audit**	• Critical parameters not included. • Wrong data generated by vendor. • Questionnaire not upgraded	Low quality API received.	cGMP norms not followed	• 100% testing of Starting material. • In case three consecutive OOS was observed, said vendor shall be hold for further supply. • No market complaint received. • Vendor questionnaire as per cGMP norms. • Quality agreement is in place. • In case any changes at RM manufacturer, same shall be informed to site. • No any critical observation. • Evaluation of each vendor on annual basis. • Annual rating above 70%. • No any critical change in equipment, process, method of analysis & facility observed. • Out of Specification not observed.	SOP No.: "Vendor Qualification"	3	2	1	6	NA	NA	NA	NA	NA
			Repeated Market complaint	Questionnaire not updated											

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S.No.	Item/ Function	Potential Failure Mode (Failure Mode)	Potential Effect of Failure	Potential Cause/ Mechanism of Failure	Current Control	Reference document No.	S	O	D	Risk Priority Number (SxOxD)	Recommended Actions (if any)	Post Risk Evaluation			
												S	O	D	RPN SxOxD
5.	**Data Integrity**	• Actual data not provided by vendor	Material received is of low quality	• Wrong COA provided • Wrong MSDS provided • Process validation not done • Stability studies not performed • Disinfectant policy not available	• 100% testing of Starting material. • In case three consecutive OOS was observed, said vendor shall be hold for further supply. • No market complaint received. • Vendor questionnaire as per cGMP norms. • Quality agreement is in place. • In case any changes at RM manufacturer, same shall be informed to site. • No any critical observation. • Evaluation of each vendor on annual basis. • Annual rating above 70%. • No any critical change in equipment, process, method of analysis & facility observed. • Out of Specification not observed.	SOP No.: "Vendor Qualification"	3	2	1	6		NA	NA	NA	NA
6.	**cGMP/Regulatory requirements**	• Updated regulatory norms not followed	Specification not updated	Auditor not trained	• 100% testing of Starting material. • In case three consecutive OOS was observed, said vendor shall be hold for further supply. • No market complaint received. • Vendor questionnaire as per cGMP norms. • Quality agreement is in place.	SOP No.: "Vendor Qualification"	3	2	1	6	NA	NA	NA	NA	NA

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S.No.	Item/ Function	Potential Failure Mode (Failure Mode)	Potential Effect of Failure	Potential Cause/ Mechanism of Failure	Current Control	Reference document No.	S	O	D	Risk Priority Number (SxOxD)	Recommended Actions (if any)	Post Risk Evaluation			
												S	O	D	RPN SxOxD
					• In case any changes at RM manufacturer, same shall be informed to site. • No any critical observation. • Evaluation of each vendor on annual basis. • Annual rating above 70%. • No any critical change in equipment, process, method of analysis & facility observed. • Out of Specification not observed.										

Where: S=Severity; O=Occurrence Probability; D=Detection

Assessment of Severity, Occurrence and Detection:

Severity Effect	Likelihood Occurrence	Likelihood of Detection	Rating
No Effect	Unlikely	Always Detected	1
Moderate Effect	Possible	Might Detect Failure	2
Serious Effect	Almost Certain (Every time)	Lack of Detection Control	3

Evaluation of RPN:

RPN Rating	Category
12 to 27	High
7 to 11	Medium
Upto 6	Low

S.No.	Recommended Action	Responsible Person	Target Date of Completion
1.	NA	NA	NA

CAPA (Required/Not Required): Required

If required, mention CAPA No.: ……..

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Reference Document No.:	Risk Assessment No.:

Quality Risk Management Team			Reviewed By Head Operations (Sign & Date)	Approved By Head QA (Sign & Date)
Name	Department	Sign & Date		

Verification of Recommended Action:

……

……

……

Remarks (if any):

……

……

……

……

……

Verified By
Operating Person QA
(Sign & Date)

Approved By
Head QA
(Sign & Date)

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9. CONCLUSION:……
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10. REFERENCES:

- Reference SOP of Risk Assessment.
- Related SOP's.

11. DOCUMENTS TO BE ATTACHED:

- Not Applicable

12. DEVIATION FROM PRE DEFINED SPECIFICATION, IF ANY:

……
……
……

13. CHANGE CONTROL, IF ANY:……
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……
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……

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14. ABBREVIATIONS:

FMEA	: Failure Mode Effect Analysis
RPN	: Risk Priority Number
CAPA	: Corrective action preventive action
SOP	: Standard Operating Procedure
QRM	: Quality Risk Management
QA	: Quality Assurance

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15. FMEAAPPROVAL:

PREPARED BY:

DESIGNATION	NAME	SIGNATURE	DATE
OPERATING PERSON (QUALITY ASSURANCE)			

REVIEWED BY:

DESIGNATION	NAME	SIGNATURE	DATE
OPERATING MANAGER (QUALITY ASSURANCE)			

APPROVED BY:

DESIGNATION	NAME	SIGNATURE	DATE
HEAD (QUALITY ASSURANCE)			