QUALITY RISK ASSESSEMENT AND MITIGATION PLAN

QRA No.:

Name of Facility/Equipment/Utility/System/Activity/Procedure **Unit Operation**: **Description:** The objective of the risk assessment is to evaluate the risk associated during the Process Validation Batch of Ciprofloxacin Hydrochloride Eye Drops BP 5 ml	**Date of Quality Risk Assessment:**

Sr. No.	Item/ Function	Potential Failure Mode (Failure Mode)	Potential Effect of Failure (Effect)	Potential Cause/ Mechanism of Failure	Current Control	Reference	S	O	D	Risk Priority Number (S*O*D)	Recommend-ended Actions (if any)	Post Risk			
												S	O	D	RPN S*O*D
1.	Before start of Dispensing	➢ Unapproved material gets dispense. ➢ Failed material gets dispense.	➢ Unapproved dispense material leads to product contamination. ➢ Fails to achieve the safety, efficacy and quality of product.	➢ Lack of Qualified source of API and excipient. ➢ Lack of testing specification. ➢ Lack of vendor management procedure.	➢ Qualification procedure is in place and also line clearance check point is available in BMR to ensure approved & release materials are available for dispensing. ➢ Testing specifications are in place. ➢ Vendor management procedure is in place.	Approved Vendor List (AVL) & Batch manufacturing record(BMR)	4	1	1	4	NA	NA	NA	NA	NA

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2.	At the time of Dispensing	➢ Fails to dispense the required quantity. ➢ Dispense material get contaminate.	➢ Inadequate result due to improper quantity dispensing and improper testing outcomes (OOS). ➢ Contamination of the area leads to product failure	➢ Due to selection of wrong capacity weighing balance. ➢ Due to lack of operational and calibration procedure of weighing balance. ➢ Due to improper environmental conditions. ➢ Due to lack of the operation and cleaning procedure for dispensing tools. ➢ Due to lack of procedure for dispensing ➢ Material dispensed by untrained personnel. ➢ No cross check during dispensing ➢ Unapproved/rejected material dispensed.	➢ Selection of weighing balance is depending on balance capacity and quantity of material. ➢ SOP is in place for operation and calibration procedure of weighing balances. ➢ Environmental condition check point is in place in line clearance checklist. ➢ Uses and cleaning of dispensing tool SOP is in place. ➢ Dispensing of API, excipient and PM SOPs are in place. ➢ Training has been imparted to concerned personnel's. ➢ In dispensing activity done by and checked by provision is available in BMR and verification done by before compounding. ➢ Check point is in place in BMR to check material is approved/released.	Operation, Cleaning, Calibration and Verification of Weighing Balances, Dispensing and issuance of RM and Dispensing of PM	3	2	1	6	NA	NA	NA	NA	NA

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3.	Component preparation	➢ Failure of Component preparation and sterilization.	➢ Improper cleaning and sterilization of component leads to contamination in product.	➢ Due to lack of unqualified sterilizer. ➢ Lack of component cleaning and component sterilization procedure. ➢ Steam lack or utility cut off during sterilization phase. ➢ Articles cleaning and sterilization by untrained person. ➢ Load pattern may not follow. ➢ Selection of wrong recipe. ➢ Sensor malfunctioning. ➢ Due to sterilization, material hold time cross	➢ Qualification of sterilizer has been completed. ➢ Component cleaning and sterilization SOP is in place. ➢ If the steam lack occurs during sterilization phase, alarm will generate and same shall be acknowledged by operator and cycle will be considered as abort. ➢ Training has been imparted to all concerned persons. ➢ Validated load patterns should be refers before start of activity as per respective SOP. ➢ Validated recipe and parameter has been set in autoclave PLC and controlled through password. ➢ Defined frequency in place for schedule calibration, Preventive maintenance and validation status. ➢ Sterilized hold time has been established and actual material hold time is track in BMR.	Operation and Cleaning of Autoclave Cum Bung Processer	3	2	1	6	NA	NA	NA	NA	NA

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4.	During Filter Integrity testing	➢ Failure in filter integrity	➢ Improper filter integrity gets direct impact on sterility of product.	➢ Unqualified equipment used. ➢ Lack of cleaning and operational SOP. ➢ Filter integrity activity performed by untrained person. ➢ No cross checks provision for filter integrity test report.	➢ Qualification of filter integrity machine has been completed. ➢ Cleaning and Operational SOP is in place ➢ Training has been imparted to all concerned persons and user ID given after completion of training. ➢ Filter integrity test report (Pre and Post) shall be checked by production person and verified by QA person.	Operation of Integrity Tester	5	1	1	5	NA	NA	NA	NA	NA

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5.	During compounding	➢ Failure in Batch manufacturing	➢ Due to improper manufacturing procedure leads to Bioburden may increase more than specification. ➢ Unexpected outcome like yield and concentration of product leads to product failure.	➢ Compounding procedure not available. ➢ Due to lack of calibration, preventive maintenance, operational and cleaning procedures. ➢ Qualification of vessel system not available. ➢ Unsterilized and unclean equipment may use. ➢ Inadequate cleaning or equipment's difficult to clean. ➢ Compounding activity handle by untrained person. ➢ Due to lack of clean equipment hold time may cross. ➢ Micro growth due to utility supply such as WFI, Compressed air and nitrogen.	➢ Detail, compounding procedure is in place in BMR. ➢ Vessel calibration, preventive maintenance, operational and cleaning procedure are in place. ➢ Qualification of vessels system is completed. ➢ In line clearance of compounding activity ensure the sterilization vessels shall be mention in BMR. ➢ Vessels CIP, SIP procedure are qualified and SOP is in place. ➢ Training has been completed for all concerned persons. ➢ CIP hold time has been established. ➢ Water system compressed air and Nitrogen are qualified.	Load Cell Verification and Calibration of Manufacturing Vessels CIP of Mixing vessel, Mixing mobile vessel, holding vessel	5	3	1	15	Sample shall be collected for QC analytical and QC microbiological to check the impact of CPP on CQA. CPP and CQA shall be evaluated after completion of process validation activity.	5	1	1	5

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6.	Filtration activity	➢ Failure in filtration of bulk solution	➢ Filtrate is not sterile leads to microbial growth. ➢ Improper filtration leads to contamination in product.	➢ Lack of procedure for sterilization of filter. ➢ Lack of procedure to check the filter integrity. ➢ Due to improper training to concerned persons. ➢ Lack of filtration procedures.	➢ SOP is in place for SIP of vessel system along with product transfer line. ➢ Filter integrity procedure is in place check points is available. ➢ Training procedures is in place. ➢ Filtration procedure is available in BMR.	SIP for Mixing Vessel/ MMV/ Holding Vessel/Buffer Vessel	5	3	1	15	Sample shall be collected for QC analytical and QC microbiological to check the effect of filtration	5	1	1	5

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7.	Filling operation	➢ Failure in filling	➢ Improper filling may result in volume variation. ➢ Improper filling activity may leads to contamination.	➢ Lack of qualification procedure. ➢ Lack of cleaning and operational procedure. ➢ Unsterile parts or article may use filling operation. ➢ Lack of environmental condition for filling. ➢ Improper handling of aseptic intervention may lead to product contamination. ➢ Operation handled by untrained and unqualified person. ➢ Due aseptic interventions ➢ Due filling duration.	➢ Qualification of filling machine has been completed. ➢ SOP for filling machine cleaning and operation is in place. ➢ Sterilization procedure for machine parts loads is in place. ➢ Filling has been carried out under class A condition (Unidirectional air flow area). ➢ Aseptic intervention has been performed as per media fill protocol and BMR. ➢ Operational training has been done for all concerned persons for aseptic. ➢ Filling duration is mentioned in BMR and same was simulated in media fill.	Operation & cleaning of Filling, Dropper fixing & Screw capping machine	5	2	2	20	If in case any unexpected intervention will happen during batch processing same shall be documented and handled through QMS.	5	1	1	5

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8.	Dropper Fixing and Screw capping operation	➢ Failure in Dropper fixing and screw capping	➢ Improper sealing is not providing leak proof sealing to the vials. ➢ Failure in sealing activity leads to product contamination.	➢ Unqualified equipment may use. ➢ Operational and cleaning procedure may not available. ➢ Untrained person may operate machine. ➢ Lack of leak test procedure for vials.	➢ Qualification for filling machine has been completed. ➢ Operational and cleaning SOP is in place. ➢ Training has been imparted to concerned persons. ➢ SOP is in place for leak test.	Operation & cleaning of Filling, Dropper fixing & Screw capping machine	5	1	1	5	NA	NA	NA	NA	NA

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9.	Labeling activity	➢ Improper labeling in product.	➢ Improper labeling leads to adverse effect on patient health.	➢ Lack of SOP of labeling machine. ➢ Lack of line clearance and physical verification. ➢ Lack of proper dispensing of packing material.	➢ SOP of labeling machine is in place. ➢ Training imparted to IPQA person for line clearance and proof check. ➢ SOP of Packing material dispensing is in place.	Dispensing and Issuance of packing material	1	1	5	5	NA	NA	NA	NA	NA

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10.	Secondary packing activity	➢ Improper packing of the product.	➢ Improper packing leads to adverse effect on patient health.	➢ Lack of SOP of carton packing. ➢ Lack of line clearance and physical verification. ➢ Lack of proper dispensing of packing material.	➢ SOP of operation & cleaning of Hi-cart carton packing machine is in place. ➢ Training imparted to IPQA person for line clearance and proof check. ➢ SOP of packing material dispensing is in place.	Operation and cleaning of Hi-cart cartooning machine	1	1	5	5	NA	NA	NA	NA	NA

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11.	Storage condition in FG	➢ Improper storage space and conditions in finished goods store.	➢ Chance of product mix-up due to lack of dedicated space. ➢ Chance of product degradation due to irrespective storage condition.	➢ Lack of SOP. ➢ Lack of dedicated storage space. ➢ Due to environmental condition not maintain.	➢ SOP for handling of finished goods is in place. ➢ Dedicated storage space is available. ➢ Environmental condition is monitoring through BMS.	Handling of finished goods	1	1	5	5	NA	NA	NA	NA	NA

Where: S=Severity; O=Occurrence Probability; D=Detection; Risk category 1-25 RPN is Low risk, 26-50 RPN is Medium Risk, 51-125 RPN is High Risk.

Name of Facility/Equipment/Utility/System/Activity/Procedure/Unit Operation: Process Validation Batch of Ciprofloxacin Hydrochloride Eye Drops BP 5 ml	**Date:** NA

S. No.	Recommended Action	Responsible Person	Target Date of Completion
1.			
2.			

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CAPA:
If required, mention CAPA No.:

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

QUALITY RISK ASSESSEMENT AND MITIGATION SUMMARY REPORT

Name of Facility/Equipment/Utility/System/Activity/Procedure:	Process Validation Batch of Ciprofloxacin Hydrochloride Eye Drops BP 5 ml

Verification of Action Plan: NA

Remarks (if any): The entire above failure mode and their Severity, Occurrence, Detection rating done and RPN No. is found between 1-25. Hence Risk is detected as low which is acceptable.

Verified By
QA
Sign & Date

Approved By
Head QA
Sign & Date