QUALITY RISK ASSESSMENT & MITIGATION PLAN

FAILURE MODE EFFECT ANALYSIS FOR TOPICAL SOLUTION IN MANUFACTURING IN FACILITY

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

STANDARD ROOT CAUSE ANALYSIS								SPECIFIC PER MANUFACTURING PROCESS										
Item No	**Process Step/Input**	**Potential Failure Mode**	**Potential Failure Effects**	**Applicability**	**Severity**	**Potential Causes**	**Occurrence**	**Current Controls**	**Detection**	**Risk RPN**	**Actions Recommended**	**Resp.**	**Actions Taken**	**Severity**	**Occurrence**	**Detection**	**Risk RPN**	**COMMENTS**
	What is the process step/ Input under investigation?	In what ways does the key input go wrong?	What is the impact on the key output variables (customer requirements) or internal requirements?	Applicable / Not Applicable	How severe is the effect to the process/product?	What causes the key input to go wrong?	How likely is the cause or failure mode?	What are the existing controls that prevent either the cause or the failure mode?	How detectable is the cause/failure before next step?		What are the actions for reducing the RPN. Should have actions only on high RPN's or easy fixes.	Who's responsible to take action?	What actions have been taken and date completed?					
Material Procurement from Vendors(API, Excipients, Primary Packaging Materials)																		
1	Receipt of materials	Receipt of raw material and packing material from the unapproved source Receipt of material not as per required grade/ specifications	• Impact on process validation study. • Impact on the product stability study. • Impact on the quality of the product.	Applicable	**6**	• Material not purchased as per approved vendor list • GRN prepare without material verification. • Material verification procedure not followed.	**3**	• Procedure for "Receipt of Raw Materials In Warehouse" and "Receipt of Packing Materials In Warehouse" is in place. • Procedure is available for verification of raw material and packing material like batch information, vendor name, material grade etc.	**1**	**18**	Current controls are in place. So no action recommended.	**NA**	**NA**	**NA**	**NA**	**NA**	**NA**	**NA**	
		Receipt of material without label/ damage label, uncleaned container/ damage container, damage material	• Contamination of area • Incomplete information of material. • Contamination of material.	Applicable	**6**	• Use of uncleaned vehicle for the material transportation. • Cleaning and dedusting procedure not followed. • Material verification procedure not followed. • Mishandling of	3	•Procedure for "Receipt of Raw Materials In Warehouse" and "Receipt of Packing Materials In Warehouse" is in place. •There is well defined procedure to receipt of materials, all material should received after checking of cleaning, weight verification, batch information and physical condition as per checklist (raw & packing material receipt checklist, SOP annexure). •Containers shall be cleaned by moping	**1**	**18**	Hence current procedure for receipt of materials reveals that there could not be chances to receipt uncleaned or damaged material received. So no action recommended.	**NA**	**NA**	**NA**	**NA**	**NA**	**NA**	**NA**	**NA**

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						containers lead damage		with dry clean cloth. •Procedure is available for dedusting of received material through De-dusting tunnel in place before entry of material inside the area. •Procedure is available for damage container labelling.										
Storage of Materials																		
2	Storage of Materials	Storage of material in in-appropriate area.	Mixup	Applicable	**10**	• Material not stored as per their dedicated place.	**1**	• Procedure for "Handling and Storage of Raw and Packing Materials In Warehouse" is in place. • Storage of materials to separate area through line marking system for different stages shall be done. (Blue colour for Quarantine Area, Yellow colour for Under Test Area, Red colour for Rejected Area and Green colour for Approved Area).	**1**	**30**	Hence current procedure for storage of materials reveals that there could not be chances to storage of material in-appropriate area. So no action recommended.	**NA**	**NA**	**NA**	**NA**	**NA**	**NA**	**NA**
		Storage of material in in-appropriate condition.	• Impact on the product stability study. • Impact on the quality of the product. • Impact on the patient health and safety. • Impact on the quality of material.	Applicable		• Material not stored as per required condition.		• Procedure for "Storage Condition of Raw and Packing Materials In Warehouse" (SOP is in place. • Material shall be stored in appropriate condition to maintain required storage condition of material (cool, dry & ambient).			Hence current procedure for storage of materials reveals that there could not be chances to storage of material in appropriate condition. So no action recommended.							

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Labeling of materials																		
3	In-house labeling of materials	Wrong labeling on material.	• Impact on the quality of the product. • Impact on the identity of the product.	Applicable	**10**	• Wrong label prepare. • Material not stored as per their dedicated place.	**1**	• Procedure for "Labeling of Receipt Raw Material Containers" is in place. There is well defined procedure for preparation of label, label checking and label verification. • Procedure for "Handling and Storage of Raw and Packing Materials In Warehouse" is in place. There is well defined procedure to storage of materials to separate area through Line marking system for different stages and storage of material according to their manufacturer name, Batch No. / Lot No., Mfg. date. retest/expiry date, Grade etc.	**1**	**30**	Hence current procedure for Labeling of materials reveals that there could not be chances to wrong labeling on material. So no action recommended.	**NA**	**NA**	**NA**	**NA**	**NA**	**NA**	**NA**
Sampling of Materials																		
4	Sampling of Materials	• Sampling done in un-controlled area. • Sampling done in un-cleaned area.	• Impact on the quality of the product. • Impact on the patient health and safety. • Sample contamination. • Impact on the	Applicable	**6**	Line clearance not followed during sampling.	**3**	• Procedure for "Line-Clearance of Raw Material Sampling & Dispensing Area" is in place. There is well defined procedure for line clearance for material Sampling. • Sampling both is available. • Sampling is being performed under RLAF. • AHU's are installed in sampling area to maintained temperature, humidity and differential pressure.	**1**	**18**	Hence current procedure for sampling of materials reveals that there could not be chances to sampling done in un-controlled and un-cleaned area. So no action recommended.	**NA**	**NA**	**NA**	**NA**	**NA**	**NA**	**NA**

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		Sampling done through un-cleaned equipment.	quality of material.	Applicable		Sampling tools not cleaned.		Procedure for "Handling and Cleaning of Raw Material Sampling Aids In Warehouse" is in place. There is well defined procedure for cleaning of sampling aid.			Hence current procedure for Sampling of Materials reveals that there could not be chances to sampling done through un-cleaned equipment. So no action recommended.							
		Sampling of wrong material.		Applicable		Wrong material sampled		• Procedure for "Sampling of Non Sterile Raw Materials" and "Sampling, Testing, Release, Approval and Rejection of Packaging Materials" is in place. There is well defined procedure to sampling of material. Material is released after satisfactory results of raw material and packing material with specification. • Labeling procedure in place.			Hence current procedure for Sampling of Materials reveals that there could not be chances to sampling of wrong material. So no action recommended.							
Dispensing																		
5	Dispensing of material	Dispensing done in un-clean area.	• Impact on the quality of the product. • Impact on the patient health and safety. • Contamination of material. • Impact on the quality of raw material.	Applicable	**6**	Line clearance not followed during dispensing.	**3**	• Procedure for "Line-Clearance of Raw Material Sampling & Dispensing Area In Warehouse" is in place. There is well defined procedure for line-clearance for material dispensing. • Dispensing is being performed under RLAF.	**1**	**18**	Hence current procedure for Dispensing of material reveals that there could not be chances to dispensing done in un-clean areal. So no action recommended.	**NA**	**NA**	**NA**	**NA**	**NA**	**NA**	**NA**
		Dispensing done through un-cleaned equipment.				Dispensing tools not cleaned.		•Procedure for "Handling and Cleaning of Dispensing Tools In Warehouse" is in place. There is well defined procedure for cleaning of dispensing tools. •Procedure for "Line-Clearance of Raw			Hence current procedure for Dispensing of material reveals that there could not be chances to dispensing done through un-cleaned							

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								Material Sampling & Dispensing Area In Warehouse" is in place. There is well defined procedure for line-clearance for material dispensing.			equipment. So no action recommended.							
		Dispensing done through un-calibratated balance.				Balance calibration not done as per schedule.		Procedure for "Operation, Cleaning, Verification and Calibration of Electronic Weighing Balances" and "Operation, Cleaning, Verification and Calibration of Weighing Balance" is in place. There is well defined procedure to verification and calibration of weighing Balance.			Hence current procedure for Dispensing of material reveals that there could not be chances to dispensing through un-calibratated balance. So no action recommended.							
		Wrong material dispensed				Dispensing not done as per procedure		Procedure for "Dispensing of Raw Materials to Production" is in place. There is well defined procedure for dispensing of material, Batch dispensing slip and identification slip generated through SAP system.			Hence current procedure for Dispensing of material reveals that there could not be chances to wrong material dispensed. So no action recommended.							
Manufacturing and Packing																		
6	Manufacturing, filling and packing.	• Parameters are not defined. • Uncalibrated instrument. • Unqualified equipment. • Uncleaned equipment. • Environmental conditions not meet	• Impact on process validation study. • Impact on cleaning validation study. • On the product stability study. • Impact on the quality of the product. • Impact on the patient health and	Applicable	**10**	• Product manufactured with un-defined parameters. • Uncalibrated instrument. • Unqualified equipment used. • Cleaning method not available. • Environmental conditions not meet.	**1**	•Once new product is received, same shall be preceded through change control procedure. •For new product, based on technology transfer documents, plant documents shall be prepared (like BMR, BPR, STS, STP etc.). • New product is manufactured based on the parameters and process flow described in Master Formula Record. •BMR is prepared based on the Master	**1**	**10**	Hence current procedure for Shifting of material, granulation, drying, sizing & milling, blending, compression, coating and packing reveals that there could not be chances to undefined parameter, uncalibrated instrument, unqualified equipment, Uncleaned equipment and deviation of environmental	**NA**	**NA**	**NA**	**NA**	**NA**	**NA**	**NA**

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		(temperature and RH)	safety. • Cross contamination			• Untrained man power.		Formula Record. •Process validation shall be performed for new product. •Stability study shall be performed for new product. •Calibration of instrument performed as per their schedule (calibration planner). •Equipment qualification activity performed at time of installation. •Re-qualification of equipment shall be performed as per their schedule (equipment planner). •Qualified equipment is used for product manufacturing. •Preventive maintenance of equipment shall be performed as per preventive maintenance planner. •Line clearance procedure is in place. •All new API considered for cleaning validation study, on the basis of MACO value cleaning study evaluated. If product comes under worst case study, then cleaning validation study shall be performed. •There is a Procedure for Monitoring of "Temperature, Relative Humidity & Differential Pressure" in place during manufacturing. •There is cleaning SOP of all equipment in place.			condition. So no action recommended.							

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								•Handling of all equipment SOP's is in place. •There is well defined procedure for Monitoring of "Temperature & Relative Humidity" .Temperature and Relative Humidity of respective areas shall be recorded initially, at every 4 hours & after Breakdown. •There is procedure for Monitoring of temperature & relative humidity during process in BMR & BPR at every 1 hour. •After completion of blending, compression, coating and packing, sample shall sent to QC for analysis. After satisfactory result of blend sample, batch proceeds for next stage. •If any failure observed during process, same shall be handled through deviation/ incident.										
Batch Release																		
7	Batch Release	Batch released without FG analysis.	• Impact on the quality of the product. • Impact on the patient health.	Applicable	**10**	Batch released without FG analysis.	**1**	• There is a Procedure for Monitoring of "Approval and Release of Finished Products for Sale / Distribution" in place. • After Completion of Batch, the Batch Production and Control Record (BPCR) shall be reviewed and finalized for its completion by the Production Officer / Executive as per the checklist. Check the BPCR for various entries at	**1**	**10**	Hence current procedure for Batch Release reveals that there could not be chances to batch can be released without FG results. So no action recommended.	**NA**	**NA**	**NA**	**NA**	**NA**	**NA**	**NA**

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								manufacturing and packing stage, reconciliation of material and product yield at the respective stages of the operation and batch shall be transferred to QA terminal inspection room for inspection purpose. • QA shall receive the batch for inspection as per SOP, "Terminal Inspection and Transfer of Finished Goods". • QA shall review the Batch Production and Control Record (BPCR) as per the checklist. • QA shall ensure the Completion of the QMS documents, COA and Batch Production and Control Record (BPCR) before release. • Batch shall release through SAP system for Sale or distribution. • Representative sample of batch shell be provided to QC for testing.										

Rating Scale - Severity
10= Hazardous without warning/Regulatory Issue
6= Loss of function
3= Minor defect
1= Little or no effect

Rating Scale - Occurrence
10= Almost inevitable Time Period- Once per week
6= Frequent/Moderate failure Time Period- Once every 3 months
3= Occasional failures Time Period- Once every 1-3 years
1= Failure unlikely

Rating Scale - Detection
10= Almost undetectable
6= Low probability of detection
4= Reasonable probability of detection
3= High probability of detection
1= Almost certain detection

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Remarks:

1.0 RPNs greater than 120 should be assessed for improvement actions. Any RPNs greater than 120 that cannot/ will not be reduced will need to be agreed with Novartis.

2.0 Recalculate the RPN this should only be done after the implementation of the action.

Prepared By	Checked By	Approved By
Sign & Date	Sign & Date	Sign & Date