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RISK ASSESSMENT & MITIGATION FOR PROCESS VALIDATION STUDY FOR 5-AMINO LEVULINIC ACID HCL (FINAL STAGE)

REPORT

FOR

RISK ASSESSMENT& MITIGATION FOR PROCESS VALIDATION STUDY

PRODUCT: 5-AMINO LEVULINIC ACID HCL

STAGE: FINAL

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REPORT Contents

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1. Report Approval

This is a specific Report for Risk assessment and Mitigation of Process Validation of 5-Amino Levulunic Acid stage final. which has been carried out in ……..

This report has been prepared, reviewed and approved by the following

Prepared By:

Name	Designation	Department	Signature	Date
		Quality Assurance		

Reviewed By:

Name	Designation	Department	Signature	Date
		Production		
		Quality Control		
		Maintenance		
		Quality Assurance		

Approved By:

Name	Designation	Department	Signature	Date
		Production		
		CQA		

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2.0 Overview

2.1 Objective:

The Objective of this Report is to adopt a systematic process for the assessment, control, communication and review of risk associated with the Process Validation of of 5-Amino Levulinic Acid which is carried out in the plant.

2.2 Purpose and Scope

The purpose of this Report is to outline a scientific and practical approach for decision making process by applying a suitable tool of risk assessment covering all aspects of risk associated with Process Validation of 5-Amino Levulinic Acid stage final.

2.3 Risk Assessment Team

- Production Executive /Officer/Manager
- Quality control Executive/Officer/Manager
- Projects Engineer/Sr. Engineer/Manager
- Maintenance Executive /Officer/Manager
- Quality Assurance Executive /Officer/Manager

2.4 Responsibility

S.No.	Department	Designation	Responsibility
1.	**Production**	Executive /Officer/ Manager	Review of Protocol & report To Provide the all relevant information that are required while undergoing Risk assessment process i.e. Quantity, Packaging etc.
2.	**Quality control**	Executive /Officer/ Manager	Review of Protocol & report To Provide information about the availability of Analytical methods Pharmacopeia reference and finally reviewing the testing procedures
3.	**Maintenance**	Executive /Officer/ Manager	Review of Protocol & report To assist the risk assessment team about the technical queries of facility & equipments
4.	**Quality Assurance**	Executive /Officer/ Manager	Preparation of Protocol & report To review all the Procedural controls both in-house and vendor To conduct audits to assess the quality management system and manufacturing facility Final approval of Protocol & report By head quality Assurance

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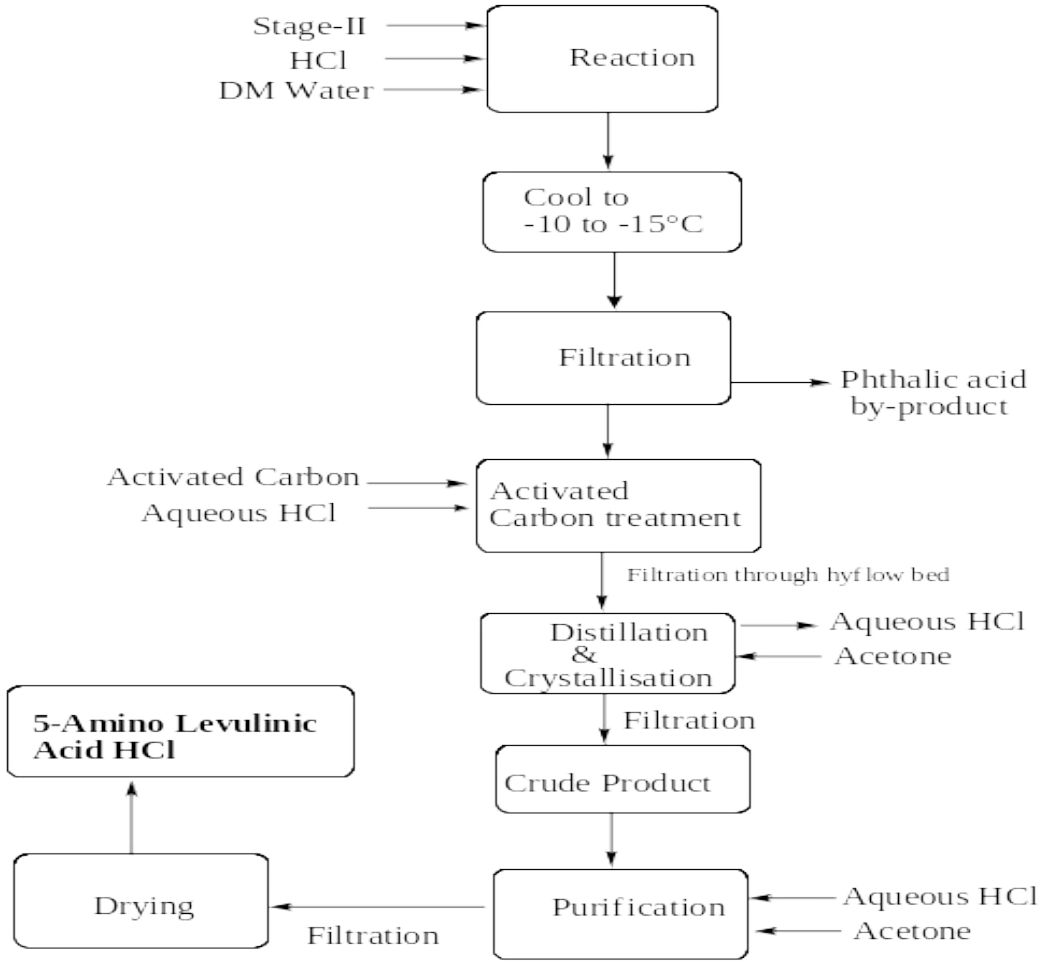
3.0 Process Flow Diagram : 5-Amino Levulunic Acid stage final produced by treatment of Stage II by purified water and HCL as explained in process flow diagram

Stage –III: Preparation of 5-Aminolevulinic Acid HCl



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4.0 Introduction

Risk analysis for Process Validation Study of 5-Amino Levulunic Acid has been performed by taking into the probability, occurance and Severity. The risk is indentified analyzed and evaluated. The risk indentified analyzed and evaluated for Equipments, Process, Raw Materials, and Process Parameters and in process Checks, Intermediate, Impurities & Extraneous Matter.

4.1 Quality Risk Management Process

Risk assessment is a systematic process of organizing information to support a risk decision to be made within a risk management process. Its consists Identification of hazards and the analysis and evaluation of risks associated with exposure to those hazards

Quality risk assessment begins with a well defined problem description or risk question.

For risk assessment process three fundamental questions are considered

- What might go wrong?
- What is likely hood **(Occurrence)** it will go wrong?
- What are the consequences **(severity)?**

- **Risk Identification**

Risk Identification is systematic use of information to identify hazards referring to risk questions or problem description. Information may include historical data theoretical analysis, informed opinions and concerns of stakeholders. risk Identification will be conducted by reviewing the types of events that might occur in both normal and unusual situations. This may be done by challenging the normal presumptions, and considering the possibilities of unanticipated situations. For each risk event, the underlying (root) cause should be determined that will create the potential risk occurrence.

Risk Identification addresses the “what might go wrong” question including identifying the possible consequences. This provides the basis for the further steps in quality risk management process.

- **Risk Analysis**

Risk analysis is the estimation of risk associated with the identified hazards.

It is the quantitative or qualitative process of linking the likelihood of occurrence and severity of harm and sometime the detectability of harm is also consider during estimation of risk.

- **Risk Evaluation**

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

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Risks are ranked by scoring various criteria with appropriate numerical ratings, adding to scores to determine the overall score of each risk, and sorting the risks into descending order based on each score. A risk scoring threshold is established, over which risks must be mitigated using adequate design and/ or process controls that will protect the system. Those risks that fall below the threshold are either unmitigated or scheduled for later mitigation. An additional threshold or characteristic of risk can be used to determine the differentiation of non- mitigation versus postponed mitigation.

- **Risk Control**

Risk control includes decision making to reduce or mitigate risk. The purpose of risk control is to reduce the risk to the acceptance level

The risk control is done by considering the following question

- Is the risk above an acceptable level?
- What can be done to reduce or eliminate risk?
- What is appropriate balance among benefits, risks and resources?
- Are new risk is introduced as a result identified risk being controlled?

- **Risk Reduction**

Risk reduction focuses on processes the mitigation or avoidance of quality risk when it exceeds the acceptable level. Risk reduction includes action taken to mitigate the severity, occurrence or probability of harm and the processes that improve the detectability of harm. It is the part of risk control strategy and involves

- Engineering Control
- Procedural Control
- Manual control etc.

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4.2 Risk Assessment Legend

A. Severity

Ranking	Effect	Criteria
10	Hazardous	Hazardous effect without warning. Safety related. Regulatory non-compliant.
9	Serious	Potential hazardous effect. Able to stop without mishap. Regulatory compliance in jeopardy.
8	Extreme	Item inoperable but safe. Customer very dissatisfied.
7	Major	Performance severely affected but functional and safe. Customer dissatisfied.
6	Significant	Performance degraded but operable and safe. Non-vital part inoperable. Customer experiences discomfort.
5	Moderate	Performance moderately affected. Fault on non-vital part requires repair. Customer experiences some dissatisfaction.
4	Minor	Minor effect on performance. Fault does not require repair. Non-vital fault always noticed. Customer experiences minor nuisance.
3	Slight	Slight effect on performance. Non-vital fault notice most of the time. Customer is slightly annoyed.
2	Very Slight	Very slight effect on performance. Non-vital fault may be noticed. Customer is not annoyed.
1	None	No effect.

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B. Probability or Occurrence

Ranking	Possible Failure	Probability of Failure
10	≥1 in 2	Almost certain.
9	1 in 3	Very high.
8	1 in 8	High.
7	1 in 20	Moderately high.
6	1 in 80	Medium
5	1 in 400	Low
4	1 in 2,000	Slight
3	1 in 15,000	Very slight.
2	1 in 150,000	Remote.
1	1 in 1,500,000	Almost impossible.

C. Detection

Ranking	Detection	Likelihood of Detection by design control
10	Absolute Uncertainty	No design control or design control will not detect potential cause
9	Very Remote	Very remote chance design control will detect potential cause.
8	Remote	Remote chance design control will detect potential cause.
7	Very Low	Very low chance design control will detect potential cause.
6	Low	Low chance design control will detect potential cause.
5	Moderate	Moderate chance design control will detect potential cause.
4	Moderately High	Moderately high chance design control will detect potential cause.
3	High	High chance design control will detect potential cause.
2	Very High	Very high chance design control will detect potential cause.
1	Almost Certain	Almost certain that the design control will detect potential cause.

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4.3 Risk Assessment Tool – Failure Mode effect Analysis (FMEA)

4.3.1 Risk Identification

Risk assessment team shall identify all possible failure modes of Process Validation of Methyl -5-Bromolevulinate (Stage-1) by reviewing the various aspects of facility design & operational features, Provisions and Adopted procedures. The risk identification involves three aspects

1. **Identification of Failure Mode of Process Validation Study of Stage-1 5-Amino Levulinic Acid**
    a. Equipment
    b. Raw Materials
    c. Process (including In process & final)
    d. Equipment Cleaning
    e. Sampling, Handling & Testing
    f. Stability Study
    g. Mix-up
    h. Packing & Storage of the Product
    i. Environment of the Plant.
2. **Identification of Potential cause**
    a. Operator Error
    b. Equipment Malfunctioning
    c. Instrument malfunctioning
    d. Non availability or Non rational Procedures
    e. Inefficient Provisions for operations etc.
3. **The consequences i.e. End results of failure mode**
    The failure Mode may leads to
    a. GMP Violation
    b. Product Quality
    c. Patient
    d. Contaminated Product
    e. Regulatory non compliance
    f. Product Recall
    g. Unsafe operating conditions

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The identification done for the risk shall have scientific rational and must be justified for its validity. The below mentioned table shall be used for Risk Identification process.

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S. No.	Failure Mode {What can go wrong}	Potential cause of Failure	What are the Consequences (Severity)	Justification
	Risk Identification			

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01	**Equipments** (Reactors and Centrifuge)	Equipment Selection Equipment Qualification Man hole Opening & Closing Awareness Equipment Malfunctioning Power failure	Product Failure GMP Violation Contamination Deviation Impact on Conversion of reaction Yield Loss	Qualified equipments are used in production of Final stage of 5-ALA. Awareness provide through training and preventive maintenance records verified. Equipments history checked no malfunctioning was found. The equipments used in 5-ALA stage final are GLR reactors, Sparkler filter, centrifuge, and Vacuum tray dryer, Multi mill & Sifter. The GLR reactor was used in Final for Reaction. The reactor is suitable as per the process Requirement The Sparkler filter was used to filter the reaction mass. The GLR reactor was used for carbon treatment. Centrifuge was used for separation of cake from mother liquid. The centrifuge usage justified according the process Requirement. The GLR reactor was used for Heating, Cooling, and Crystallization. The reactor is suitable for crystallization justified according the process Requirement ……. was used for Extract the wet material. ……. was use for drying operation and achieves the LOD. ……. was use for Milling operation. ……. was used for sifting the material.
S. No.	**Failure Mode {What can go wrong}**	**Potential cause of Failure**	**What are the Consequences (Severity)**	**Justification**

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	Risk Identification			
02	**Process**	Technology transfer Product stability Product knowledge Analytical method validation	Product validation Stability Filling Customer commitment Business impact Campaign failure	5-ALA final stage was develop in R&D. The R&D and Plant validation batches are kept on Stability Time Study. Based on ROS and process package development batches are taken batches were comply with the Specification After development batches evolution of quality and yield performed. Based on success of development batches the validation batches had been taken. All the batches comply with the specification. Based on R&D lab batches, Development batches and validation batches it is concluded that process is robust.

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S.No.	Failure Mode {What can go wrong}	Potential cause of Failure	What are the Consequences (Severity)	Justification
	Risk Identification			
03	**Raw Materials**	Vendor Sampling Testing and specification Awareness Material handling and storage	Quality Product Failure GMP Violation Conversion of reaction Yield	Awareness regarding sampling, testing and handling of raw material provided. Material procured from approved vendors. Vendors were qualified as per SOP on vendor management. Raw materials are tested as per approved specification. Only approved raw materials are used in manufacturing of 5 ALA. MSDS was followed for handling, sampling and storage of raw materials. Batches are taken as per Approved BPRs. All the in process parameter comply with specification. All the batches of 5-ALA final stage comply with the specification. Yield of all the batches was within range. Based on the yield, quality, in process checks good laboratory practices and cGMP. it is concluded that the raw materials are of good quality and handled sampled and tested appropriately

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S.No.	Failure Mode {What can go wrong}	Potential cause of Failure	What are the Consequences (Severity)	Justification
04	**Process Parameters and In process Checks**	Awareness Written Procedure Selection of Equipments Raw Materials Sampling & Handling	Deviation Product Failure Yield Contamination	All the batches are taken as per approved BPR's. in-process checks are defined in BPR's. Sampling and testing performed as per specification. Critical parameters were performed as per BPR's and Checked by Shift Incharge. All the critical process parameters are identified as per process package of Product. Indentified in BPR marked as Bell.
Risk Identification				
05	**Intermediate**	Sampling, Testing Material handling and storage	Contamination Yield and Quality	Structure elucidation had been performed at R&D.Analytical procedure are developed and apply. On all R&D Batches. Awareness provided before starting the campaign. Equipments are selected keeping in observation of Impurities generation and heating cooling impact. Based on Evaluation of quality and yield data all the batches of 5-ALA. That batches are taken in suitable equipments under the supervision of trained man power

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S.No.	Failure Mode {What can go wrong}	Potential cause of Failure	What are the Consequences (Severity)	Justification
06	**Impurities**	Raw Material Awareness Equipments Selection Batch size Analytical Procedure	Product Failure Product Contamination Deviation Yield and Quality	Final Stage of 5-ALA Manufactured in LA Block. All the raw material charged using PPE. Before charging of batch equipment surfaced is cleaned. The Floor and Walls of the facility are good condition. Inappropriate door opening & Closing give a chance for the Extraneous Matter incursion inside the facility which thereafter can move into the Material flow line And results into contamination. Bioburdan tests performed of all validation batches. All parameters are comply With the specification

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S.No.	Failure Mode {What can go wrong}	Potential cause of Failure	What are the Consequences (Severity)	Justification
	Risk Identification			
07	**Extraneous Matter**	Inappropriate door Opening &Closing Non Availability of Standard Procedure for cleanliness verification of entering person	Raw Material Packing Material Equipment Surface Floor & Walls of the facility	Stage final of 5-ALA Manufactured in LA Block. The operation of final crystallization was performed in closed Room. The centrifuging, drying packing was performed in the classified area. All the operations were performed by trained manpower by following gowning procedure. All the equipments were cleaned after every batch processing.
08	**Micro Organism**	Awareness Testing procedure	Contamination	Stage final of 5-ALA three batches are tested for Bioburden.All the batches comply to the specification. Hence existing awareness and testing procedure is appropriate
09	**Packing and Storage**	Awareness Written Procedure	GMP Violation Contamination Complaint and recall	Final Stage activity has been done in Class D Closed Area. No other manufacturing activity has been undertaken therein. Each room in classified area is separated by gallery having more positive pressure as compare to rooms

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4.3.2 Risk Analysis

Risk Analysis is the second step of risk identification Process. It involves the assessment of the

1. Severity of the Consequence of failure Mode
2. The Probability or Occurrence of Failure mode by reviewing effectiveness of the existing Design control
3. its detectability under the existing design control

Base upon the analysis Risk priority number will be assigned to the particular failure Mode as per the formula

RPN = Severity X Occurrence X Detection

Each index ranges from 1 (lowest risk) to 10 (highest risk). The overall risk of each failure is called Risk Priority Number (RPN) and the product of Severity (S), Occurrence (O), and Detection (D) rankings: RPN = S × O × D. The RPN (ranging from 1 to 1000) is used to prioritize all potential failures to decide upon actions leading to reduce the risk, usually by reducing likelihood of occurrence and improving controls for detecting the failure

The below mentioned table shall be used for Risk Analysis process

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4.3.2 Risk Analysis

S.No.	Failure Mode {What can go wrong}	Potential cause of Failure	What are the Consequences	Existing Design Control	Severity	Probability	Detection	Risk Priority Number
					(S)	(P)	(D)	RPN=S x P x D
	Risk Analysis							Risk valuation

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01.	Equipments (Reactors and Centrifuge)	Equipment Selection Equipment Qualification Man hole Opening & Closing Awareness Equipment Malfunctioning Power failure	Product Failure GMP Violation Contamination Deviation Impact on Conversion of reaction Yield Loss	Qualified equipments (DQ,IQ,OQ,PQ) Preventive Maintenance of Equipments Training to concerned persons Work order system to rectify any breakdown of equipments	4	6	2	RPN = 4X6X2 = 48

S.No.	**Failure Mode {What can go wrong}**	**Potential cause of Failure**	**What are the Consequences**	**Existing Design Control**	**Severity**	**Probability**	**Detection**	**Risk Priority Number**
					(S)	**(P)**	**(D)**	**RPN=S x P x D**
	Risk Analysis							**Risk valuation**

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02	Process	Technology transfer Product stability Product knowledge Analytical method validation	Product validation Stability Filling Customer commitment Business impact Campaign failure	Technology transfer documents are provided from R& D to plant Trained Operators w.r.t process Method Validated	2	6	2	RPN = 2X6X2 = 24

S.No.	**Failure Mode {What can go wrong}**	**Potential cause of Failure**	**What are the Consequences**	**Existing Design Control**	**Severity**	**Probability**	**Detection**	**Risk Priority Number**
					(S)	**(P)**	**(D)**	**RPN=S x P x D**

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	Risk Analysis							Risk valuation
03	Raw Materials	Vendor Sampling Testing and specification Awareness Material handling and storage	Quality Product Failure GMP Violation Conversion of reaction Yield	SOP for dispensing of material (Ref……) Provision of PPEs SOP for cleaning of scoop and scrapersTrained Operators Procedure for the destruction floor sweep material (Ref……) Separate De-dusting facility are provided for both raw materials & packing materials. MSDS are available wrt materials	2	6	2	RPN = 2X6X2 = 24

S.No.	Failure Mode {What can go wrong}	Potential cause of Failure	What are the Consequences	Existing Design Control	Severity	Probability	Detection	Risk Priority Number
					(S)	(P)	(D)	RPN=S x P x D

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	Risk Analysis							Risk valuation
04	Process Parameters and In process Checks	Awareness Written Procedure Selection of Equipments Raw Materials Sampling & Handling	Deviation Product Failure Yield Contamination	Process design for filtration to prevent Extraneous matter incursion in the API like particle, rust etc (Ref Manufacturing BPRs) Procedural control to check the Layer separation by visual inspection by sight glass & verification through BPR Instruction	2	6	2	RPN = 2X6X2 = 24
05	Intermediate	Sampling, Testing Material handling and storage	Contamination Yield and Quality	Specification & STP are provided to analyst Trained analyst	2	6	2	RPN = 2X6X2 = 24

S.No.	Failure Mode {What can go wrong}	Potential cause of Failure	What are the Consequences	Existing Design Control	Severity	[illegible]	Detection	Risk Priority Number

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					(S)	(P)	(D)	RPN=S x P x D
	Risk Analysis							**Risk valuation**
06	Impurities	Raw Material Awareness Equipment's Selection Batch size Analytical Procedure	Product Failure Product Contamination Deviation Yield and Quality	Specification & STP are provided to analyst Qualified Instrument are Method Validation are provided to analyst Provision of PPEs Trained analyst	4	6	2	RPN =4X6X2 = 48

S.No.	Failure Mode {What can go wrong}	Potential cause of Failure	What are the Consequences	Existing Design Control			Detection	Risk Priority Number

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					(S)	(P)	(D)	RPN=S x P x D
	Risk Analysis							**Risk valuation**
07	Extraneous Matter	Inappropriate door Opening &Closing Non Availability of Standard Procedure for cleanliness verification of entering person	Raw Material Packing Material Equipment Surface Floor & Walls of the facility	Work order system to rectify the failure of door functioning. Air curtains are installed on the entry doors for the plants The SOP to verify personnel hygienic which allows verification through checklist for cleanliness for the operating persons	5	6	2	RPN = 5X6X2 =60
08	Micro Organism	Awareness Testing procedure	Contamination	Classified area for Final product processing.AHU qualified as per frequency. Enviournment monitoring done monthly	2	6	2	RPN=2x6x2=24
09	Packaging	Awareness Written Procedure	GMP Violation Contamination	Final packing performed by trained manpower. Qc perform the sampling and testing after final Packing. The labeling and sealing performed in the presence of QA	2	6	2	RPN =2x6x2=24

4.3.3 Risk Reduction or Mitigation

The Risk Reduction or Mitigation is the Third step of Risk assessment process. if the Existing design control cannot lead the risk priority number to the acceptable level then additional design control shall be worked by providing

1. New or Improved Provisions or Procedures
2. Modification in the existing facility design
3. Additional resources
4. Improved control strategy etc.

   The additional design control shall be appropriately worked out to reduce the risk to its acceptable level. The below mentioned table shall be used for the Risk Reduction or Mitigation process

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4.3.3 Risk Reduction or Mitigation

S.No.	Failure Mode {What can go wrong}	Potential cause of Failure	Existing Design Control	Severity (S)	Probability (P)	Detection (D)	Risk Priority Number (RPN)	Additional Design Control	Severity (S)	Probability (P)	Detection (D)	Risk Priority Number (RPN)
	Risk Mitigation											
1.	Equipments (Reactors and Centrifuge)	Equipment Selection Equipment Qualification Man hole Opening & Closing Awareness Equipment Malfunctioning Power failure	Qualified equipments (DQ,IQ,OQ,PQ) Preventive Maintenance of Equipments Training to concerned persons Work order system to rectify any breakdown of equipments	4	6	2	48	Existing design control keep the risk at acceptable level.	4	6	2	48

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S.No.	Failure Mode {What can go wrong}	Potential cause of Failure	Existing Design Control	Severity (S)	Probability (P)	Detection (D)	Risk Priority Number (RPN)	Additional Design Control	Severity (S)	Probability (P)	Detection (D)	Risk Priority Number (RPN)
	Risk Mitigation											
02	Process	Technology transfer Product stability Product knowledge Analytical method validation	Technology transfer documents are provided from R& D to plant Trained Operators w.r.t process Method Validated	2	6	2	24	Existing design control keep the risk at acceptable level.	2	6	2	24

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S.No.	Failure Mode {What can go wrong}	Potential cause of Failure	Existing Design Control	Severity (S)	Probability (P)	Detection (D)	Risk Priority Number (RPN)	Additional Design Control	Severity (S)	Probability (P)	Detection (D)	Risk Priority Number (RPN)
	Risk Mitigation											
03	Raw Materials	Vendor Sampling Testing and specification Awareness Material handling and storage	SOP for dispensing of material Provision of PPEs.SOP for cleaning of scoop and scrapers. Trained Operators Procedure for the destruction floor sweep material Separate De-dusting facility are provided for both raw materials & packing materials MSDS are available w.r.t materials	2	6	2	24	Existing design control keep the risk at acceptable level.	2	6	2	24

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S.No.	Failure Mode {What can go wrong}	Potential cause of Failure	Existing Design Control	Severity (S)	Probability (P)	Detection (D)	Risk Priority Number (RPN)	Additional Design Control	Severity (S)	Probability (P)	Detection (D)	Risk Priority Number (RPN)
	Risk Mitigation											
4.	Process Parameters and In process Checks	Awareness Written Procedure Selection of Equipments Raw Materials Sampling & Handling	Process design for filtration to prevent Extraneous matter incursion in the API like particle, rust etc (Ref Manufacturing BPRs) Procedural control to check the Layer separation by visual inspection by sight glass & verification through BPR	2	6	2	24	Existing design control keep the risk at acceptable level.	2	6	2	24

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S.No.	Failure Mode {What can go wrong}	Potential cause of Failure	Existing Design Control	Severity (S)	Probability (P)	Detection (D)	Risk Priority Number (RPN)	Additional Design Control	Severity (S)	Probability (P)	Detection (D)	Risk Priority Number (RPN)
	Risk Mitigation											
5.	Intermediate	Sampling, Testing Material handling and storage	Specification & STP are provided to analyst Trained analyst	2	6	2	24	Existing design control keep the risk at acceptable level.	2	6	2	24
6.	Impurities	Raw Material Awareness Equipment's Selection Batch size Analytical Procedure	Specification & STP are provided to analyst Qualified Instrument are Method Validation are provided to analyst Provision of PPEs Trained analyst	4	6	2	48	Existing design control keep the risk at acceptable level.	4	6	2	48

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RISK ASSESSMENT & MITIGATION FOR PROCESS VALIDATION STUDY FOR 5-AMINO LEVULINIC ACID HCL (FINAL STAGE)

S.No.	Failure Mode {What can go wrong}	Potential cause of Failure	Existing Design Control	Severity (S)	Probability (P)	Detection (D)	Risk Priority Number (RPN)	Additional Design Control	Severity (S)	Probability (P)	Detection (D)	Risk Priority Number (RPN)
	Risk Mitigation											
7.	Extraneous Matter	Inappropriate door Opening &Closing Non Availability of Standard Procedure for cleanliness verification of entering person	Work order system to rectify the failure of door functioning Air curtains are installed on the entry doors for the plants The SOP to verify personnel hygienic which allows verification through checklist for cleanliness for the operating persons	5	6	2	60	Existing design control keep the risk at acceptable level. Layout Display for the Man & Material Movement in the plant	5	6	2	60

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S.No.	Failure Mode {What can go wrong}	Potential cause of Failure	Existing Design Control	Severity	Probability	Detection	Risk Priority Number	Additional Design Control	Severity	Probability	Detection	Risk Priority Number
				(S)	(P)	(D)	(RPN)		(S)	(P)	(D)	(RPN)
	Risk Mitigation											
08	Micro Organism	Awareness Testing procedure	Classified area for Final product processing.AHU qualified as per frequency. Enviournment monitoring done monthly	2	6	2	RPN = 2X6X2 = 24	Existing design control keep the risk at acceptable level.	2	6	2	RPN = 2X6X2 = 24
09	Packaging	Awareness Written Procedure	Final packing performed by trained manpower. Qc perform the sampling and testing after final Packing. The labeling and sealing performed in the presence of QA	2	6	2	RPN = 2X6X2 = 24	Existing design control keep the risk at acceptable level.	2	6	2	RPN = 2X6X2 = 24

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5.0 Acceptance Criteria

The Risk Priority Number shall be within the range 0<RPN<100

6.0 Risk Control Strategy

S.No.	Risk Priority Number	Risk Decision	Risk control strategy
1.	0<RPN<100	Risk Acceptable	No control is required
2.	100<RPN<500	Risk Reduction	Additional Procedural Control
			Manual Control
			Documentary Evidence
3.	500<RPN<1000	Risk Reduction	Rugged Procedural control
			Additional Manual Control
			Auditing
			Engineering controls (if Possible)

7.0 Summary and Conclusion

The Risk assessment of 5-ALA Product had been performed taking in to consideration Manual operations, operator involvements, cross contamination and handling of hazardous materials.
Risk has been evaluated and found risk priority number below 100. As per protocol if RPN is less than 100 risk is acceptable. As per risk analysis the RPN no is maximum 60. Hence it is concluded that based on risk analysis that risk is acceptable. As all the personnel are qualified & trained, equipments are qualified. Batches are taken as approved BPR.All the critical Process Parameter has been identified. there is no product failure, no deviation found during manufacturing of 5-ALA.Hence Risk is LOW & is below 100.

8.0 Report Approval.

The report has been prepared by evaluating all possible risks and finally approved by Quality Assurance head.

9.0 References:

1. Risk Management Master Plan (RMMP)
2. ICH Q9
3. PICS Annexure – 20.

4. Annexure :01

Annexure – 01

List of Reference Documents

Facility :	
Location:	
No. of Pages:	

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RISK ASSESSMENT & MITIGATION FOR PROCESS VALIDATION STUDY FOR 5-AMINO LEVULINIC ACID HCL (FINAL STAGE)

List of reference documents

S.No.	Document Title	Document No
1.	SOP on Vendor Assessment, Evaluation and Approval	
2.	SOP on Prepration,Control,Issuance and Revision of Batch Production Records and Batch Records for cleaning	
3.	SOP on Document and Data Control	
4.	SOP on Change Control Procedure	
5.	Approval and Release of Finished goods/intermediate.	
6.	SOP on Labeling of Raw Material, Packing Material, Intermediate and Finished API	
7.	SOP on Procedure on Handling of Deviation	
8.	SOP on Batch Numbering System	
9.	SOP on Technology Transfer	
10.	SOP on Handling of Customer Complaints	
11.	SOP on Equipment Qualification and Validation of System and Process	
12.	Rectification of Errors	
13.	SOP on Procedure for Training of Employees	
14.	SOP for Personal Hygiene of Employees	
15.	Recruitment of employee	
16.	SOP for Calibration of Reactor, Receiver and Tank	
17.	SOP on Operation of Scrubber	
18.	SOP on Issuance, Usage and Disposal of Centrifuge Bags	
19.	SOP on movement of Dispensed Raw Material	
20.	SOP on Disposal of Floor Swiping	
21.	SOP on Receipt, Sampling, Testing, Approval & Rejection of Packaging Material	
22.	SOP on Calibration & Preventive Maintenance of Laboratory Instruments	
23.	SOP on Testing and Release of In-Process Samples	
24.	SOP on qualification of Analysts	
25.	SOP on Retention Samples of Critical raw Materials & Intermediates	
26.	SOP on Passwords Protection and Audit Trail for critical QC Instruments	

RISK ASSESSMENT & MITIGATION FOR PROCESS VALIDATION STUDY FOR 5-AMINO LEVULINIC ACID HCL (FINAL STAGE)

27.	SOP on Good Laboratory Practice	