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QUALITY ASSURANCE DEPARTMENT

QUALITY RISK ASSESSEMENT AND MITIGATION PLAN (FMEA TOOL) RISK ASSESSMENT

QRA No.:

Name of Facility/Equipment/Utility/System/Activity/Procedure/ **Unit Operation:** Cyclosporine Eye Drops	**Date Of Quality Risk Assessment:**

S.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
AREA:															
1.	**Dispensing & Sampling**	Cyclosporine Got exposed	➢ Probability of Cross-Contamination of Cyclosporine with other Raw materials being Sampled/ dispensed in same facility.	➢ If sampling & dispensing activity is carried out for more than one raw material at a time. ➢ Post cleaning activity not performed after molecule change over. ➢ Sampling/dispensing activity not performed by trained personnel. ➢ Dedicated tools not provided for sampling & dispensing activity. ➢ Approved gowning procedure not available.	➢ Sampling/dispensing activity is performed only for one raw material at a time. ➢ Post cleaning procedure in place for sampling/ dispensing area during API molecule change over ➢ Sampling/dispensing activity is performed by trained personnel in the presence of QA personnel after QA line clearance. ➢ Equipment Qualification of RLAF performed with respect to Air flow pattern (vertical flow from top) and reverse flow towards the RLAF return riser to protect the personnel during sampling/ dispensing operation.	➢ SOP No. ➢ BMR	10	7	4	280	PAPR snoods to be used. Ensure that personnel involved in dispensing of Cyclosporine are wearing PAPR gowning (separate gowning) Dedicated Sampling/ Dispensing tools to be used during sampling & dispensing of cyclosporine. Used sampling & dispensing tools shall be cleaned immediately after Sampling/ Dispensing activities.	7	7	1	49

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												S	O	D	RPN S*O*D
		Direct exposure to Personnel	➢ Probability of Cyclosporine exposure to personnel involved in activity.	➢ Sampling/Dispensing Activity Not Done By Trained Personnel ➢ Separate gowning procedure not available	➢ Sampling/Dispensing activity is performed by trained personnel in the presence of QA Personnel after QA line clearance ➢ Protective gowning procedure is available with secondary gowning over the existing uniform and snood / face mask also eyes are protected with goggles and hence no part of the body is exposed.		10	7	4	280	PAPR gowning (separate gowning) Decontaminati on is performed with procedure using 2.5% sodium hypochlorite solution Decontaminati on of area is performed with procedure using 2.5% sodium hypochlorite solution	7	7	1	49

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												S	O	D	RPN S*O*D
	Riser filter cleaning	➢ Riser filter not cleaned properly	➢ Cross contamination	➢ Filter cleaning area not available ➢ Personnel doing cleaning not Trained ➢ SOP of filter cleaning not followed	➢ Filter cleaning area available ➢ Training to be provided ➢ SOP of filter cleaning available	➢ SOP No.:	7	7	1	49 Low category and Risk accepted	Filters to be decontaminated by 2.5% of Sodium Hypochlorite solution	NA	NA	NA	NA

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												S	O	D	RPN S*O*D
2	**Manufacturing Stage (Bulk preparation)**	➢ Impact on Product Quality ➢ Impact of Cyclosporine on Personnel health	➢ Probability of Cross-Contamination of Cyclosporine product with other general product being manufactured in the same area. ➢ Probability of Cyclosporine exposure to personnel involved in manufacturing activity.	➢ If Post cleaning activity after Production of Cyclosporine product not in place or inadequate. ➢ Cleaning procedure is not validated. ➢ If manufacturing activity is performed by untrained personnel. ➢ Other general product material can contaminate the cyclosporine products while manufacturing	➢ Manufacturing activity performed under controlled. Environmental condition of temperature, RH & Pressure differential. ➢ Protective gowning procedure is available with secondary gowning over the existing uniform and snood /face mask. Also eyes are protected with goggles and hence no part of the body is exposed. ➢ Cyclosporine's Product manufacturing shall be limited to specific manufacturing Area.	➢ SOP No.	10	7	4	280	PAPR gowning (separate gowning) to be used. Decontamination is performed with procedure using 2.5% sodium hypochlorite solution Decontamination of area is performed with procedure using 2.5% sodium hypochlorite solution	7	7	1	49

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												S	O	D	RPN S*O*D
	Riser filter cleaning	➢ Riser filter not cleaned properly	➢ Cross contamination	➢ Dedicated filter cleaning area not available ➢ Personnel doing cleaning not Trained ➢ SOP of filter cleaning not followed	➢ Dedicated area available ➢ Training to be provided ➢ SOP of filter cleaning available	➢ SOP No.:	7	7	1	49 Low category and Risk accepted	Filters to be decontaminated by 2.5% of Sodium Hypochlorite solution	NA	NA	NA	NA

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												S	O	D	RPN S*O*D
3.	**Bulk Filtration**	Failure of Pre and Post Bubble Test Differential pressure of filtration area with respect to Aseptic Area Corridor is not within specified Range Holding vessels, filters and Accessories are not cleaned and sterilized. Environmental condition in filtration area is not maintained. Dedicated filtration assembly is not used	Contamination Cross contamination Loss of efficacy, Productivity	Fail to follow SOP Inadequate Training Other general product material can contaminate the cyclosporine products while manufacturing Other general product material can contaminate the cyclosporine products while manufacturing.	Line clearance Procedures SOP Trainings Cleaning procedures Dedicated filtration assembly is used with tubing.	BMR Line Clearance procedures	10	4	1	40 Low category and Risk accepted	(Not Applicable) Since RPN is 40 and it is in the low risk category.	NA	NA	NA	NA

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S.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
	Riser filter cleaning	➢ Riser filter not cleaned properly	➢ Cross contamination	➢ Dedicated filter cleaning area not available ➢ Personnel doing cleaning not Trained ➢ SOP of filter cleaning not followed	➢ Dedicated area available ➢ Training to be provided ➢ SOP of filter cleaning available	➢ SOP No.:	7	7	1	49 Low category and Risk accepted	NA	**NA**	**NA**	**NA**	**NA**
4.	**Sterilization process**	Line clearance failure Improper cleaning, drying and sterilization of equipments Improper working of LAF Improper cleaning of Autoclave	Contamination Cross-contamination Loss of efficacy	Fail to follow SOP Inadequate Training	Line clearance Procedures SOP Trainings	BMR Line Clearance procedures,	10	4	1	40 Low category and Risk accepted	(Not Applicable) Since RPN is 40 and it is in the low risk category.	NA	NA	NA	NA
5.	**Processing of Machine Parts and Accessories.**	Line clearance failure or Cleaning not done as per the check-list within the SOP Improper cleaning and sterilization of equipment and Accessories	Contamination Cross-contamination Loss of efficacy, Productivity	Fail to follow SOP In-adequate Training Cleaning procedures	Line clearance Procedures SOP Trainings Decontamination of Assemblies (Filling & Filtration Assembly).	BMR Line Clearance procedures,	10	4	1	40 Low category and Risk accepted	Decontaminati on g of area is performed with procedure using 2.5% sodium hypochlorite solution	NA	NA	NA	NA

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QRA No.:

Name of Facility/Equipment/Utility/System/Activity/Procedure/ **Unit Operation:** Cyclosporine Eye Drops	**Date Of Quality Risk Assessment:**

S.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
6.	**Preparation of Garments**	Line clearance failure Improper cleaning and sterilization of equipment and Accessories	Contamination Cross contamination	Fail to follow sop In-adequate Training	Line clearance Procedures SOP Trainings	BMR Line Clearance procedures,	10	4	1	40 Low category and Risk accepted	Decontaminati on is performed with procedure using 2.5% sodium hypochlorite solution	NA	NA	NA	NA
7.	**Bulk transfer to Aseptic area**	➢ Material may got exposed	➢ Probability of Cross-Contamination of Cyclosporine Products with other general products being manufactured in the same facility. ➢ Probability of Cyclosporine exposure to personnel involved in manufacturing activity.	➢ If Post cleaning activity after Production of Cyclosporine product not in place or inadequate. ➢ Cleaning procedure is not validated. ➢ If manufacturing activity by untrained personnel	➢ This activity is performed under controlled environmental condition of temperature, RH & Pressure differential. ➢ Protective gowning procedure is available with secondary gowning over the existing uniform and snood / face mask also eyes are protected with goggles and hence no part of the body is exposed. ➢ Cleaning validation to be performed considering (Cyclosporine) as a marker on the basis of its Solubility, Potency & Toxicity.	➢ BPCR	10	7	4	280	PAPR gowning (separate gowning) to be used. Decontaminati on is performed with procedure using 2.5% Sodium Hypochlorite solution.	7	7	1	49

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S.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
	Riser filter cleaning	➢ Riser filter not cleaned properly	➢ Cross contamination	➢ Dedicated filter cleaning area not available ➢ Personnel doing cleaning not Trained ➢ SOP of filter cleaning not followed	➢ Dedicated area available ➢ Training to be provided ➢ SOP of filter cleaning available		7	7	1	49 Low category and Risk accepted	NA	NA	NA	NA	NA

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S.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
8.	**Filling & Sealing**	Line clearance failure Environmental conditions failure Unclean equipments Improper gowning Filling Nozzles are not calibrated Improper working of LAF Inadequate Media settle plates Pre-sterilized Vials, Dropper and screws caps not release from QC. Machines Parts and other Aids used in Aseptic filling is not sterilized. Filtered solution is not kept under LAF	➢ Probability of Cross-Contamination of Cyclosporine Products with other general product being manufactured in same facility. ➢ Probability of Cyclosporine exposure to personnel involved in manufacturing activity.	➢ If Post cleaning activity after Production of Cyclosporine product not in place or inadequate. ➢ Cleaning procedure is not validated. ➢ If manufacturing activity is performed by untrained personnel ➢ HVAC system is not provided in area	➢ Product inspection activity performed under controlled environmental condition of temperature, RH & Pressure differential. ➢ Protective gowning procedure is available with secondary gowning over the existing uniform and snood / face mask. Also eyes are protected with goggles and hence no part of the body is exposed. ➢ HVAC System is qualified. Line clearance Procedures, SOP Trainings	➢ BPCR ➢ HVAC protocol	7	7	1	49	Low risk	NA	NA	NA	NA

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												S	O	D	RPN S*O*D
		Non-Viable particle count is not performed before line set up and the results are not within acceptance criteria. Line clearance failure Environmental conditions failure Unclean equipments Improper working of LAF Inadequate Media settle plates	Contamination Cross contamination. Loss of efficacy, Productivity	Fail to follow sop In-adequate Training	➢ During Product Change over, Swab & rinse analysis is carried out as per validated analytical method. ➢ Product inspection is performed by trained personnel in the presence of QA personnel after line clearance. ➢ SOP for Handling & Decontamination of In-Process rejection of Cyclosporine to be implemented with next campaign of production ➢ Also Inspected Cyclosporine Products are kept in double lined poly bags with proper tighten with tie.	BMR As per SOP	10	4	1	40 Low category and Risk accepted	(Not Applicable) Since RPN is 40 and it is in the low risk category.	NA	NA	NA	NA

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												S	O	D	RPN S*O*D
	Riser filter cleaning	➢ Riser filter not cleaned properly	➢ Cross contamination	➢ Dedicated filter cleaning area not available ➢ Personnel doing cleaning not Trained ➢ SOP of filter cleaning not followed	➢ Dedicated area available ➢ Training to be provided ➢ SOP of filter cleaning available	➢ SOP No.:	7	7	1	49 Low category and Risk accepted	NA	NA	NA	NA	NA
9.	**Visual inspection**	Contamination Cross contamination	Contamination Cross contamination Loss of efficacy, Productivity	Fail to follow SOP (Standard Procedure) In-adequate Training Qualification of Visual Inspector not done	Line clearance Procedures, SOP No.-QAH/012 SOP Trainings Visual Inspector as per SOP	BMR As per SOP	10	4	1	40 Low category and Risk accepted	(Not Applicable) Since RPN is 40 and it is in the low risk category.	NA	NA	NA	NA
		Uncleaned Area/ Waste bin.	1) Contamination 2) Cross Contamination 3) Dust Problem 4) Affect Product efficacy 5) GMP Deviation	1) Fail to follow SOP 2) Inadequate training 3) Failure of Line clearance procedure	➢ Line clearance Procedures, SOP No.-QAH/012 ➢ Follow SOP ➢ 3) Provide Training	➢ BPR ➢ As per SOP	7	7	1	49 Low category and Risk accepted	NA	NA	NA	NA	NA
		Personnel doing inspection not qualified	➢ Defective vials not get rejected	➢ SOP not followed	➢ SOP available	As per SOP	7	7	1	49 Low category and Risk accepted	NA	NA	NA	NA	NA

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												S	O	D	RPN S*O*D
10.	**Cleaning**	➢ Cleaning not done by trained personnel	➢ Contamination & Cross-contamination	➢ Fail to follow Area Cleaning SOP ➢ Inadequate training of Personnel ➢ Improper Line Clearance	➢ During Product Change over, Swab & rinse analysis is carried out as per validated analytical method. ➢ Follow Cleaning SOP ➢ Training to be provided ➢ Follow SOP of Line Clearance	➢ BPR ➢ As per SOP	7	7	1	49 Low category and Risk accepted	NA	NA	NA	NA	NA
EQUIPMENTS															
1.	**Sampling & Dispensing Tools**	➢ Improper Cleaning & Improper Sterilization	➢ Contamination & Cross Contamination	➢ SOP of cleaning & sterilization not followed ➢ Cleaning validation not performed ➢ Cleaning verification results of Swab & Rinse not verified ➢ Untrained personnel	➢ Training on Cleaning SOP ➢ Cleaning validation to be performed ➢ Sampling to be done after verification of Swab & Rinse results	SOP No.:	7	7	1	49 Low category and Risk accepted	Decontaminati on is performed with procedure using 2.5% sodium hypochlorite solution	NA	NA	NA	NA
		➢ Cleaned Sampling & Dispensing tool not used within specified Hold time period	➢ Microbial contamination	➢ Cleaned equipment & Dirty equipment hold time not performed	➢ Cleaned & Dirty hold time to be performed for Sampling & Dispensing tools ➢ Labeling to be done for Hold time period for certain tools	➢ BMR ➢ SOP No.:	7	7	1	49 Low category and Risk accepted	NA	NA	NA	NA	NA

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												S	O	D	RPN S*O*D
		➢ Dedicated tools not used	➢ Cross contamination	➢ Improper training	➢ Dedicated tools to be provided for Cyclosporine	➢ BMR ➢ As per SOP	7	7	1	49 Low category and Risk accepted	NA	NA	NA	NA	NA
		➢ Dedicated tool box & area not provided for Cyclosporine	➢ Contamination	➢ Dedicated area not provided ➢ Identification not provided on tool box	➢ Dedicated tool box to be provided for Cyclosporine	➢ BMR ➢ As per SOP	7	7	1	49 Low category and Risk accepted	NA	NA	NA	NA	NA
		➢ Controlled environment not provided for tool storage	➢ Uncontrolled environment may lead to microbial growth	➢ Temperature & RH not maintained	➢ Area should be qualified	➢ As per SOP	7	7	1	49 Low category and Risk accepted	NA	NA	NA	NA	NA
2.	**RLAF & LAF**	➢ Improper Cleaning	➢ Contamination	➢ SOP of cleaning not followed ➢ Cleaning verification results of Swab & Rinse not verified ➢ Untrained personnel	➢ Training on Cleaning SOP ➢ Sampling to be done after verification of Swab & Rinse results	➢ As per SOP	7	7	1	49 Low category and Risk accepted	NA	NA	NA	NA	NA
		➢ Line clearance	➢ Contamination	➢ SOP not followed	➢ Training on Line Clearance SOP	➢ BMR	7	7	1	49 Low category and Risk accepted	NA	NA	NA	NA	NA
		➢ Preventive maintenance not done	➢ Breakdown during process	➢ Preventive maintenance schedule not followed ➢ SOP not followed.	➢ Preventive maintenance to be done as per schedule	➢ Preventive Maintenanc e Schedule ➢ As per SOP	7	7	1	49 Low category and Risk accepted	NA	NA	NA	NA	NA
		➢ LAF & RLAF not qualified	➢ Breakdown during process ➢ Contamination	➢ Equipment not qualified as per schedule ➢ VMP not followed	➢ VMP available ➢ Qualification schedule available	➢ Qualification documents ➢ VMP ➢ As per SOP	7	7	1	49 Low category and Risk accepted	NA	NA	NA	NA	NA

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												S	O	D	RPN S*O*D
		➢ Pressure difference among filters not maintained	➢ Air velocity got disturbed	➢ Filter leakage ➢ Choking of Filters ➢ Pressure gauges not calibrated	➢ SOP of Operation of LAF& RLAF to be followed ➢ Pressure Gauges to be calibrated as per schedule	➢ As per SOP	7	7	1	49 Low category and Risk accepted	NA	NA	NA	NA	NA
		➢ UPS failure	➢ Breakdown during Process failure	➢ Electrical failure ➢ Overload on UPS	➢ Additional UPS available	➢ As per SOP	7	7	1	49 Low category and Risk accepted	NA	NA	NA	NA	NA
		➢ Velocity got disturbed	➢ Contamination	➢ Filter choking	➢ Online Anemometer available ➢ Qualification done as per schedule	➢ Performance qualification ➢ As per SOP	7	7	1	49 Low category and Risk accepted	NA	NA	NA	NA	NA
3.	**Silicon Tubing**	➢ Not cleaned & Sterilized properly	➢ Cross-contamination ➢ Contamination	➢ Untrained personnel	➢ Dedicated Silicon Tubes available ➢ Additional Silicon Tubes available	➢ As per SOP	7	7	1	49 Low category and Risk accepted	Decontaminati on is performed with procedure using 2.5% sodium hypochlorite solution.	NA	NA	NA	NA
4.	**Cartridge Filters**	➢ Not properly cleaned & sterilized ➢ Fail in integrity	➢ Cross-contamination ➢ Contamination & cross-contamination ➢ Microbial contamination	➢ Untrained personnel	➢ Dedicated Silicon Tubes available ➢ Additional Silicon Tubes available	➢ BMR ➢ As per SOP	7	7	1	49 Low category and Risk accepted	Decontaminati on is performed with procedure using 2.5% sodium hypochlorite solution	NA	NA	NA	NA

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												S	O	D	RPN S*O*D
5.	**Compounding Vessel**	➢ Not cleaned & sterilized properly	➢ Cross-contamination	➢ Untrained personnel ➢ Fail to follow SOP	➢ Cleaning SOP available ➢ Training given	➢ BMR ➢ As per SOP	7	7	1	49 Low category and Risk accepted	NA	NA	NA	NA	NA
6.	**Holding Vessel With High Shear Homogenizer**	➢ Not cleaned & sterilized properly	➢ Cross-contamination	➢ Untrained personnel ➢ Fail to follow SOP	➢ Cleaning SOP available ➢ Training given	➢ BMR ➢ As per SOP	7	7	1	49 Low category and Risk accepted	NA	NA	NA	NA	NA
7.	**Holding vessel cleaning & Filter Cleaning**	➢ Not cleaned & sterilized properly	➢ Cross-contamination	➢ Untrained personnel ➢ Fail to follow SOP	➢ Cleaning SOP available ➢ Training given	➢ BMR ➢ As per SOP	7	7	1	49 Low category and Risk accepted	NA	NA	NA	NA	NA
8.	**CIP- SIP Module**	➢ By pass system	➢ Microbial contamination	➢ Untrained personnel ➢ Fail to follow SOP	➢ Training given ➢ Rinse sample report to be verified	➢ BMR ➢ As per SOP	7	7	1	49 Low category and Risk accepted	NA	NA	NA	NA	NA
9.	**Three piece filling machine**	➢ Preventive maintenance not done	➢ Break down during process	➢ Untrained personnel ➢ Fail to follow Preventive maintenance schedule	➢ Preventive maintenance schedule available ➢ Training given	➢ BMR ➢ As per SOP	7	7	1	49 Low category and Risk accepted	NA	NA	NA	NA	NA
		➢ Nitrogen system failure	➢ Microbial growth in product	➢ Preventive maintenance not done ➢ Untrained personnel	➢ Preventive maintenance schedule available ➢ Training given	➢ Performance qualification	7	7	1	49 Low category and Risk accepted	NA	NA	NA	NA	NA
		➢ Compressed air system failure	➢ Filling not proper may lead to spillage	➢ Preventive maintenance not done ➢ Untrained personnel	➢ Preventive maintenance schedule available ➢ Training given	➢ Performance qualification	7	7	1	49 Low category and Risk accepted	NA	NA	NA	NA	NA

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QUALITY ASSURANCE DEPARTMENT

QUALITY RISK ASSESSEMENT AND MITIGATION PLAN (FMEA TOOL) RISK ASSESSMENT

QRA No.:

Name of Facility/Equipment/Utility/System/Activity/Procedure/ **Unit Operation:** Cyclosporine Eye Drops	**Date Of Quality Risk Assessment:**

S.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
		➢ Accessories not cleaned & sterilized properly	➢ Cross-contamination	➢ Untrained personnel	➢ SOP of cleaning available	➢ BMR ➢ As per SOP	7	7	1	49 Low category and Risk accepted	Decontamination is performed with procedure using 2.5% sodium hypochlorite solution	NA	NA	NA	NA
10.	**Pre filter& final filter (Mfg.)**	➢ Not properly cleaned & sterilized	➢ Contamination & cross-contamination	➢ Untrained personnel	➢ SOP of cleaning available	➢ BMR ➢ As per SOP	7	7	1	49 Low category and Risk accepted	Decontamination is performed with procedure using 2.5% sodium hypochlorite solution	NA	NA	NA	NA
		➢ Fail in integrity	➢ Microbial contamination	➢ Ruptured filter	➢ Additional filter available	➢ As per SOP	7	7	1	49 Low category and Risk accepted	NA	NA	NA	NA	NA
11.	**pH Meter**	➢ Not cleaned properly	➢ Cross contamination	➢ Person not trained ➢ Fail to follow SOP	➢ SOP available	➢ As per SOP	7	7	1	49 Low category and Risk accepted	NA	NA	NA	NA	NA
		➢ Not calibrated	➢ Error in results	➢ Calibration schedule not followed	➢ Calibration schedule available	➢ Calibration schedule ➢ As per SOP	7	7	1	49 Low category and Risk accepted	NA	NA	NA	NA	NA

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												S	O	D	RPN S*O*D
12.	**Electronic Balance**	➢ Not cleaned properly	➢ Cross contamination	➢ Person not trained ➢ Fail to follow SOP	➢ SOP available	➢ As per SOP	7	7	1	49 Low category and Risk accepted	NA	NA	NA	NA	NA
		➢ Not calibrated	➢ Error in weight	➢ Calibration schedule not followed	➢ Calibration schedule available	➢ Calibration schedule ➢ As per SOP	7	7	1	49 Low category and Risk accepted	NA	NA	NA	NA	NA
PRODUCT:															
1.	**Product Spillage**	➢ Product got spilled while sampling, dispensing or manufacturing	➢ Health effect ➢ Contamination & Cross-contamination	➢ Mishandling during process	➢ Product handling SOP to be followed	➢ As per SOP	7	7	1	49 Low category and Risk accepted	Decontaminati on is performed with procedure using 2.5% sodium hypochlorite solution.	NA	NA	NA	NA
2.	**Rejected filled bottles**	➢ Rejected filled bottles got spilled	➢ Health effect ➢ Contamination & Cross-contamination	➢ Mishandling during process	➢ Product handling SOP to be followed	➢ As per SOP	7	7	1	49 Low category and Risk accepted	Decontaminati on is performed with procedure using 2.5% sodium hypochlorite solution	NA	NA	NA	NA
PERSONNEL:															

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												S	O	D	RPN S*O*D
1.	**Gowning**	➢ Separate gowning not used	➢ Cross contamination	➢ SOP not followed	➢ SOP of gowning available	➢ As per SOP	7	7	1	49 Low category and Risk accepted	NA	NA	NA	NA	NA
		➢ Gowning not proper	➢ Contamination ➢ Health hazardous	➢ SOP not followed	➢ SOP of gowning available	➢ As per SOP	7	7	1	49 Low category and Risk accepted	NA	NA	NA	NA	NA
2.	**Personnel Health**	➢ Health related problems	➢ Contamination	➢ Personnel more sensitive to product	➢ Proper gowning ➢ PAPR snood to be used	➢ As per SOP	10	7	4	280	Ensure that the personal involved in manufacturing should be medically fit	7	7	1	49
3.	**Untrained Personnel**	➢ Person not trained to perform activity	➢ Contamination & Cross contamination	➢ Unawareness	➢ Training to be given	➢ As per SOP	7	7	1	49 Low category and Risk accepted	NA	NA	NA	NA	NA
ENVIRONMENT:															
1.	**Pressure Differential**	➢ Pressure difference not maintained	➢ Cross contamination	➢ Pressure gauge not calibrated ➢ Door not closed properly ➢ Door opened for long time	➢ Pressure differential to be monitored as per SOP ➢ GMP training	➢ As per SOP	7	7	1	49 Low category and Risk accepted	NA	NA	NA	NA	NA
2.	**Temperature & RH**	➢ Temperature & RH of area not maintained	➢ Microbial contamination will increase	➢ Data logger not calibrated ➢ Door not closed properly ➢ Door opened for long time	➢ Temperature & RH to be monitored as per SOP	➢ BMR ➢ Performance Qualification	7	7	1	49 Low category and Risk accepted	NA	NA	NA	NA	NA

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S.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
3.	**Non-viable & Viable particle count**	➢ Non-viable particle not verified at the start of process ➢ Viable particle count not performed	➢ Contamination ➢ Microbial contamination	➢ Unawareness ➢ Improper line clearance ➢ Fail to follow SOP	➢ SOP available ➢ Training to be given	➢ BMR ➢ As per SOP	7	7	1	49 Low category and Risk accepted	NA	NA	NA	NA	NA
SERVICE FLOOR:															
1.	**HVAC**	➢ Ruptured Return riser filter ➢ Ruptured Exhaust filter	Cross contamination	➢ Preventive maintenance not done as per schedule ➢ Filters not verified visually at the time of cleaning ➢ Fail to follow SOP	➢ Preventive maintenance schedule to be followed ➢ SOP to be followed	➢ Preventive maintenanc e schedule ➢ As per SOP	7	7	1	49 Low category and Risk accepted	➢ HEPA filters to be installed for purge air & exhaust air.	NA	NA	NA	NA

Where: S=Severity; O=Occurrence Probability; D=Detection
Abb.- PAPR - Power Air Purifying Respirator
NA: Not Applicable

Remarks (if any):

- On the basis of above risk assessment, there is less risk with respect to cross contamination of product in sampling/dispensing area as only one material is being handled at a given time trained personnel and cleaning procedure after molecule change over is in place.
- As Risk involved in sampling & Dispensing room due to exposure of Cyclosporine in sampling/dispensing room is very less, i.e., very less exposure time with respect to Cyclosporine exposure and proper gowning procedure in place to avoid any occupational health risk.
- Sampling /dispensing tools provided for handling of Cyclosporine's products to avoid any risk of cross contamination of general molecule.
- During dispensing manufacturing operation of Cyclosporine's products, all personnel having protective gowning including double gloves in hands, 3M Masks and safety goggles to avoid any exposure to product.

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- In manufacturing area of Cyclosporine, Product manufacturing persons allowed to work only 4 hours to reduce occupational exposure limit of Cyclosporine and person working inside the manufacturing area wearing Gloves, Goggles, Protective Clothing (PAPR snoods) and Filter Mask.
- Decontamination process of Area/Equipment & Rejected Drops Bottles shall be done using 2.5% Sodium Hypochlorite solution.
- Training to be imparted to all concerned persons regarding proper gowning (PAPR snoods).

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/Unit Operation: Cyclosporine Eye Drops		Date:	
S.No.	**Recommended Action**	**Responsible Person**	**Target Date of Completion**
1.	Cyclosporine product manufacturing to be taken in campaign to avoid frequent changeover during manufacturing activity on same line	Production/QA	During campaign manufacturing
2.	Ensure that personnel involved in dispensing of Cyclosporine are wearing PAPR gowning (separate gowning)	Production/QA	
3.	Dedicated Sampling/Dispensing tools to be used during sampling & dispensing of cyclosporine.	Production/QA	
4.	Used sampling & dispensing tools shall be cleaned immediately after Sampling/Dispensing activities.	Production/QA	
5	Decontamination of Equipments is performed with procedure using 2.5% sodium hypochlorite solution	Production/QA	
6.	Decontamination of area is performed with procedure using 2.5% sodium hypochlorite solution	Production/QA	
7.	Filters to be decontaminated by 2.5% of Sodium Hypochlorite solution	Production/QA	
8.	Ensure that the personal involved in manufacturing should be medically fit	Production/QA	
9.	HEPA filters to be installed for purge air & exhaust air.	Production/QA	

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Verification of Action Plan:

All the above agreed actions completed,/Not Completed.

(*incase any recommendations not completed, to be tracked through CAPA System)

Remarks (if any): NA

Verified By
QA
Sign & Date

Approved By
Head QA
Sign & Date