QUALITY RISK ASSESSEMENT AND MITIGATION PLAN FOR CROSS CONTAMINATION

QRA No.:

Name of Facility/Equipment/Utility/System/Activity/Procedure **Unit Operation:** Cross Contamination	**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
Products Cross contamination:															
1.	Facility design Flow	➢ Improper design of building / facilities	➢ Cross contamination of products. ➢ Product failure	➢ Qualification of facility is not meeting the GMP requirement. ➢ Men and material flow is not adequate.	➢ Interior surfaces e.g. walls, floors, ceiling are complying GMP requirements like; smooth, free from cracks and no open joints and are designed for effective cleaning. ➢ Pipe work, ventilation light points and other services are designed to avoid creation of recesses which are difficult to clean. ➢ Entry and exit procedure is in place to avoid un-authorized activity in area of production, packing. ➢ Appropriately designed air locks, pressure differentials air supply and extraction system are in place.	As per facility Qualification & Layouts	4	1	2	8 Low category & Risk Accepted	Adequate procedure no recommendation required.	NA	NA	NA	NA
2.	HVAC System	➢ Improper arrangement of HVAC System	➢ Cross contamination	➢ Area not classified with respect to HVAC zone criteria ➢ Air flow procedure (ACPH) is not adequate ➢ Dedicated HVAC is not available in each process areas ➢ HVAC designs area not adequate	➢ Areas are classified as per HVAC zone ➢ Air flow procedure is available (ACPH is available and checked annually) ➢ Dedicated HVAC is available in each process areas ➢ HVAC designs area adequate.	DQ,IQ,OQ & PQ OF AHU	4	2	2	16 Low category & Risk Accepted	Adequate procedure no recommendation required.	NA	NA	NA	NA

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		➢ Breakdown/failure of HVAC system causing excursion of temperature, humidity and loss of differential pressure between areas	➢ Cross contamination ➢ Manufacturing disruption ➢ Material and production failure ➢ Increase in deviation situation	➢ Preventive maintenance plan implementation failure ➢ HEPA filter integrity failure	➢ Preventive Maintenance procedure is available ➢ HVAC qualification is available ➢ Routine environmental conditions monitoring plan exists and is followed ➢ Process area is segregated into air pressure zones.	DQ,IQ,OQ & PQ OF AHU	4	1	2	8 Low category & Risk Accepted	Adequate procedure no recommendation required.	NA	NA	NA	NA
3.	Purified Water System	➢ Breakdown/ failure of purified water system	➢ Manufacturing disruption ➢ Purified water quality failure	➢ Preventive maintenance plan implementation failure ➢ Water system validation plan not available or is not followed.	➢ Preventive maintenance plan exists and is followed ➢ Periodic sanitization plan exists and is followed ➢ Routine purified water system monitoring plan exists and is followed. ➢ Usage of purified water after satisfactory analytical report	As Per SOP & Validations	4	2	2	16 Low category & Risk Accepted	Adequate procedure no recommendation required.	NA	NA	NA	NA
4.	Electricity	➢ Breakdown in power generation plant ➢ Breakdown in Transformer	➢ Manufacturing disruption ➢ Material and production failure ➢ Increase in power failure situation	➢ Natural electricity supply failure in power plant ➢ Preventive maintenance implementation plan failure	➢ Preventive maintenance plan exists and is followed ➢ Standard diesel generator exists ➢ UPS exists for critical quality instrumentation	As Per SOP	4	2	2	16 Low category & Risk Accepted	Adequate procedure no recommendation required.	NA	NA	NA	NA
5.	Compressed air	➢ Breakdown of air compressor ➢ Compressed air line filter integrity failure	➢ Contamination of products	➢ Preventive maintenance plan implementation failure ➢ Routine monitoring of compressed air system not done	➢ Preventive maintenance plan exists and is followed ➢ Routine monitoring of compressed air system is available	As Per SOP & Validations	4	2	1	8 Low category & Risk Accepted	Adequate procedure no recommendation required.	NA	NA	NA	NA

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6.	Faulty fabrics of plant	➢ Wear and tear of facility fabrics e.g., doors, wall, floor etc	➢ Cross contamination	➢ Poor maintenance of facility fabrics e.g., doors, wall, floor etc	➢ Floor furnished with suitable material. ➢ Periodic maintenance of the building premises exists	As per facility Qualification & Layouts	5	1	1	5 Low category & Risk Accepted	Adequate procedure no recommendation required.	NA	NA	NA	NA
7.	Dispensing Booth	➢ Breakdown of dispensing booth ➢ Balance calibration failure	➢ Cross contamination ➢ Dispensing error ➢ Area not qualified	➢ Preventive maintenance plan failure ➢ Calibration schedule procedure is not available.	➢ Requalification plan for dispensing booth exists and is followed ➢ Calibration schedule procedure is available.	As Per SOP & Validations	4	2	2	16 Low category & Risk Accepted	Adequate procedure no recommendation required.	NA	NA	NA	NA
8.	Dispensing procedure	➢ API calculation, dispensing and documenting	➢ Error in material dispensing ➢ Product failure	➢ API calculation verification is not available. ➢ Balance calibration plan failure.	➢ API calculation verification is available. ➢ Balance calibration procedure exists and is followed. ➢ Trained personnel are involved in dispensing. ➢ Production and quality supervision is available	As Per SOP	5	2	1	10 Low category & Risk Accepted	Adequate procedure no recommendation required.	NA	NA	NA	NA
9.	Area Cleanness	➢ Area not qualified	➢ Cross contamination ➢ Product failure	➢ Area not designed as per GMP and product requirement ➢ HVAC system failure	➢ Classified condition is available under dispensing booth	As Per SOP & Area qualification record	5	1	1	5 Low category & Risk Accepted	Adequate procedure no recommendation required.	NA	NA	NA	NA

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10.	RM Sampling, Handling & Dispensing	➢ Cross contamination ➢ Personnel/ Environment contamination while handling material/product along with general products	➢ Poor quality ➢ products or materials being handled pose a risk to the operators and/or the public and/or the environment	➢ Inadequate area / Environment for sampling ➢ Inadequate handling of Product/material while Sampling ➢ Inadequate Gowning procedure ➢ No defined procedure for sampling to avoid cross contamination. ➢ Inadequate control on sampling tools ➢ Inadequate cleaning procedure for sampling device ➢ Lack of training	➢ Dedicated sampling area has been provided for sampling of RM. ➢ Adequate sampling procedure has in place. ➢ Sampling area has been provided for sampling of RM, due to that there is no chance of cross contamination. ➢ Cleaning procedure for Sampling tools defined based on cleaning validation. ➢ Sampling SOP is in place. ➢ Training has been imparted to concerned personnel on adequate sampling and gowning procedure.	As Per SOP	4	2	1	8 Low category & Risk Accepted	Adequate procedure no recommendation required.	NA	NA	NA	NA
		➢ Material spillage	➢ Loss of the quantity and contamination of sampling area.	➢ Adequate sampling procedure not followed. ➢ Appropriate sampling tools not used. ➢ Lack of trained personnel.	➢ Any spillage of material while handling considered as handling loss and same handled using the spillage kit to avoid any injury to chemist or operator working. ➢ Procedure for Collection & Handling are in place. ➢ Training has been imparted to concerned employees.	As Per SOP	4	2	1	8 Low category & Risk Accepted	Adequate procedure no recommendation required.	NA	NA	NA	NA

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												S	O	D	RPN S*O*D
		➢ Proper cleaning not done in dispensing area	➢ Risk of contamination of Raw Material.	➢ SOP for cleaning not followed. ➢ Lack of training	➢ Material dispensing has been done in dispensing area and area has been cleaned by following appropriate cleaning procedure as per SOP.	As Per SOP	4	2	1	8 Low category & Risk Accepted	Adequate procedure no recommendation required.	NA	NA	NA	NA
		➢ Malfunctioning of Dispensing / Sampling Booth (RLAF)	➢ Cross contamination.	➢ No Qualification and maintenance program for dispensing booth/Sampling Booth.	➢ For dispensing and sampling area, RLAF has been provided and same has been qualified before usage and periodic validation will also be done as per schedule. Daily monitoring of differential pressure has been done. ➢ Preventive maintenance schedule has been prepared and followed.	DQ, IQ, OQ & PQ OF RLAF	4	2	1	8 Low category & Risk Accepted	Adequate procedure no recommendation required.	NA	NA	NA	NA
		➢ Inaccuracy of weighing balance during dispensing	➢ It can be cause of variation in weight of RM during weighing and also cause variation in assay of product.	➢ Due to out of calibration of weighing balance	➢ Calibration of weighing balance is done on monthly basis and daily verification of weighing balance is also done to check its accuracy.	As Per SOP	4	2	1	8 Low category & Risk Accepted	Adequate procedure no recommendation required.	NA	NA	NA	NA

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		➢ Personnel/ Environment contamination while handling material/product along with general products	➢ Personnel/ Environmental contamination ➢ Cross contamination ➢ Poor Quality	➢ Inadequate area / Environment for sampling ➢ Inadequate handling of Product/material while Dispending ➢ Inadequate Gowning procedure ➢ Lack of training	➢ Dedicated dispensing area has been provided for dispensing of raw material ➢ Training has been imparted to all concerned employees. ➢ Only trained persons have been authorized to enter in dispensing area.	As per SOP & Training	3	1	1	3 Low category & Risk Accepted	Adequate procedure no recommendation required.	NA	NA	NA	NA
		➢ RM is not of appropeate quality	➢ It can be cause of low assay and low stability of finish product.	➢ RM testing not done during receiving of RM. ➢ Receiving of Raw material from an unapproved vender.	➢ There is a provision for sampling & testing of all raw materials and all raw materials have been sampled and tested as per the written procedures and only after that QC approved RM is used for further processes. ➢ Before procurement of materials all venders has been qualified & approved as per our written procedure for vender management.	As Per SOP	4	1	1	4 Low category & Risk Accepted	Adequate procedure no recommendation required.	NA	NA	NA	NA
		➢ Unapproved al material used for dispensing process	➢ It can be very harmful for whole batch and could be cause of low assay of finish product.	➢ Due to not proper testing by quality control department.	➢ There is a proper provision for sampling, testing and labeling (approved or rejected) of raw material and before dispensing raw material verified by quality assurance department for its approved status.	As Per SOP	4	1	1	4 Low category & Risk Accepted	Adequate procedure no recommendation required.	NA	NA	NA	NA

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		➢ Gowning procedure not followed for dispensing	➢ There might be a chance of contamination of Raw Material.	➢ If untrained person will enter in the dispensing area.	➢ Only trained persons are authorized to enter in dispensing area followed by the authorized person list with a proper gowning.	As Per SOP	3	2	1	6 Low category & Risk Accepted	Adequate procedure no recommendation required.	NA	NA	NA	NA
		➢ Temperature and RH out of limit during dispensing	➢ It can be effects the property of Raw material and due to more RH, it can create moisture in Raw material.	➢ Failures of HVAC system or unqualified AHU'S are in use.	➢ Qualified HVAC System is used in the facility and also have a provision of BMS system for controlling and monitoring of Temp. & RH.	As Per SOP	3	3	1	9 Low category & Risk Accepted	Adequate procedure no recommendation required.	NA	NA	NA	NA
		➢ No proper cleaning during dispensing process	➢ There might be a chance of contamination of Raw Material.	➢ SOP for cleaning not followed. ➢ No training provided to person.	➢ Written procedures are available for cleaning processes and trained quality assurance person daily verify the cleaning of dispensing room.	As Per SOP	3	3	1	9 Low category & Risk Accepted	Adequate procedure no recommendation required.	NA	NA	NA	NA
		➢ Malfunctioning of Dispensing Booth	➢ Due to that cross contamination of raw material will occurred.	➢ No proper maintenance is there for dispensing booth and Unqualified dispensing booth used for dispensing.	➢ Qualified Dispensing booth is using for dispensing purposes and there is a provision for daily monitoring of differential pressure of dispensing booth through its Magnehelic gauges. ➢ There is also a written procedure for preventive maintenance of all equipment including with dispensing booth.	As Per SOP	4	2	1	8 Low category & Risk Accepted	Adequate procedure no recommendation required.	NA	NA	NA	NA

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11.	Material safety	➢ Improper handling and storage ➢ Improper physical and chemical properties ➢ Improper personal protection	➢ Cross contamination ➢ Poor product quality ➢ Individual protection of eye, skin, respiratory, and general hygiene	➢ Inadequate procedure to handle materials.	➢ Training has been imparted to all employees on following personnel hygiene and safety. ➢ MSDS is in place providing details over how to handle material, individual safety measures also mentioned under the MSDS. ➢ Material is stored as per label instruction and by following respective procedure.	As Per SOP & MSDS	5	1	1	5 Low category & Risk Accepted	Adequate procedure no recommendation required.	NA	NA	NA	NA
12.	Transfer the dispensed material from store to Manufacturing.	➢ Material spillage ➢ Material misplace during transfer.	➢ Directly impacted to the product manufacturing & product quality.	➢ Not Proper handling during transferring of materials.	➢ After dispensing all materials are kept in dispensing bags and close with cable tie with a specific numbering on each material. ➢ A provision is in place to transfer all the dispensed materials in a closed SS Container. ➢ Procedure for collection and handling are in place.	As Per SOP	4	1	1	4 Low category & Risk Accepted	Adequate procedure no recommendation required.	NA	NA	NA	NA

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13.	Equipment usage and Man movement	➢ Equipment cleaning failure ➢ Uncontrolled man movement	➢ Cross contamination ➢ Product failure	➢ Non validated cleaning procedure ➢ Non-availability of entry /exit and gowning procedures	➢ Cleaning validation is done ➢ Hold time study for cleaned equipment usage is available. ➢ Closed manufacturing equipments and dedicated transfer hose pipe is available. ➢ Trained manpower is dedicated for each process cubicle. ➢ SOP for gowning procedure is available and is adhered by all concerned.	As Per SOP	4	2	2	16 Low category & Risk Accepted	Adequate procedure no recommendation required.	NA	NA	NA	NA
		➢ Line clearance	➢ Cross contamination ➢ Product failure	➢ Inadequacy in line clearance checklist	➢ Line clearance SOP and checklist exists	As Per SOP	4	1	1	4 Low category & Risk Accepted	Adequate procedure no recommendation required.	NA	NA	NA	NA
14.	Garment sterilization	➢ Garments are not sterilized by utilizing the validated parameters.	➢ Risk of Contamination and Microbial growth if not sterilized properly.	➢ Unqualified autoclave used for sterilization process ➢ Un-qualified load patterns used. ➢ Mechanical problem in autoclave. ➢ Working personnel lack of adequate knowledge.	➢ Washing will be done after uses, Followed by sterilization hence there's no risk of contamination. ➢ Autoclave qualification has been done and a validated load pattern is provided to production. ➢ Preventive maintenance is done as per schedule. ➢ Trained Person handles the all autoclave processes.	As Per SOP & Autoclave Qualification Report	3	1	1	3 Low category & Risk Accepted	Adequate control in place. No recommendation required.	NA	NA	NA	NA

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15.	Sterile Garment storage	➢ Sterile garments cabinet not working properly.	➢ Microbial contamination increase in sterile garments stored in sterile garments cabinet.	➢ Mechanical error in sterile garments cabinet. ➢ Unqualified equipment is in use. ➢ Handle by untrained person.	➢ Preventive maintenance is done as per schedule. ➢ Qualification of Sterile garments cabinet is done and used after qualification. ➢ Trained person handle the sterile garments cabinet.	As Per SOP & Validation record	3	3	1	9 Low category & Risk Accepted	Adequate procedure no recommendation required.	NA	NA	NA	NA
16.	Quality control	➢ Personnel/ Environment contamination while handling material/product along with general products.	➢ products or materials being handled pose a risk to the operators and/or the public and/or the environment.	➢ Inadequate handling of Product/material while QC Analysis ➢ Inadequate Gowning procedure ➢ Lack of training	➢ Isolator/ glove box has been provided to avoiding Personnel contamination while handling powder. ➢ Training has been imparted to all concerned employees. ➢ An only trained person has been authorized to enter in sampling area.	As Per SOP & Training	3	2	1	6 Low category & Risk Accepted	Adequate control in place. No recommendation required.	NA	NA	NA	NA

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17.	Personnel	➢ Inadequate gowning (uncleaned/damaged garment, Deficient procedure) ➢ Not following personnel hygiene	➢ Cross contamination ➢ Poor Product quality	➢ Inadequate instructions/procedure on gowning of personnel ➢ Inadequate instructions/procedure on personnel hygiene ➢ Inadequate instructions/procedure on entry exit ➢ No training provided to personnel.	➢ Training has been imparted to all employees on following personnel hygiene and entry exit procedure. Personnel hygiene and gowning strictly followed. ➢ Personnel are trained on Good manufacturing practice and Aseptic practices. Only trained personnel are allowed to work under aseptic area. ➢ Operators are provided with all PPEs while performing activities. ➢ Medical checkup plan is in place for all employees. New employees are examined for medical fitness and then only allowed to perform manufacturing operations.	As Per SOP	4	2	1	8 Low category & Risk Accepted	Adequate control in place. No recommendation required.	NA	NA	NA	NA
18.	Access Control	➢ Un Controlled access	➢ Movement of unauthorized personnel	➢ Malicious intent	➢ PLC based equipment is available ➢ Authorized persons list is available for all applications ➢ Supervisory control exists and is followed.	As Per SOP & Equipments Details	5	1	1	5 Low category & Risk Accepted	Adequate control in place. No recommendation required.	NA	NA	NA	NA
19.	Entry Exit Procedure in manufacturing area	➢ Cross Contamination ➢ Area contamination	➢ Inadequate Man movement in manufacturing area lead to cross contamination/ Area contamination	➢ No separate passage for manufacturing area. ➢ Inadequate Man movement ➢ Inadequate Entry Exit procedure	➢ All manufacturing areas have their own separate entries for man & material movements, so that there is no chance for cross contamination. ➢ Training has been provided to all personal.	As Per SOP & Training	5	1	1	5 Low category & Risk Accepted	Adequate control in place. No recommendation required.	NA	NA	NA	NA

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20.	Manufacturing Process	➢ Sterilization not done of manufacturing tank.	➢ Chemical & Microbial contamination increases in manufacturing vessel.	➢ SOP for Cleaning & sanitization not followed. ➢ Working personnel lack of adequate knowledge.	➢ Written procedures are available for cleaning & sanitization processes and quality assurance person verify the sterilization process of manufacturing tank. ➢ Online SIP (Sterilization in Place) system is available for sterilization.	As Per SOP	4	1	1	4 Low category & Risk Accepted	Adequate procedure no recommendation required.	NA	NA	NA	NA
21.	Manufacturing Process	➢ Cross contamination ➢ Personnel/ Environment contamination while handling material/product along with general products	➢ Products or materials being handled pose a risk to the operators and/or the public and/or the environment. ➢ Poor product quality.	➢ Inadequate handling of material/Product. ➢ Inadequate Gowning procedure ➢ Inadequate cleaning procedure ➢ Lack of training ➢ Lack of supervision of working behavior to ensure training effectiveness and compliance with relevant procedure.	➢ Dedicated manufacturing area has been provided for material exposure and manufacturing to avoid cross contamination. ➢ Product wise BMR/instructions are followed for execution of batch and person involved in process are well trained. ➢ A Validate cleaning procedure is in place and using validated cleaning method clean the all equipments, so there is no chance of previous product residue to contaminate the nest product. ➢ Batch to batch and Change over cleaning procedure are in place. Cleaning samples (Swab/Rinse) has been tested for allowable previous product residue.	As Per SOP &Batch Manufacturing Record	5	1	1	5 Low category & Risk Accepted	Adequate control in place. No recommendation required.	NA	NA	NA	NA

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22.	Mixing tank to Holding tank Transfer line	➢ Cleaning not done of mixing tank to holding tank transfer line.	➢ Microbial contamination increases in transfer line. ➢ There might be a chance of contamination of product.	➢ Online monitoring for cleaning of product line not available ➢ Cleaning process of transfer line interrupted. ➢ Cleaning of transfer line not followed as per SOP. ➢ No proper procedure for cleaning of transfer line.	➢ Product line cleaned with manufacturing tank and online conductivity sensor has been installed at the end of Drain line and validate recipe has been set when conductivity not achieve then cleaning continue still get required conductivity. ➢ Print facility available for reviewing of cleaning Process	As Per SOP & BMR	5	1	1	5 Low category & Risk Accepted	Adequate procedure no recommendation required.	NA	NA	NA	NA
23.	Mixing tank to Holding tank Transfer line	➢ Sterilization not done of mixing tank to holding tank transfer line.	➢ Directly impacted to Product Sterility & Quality. ➢ Product gets contaminated after filtration.	➢ Due to assembling of Product line after sterilization, intact line and online sterilization facility not available.	➢ Product line Sterilized with manufacturing tank and online temperature sensor has been installed at the end of product line and recipe has been set sterilization hold cycle not started when temperature not achieve at that end point of product line. ➢ Print facility available for reviewing of sterilization Process.	As Per SOP & BMR	4	1	1	4 Low category & Risk Accepted	Adequate procedure no recommendation required.	NA	NA	NA	NA
24.	Product Filter	➢ Integrity test failure ➢ Cross contamination	➢ Product contaminated ➢ Batch failure.	➢ Filter use more than recommended cycle ➢ Filter Use without Integrity testing	➢ Dedicated filters use for all products for filtration. ➢ Filter use as per recommended cycle & maintained in log book for their cycle. ➢ Final Filter integrity done before & After Filtration process.	As Per SOP	4	2	1	8 Low category & Risk Accepted	Adequate procedure no recommendation required.	NA	NA	NA	NA

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25.	Product Filter	➢ Aseptically not handling After Sterilization of product filter. ➢ Inadequate handling of Filter after Sterilization	➢ Directly impacted to Product Sterility & Quality	➢ On line product sterilization facility not available.	➢ Product filter sterilized with tank & Product line and after that no any manual interference allowed.	As Per SOP	4	2	1	8 Low category & Risk Accepted	Adequate procedure no recommendation required.	NA	NA	NA	NA
26.	Filtration Process	➢ Cleaning not done of Filtration tank before filtration process.	➢ There might be a chance of contamination of product.	➢ SOP for cleaning (CIP) not followed. ➢ Working personnel lack of adequate knowledge.	➢ Written procedures are available for cleaning processes of holding tank and trained quality assurance person daily verify the cleaning of manufacturing & Holding tank. ➢ Online CIP (Clean in Place) system is available for cleaning. ➢ Online conductivity meter is available. ➢ Print facility available of reviewing sterilization process.	As Per SOP	4	1	1	4 Low category & Risk Accepted	Adequate procedure no recommendation required.	NA	NA	NA	NA
27.	Filtration Process	➢ Sterilization not done of filtration tank before filtration process.	➢ Chemical & Microbial contamination increases in holding vessel.	➢ SOP for Cleaning & sanitization not followed. ➢ Working personnel lack of adequate knowledge.	➢ Written procedures are available for cleaning & sanitization processes and quality assurance person verify the sterilization process of manufacturing tank. ➢ Online SIP (Sterilization in Place) system is available for sterilization.	As Per SOP	4	1	1	4 Low category & Risk Accepted	Adequate procedure no recommendation required.	NA	NA	NA	NA

QUALITY RISK ASSESSEMENT AND MITIGATION PLAN FOR CROSS CONTAMINATION

QRA No.:

Name of Facility/Equipment/Utility/System/Activity/Procedure **Unit Operation:** Cross Contamination	**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
28.	Filtration Process	➢ Availability of non-sterile solution for aseptic filling.	➢ There might be a chance of Product Contamination.	➢ Integrity failure of 0.22µ sterile filter and/or use of unsterilized articles during filtration process.	➢ Pre and post filter integrity has been done before and after filtration process to ensure integrity of 0.22µ sterile filter. ➢ On line CIP & SIP System is in place for providing a better process result so that all equipment's should be sterile for filtration process.	As Per SOP	4	1	1	4 Low category & Risk Accepted	Adequate procedure no recommendation required.	NA	NA	NA	NA
29.	Filtration Process	Filtered Solution not aseptically transfers from Filtration room to filling room.	➢ Product gets contaminated. ➢ Chemical & Microbial contamination increases in solution.	➢ Aseptically not handling during transfer of solution. ➢ Working personnel lack of adequate knowledge.	➢ Filtered solution transfer through integrated transfer line from holding tank to buffer tank in filling room and integrated line available for prevent to cross contamination.	As Per SOP	4	1	1	4 Low category & Risk Accepted	Adequate procedure no recommendation required.	NA	NA	NA	NA
30.	Filtration process	➢ Non-Integral filters used for filtration process	➢ Filled product remains non-sterile. ➢ High bio-burden results after pre filter. ➢ Chemical & Microbial contamination increases in solution.	➢ Damaged/faulty filters used for filtration process. ➢ Human error. ➢ Working personnel lack of adequate knowledge.	➢ Each filter has a "certificate of test" from supplier. ➢ Pre and post integrity test are conducted before and after filtration process respectively and print out attached with Batch manufacturing record. ➢ Training provided to persons.	As Per SOP & BMR	5	2	1	10 Low category & Risk Accepted	Adequate procedure no recommendation required.	NA	NA	NA	NA

QUALITY RISK ASSESSEMENT AND MITIGATION PLAN FOR CROSS CONTAMINATION

QRA No.:

Name of Facility/Equipment/Utility/System/Activity/Procedure **Unit Operation:** Cross Contamination	**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
31.	Machine parts & Filling Assembly	➢ Materials/ machine parts are not sterilized by utilizing the validated parameters.	➢ Machine parts not sterilized properly.	➢ Unqualified autoclave used for sterilization process ➢ Un-qualified load patterns used. ➢ Mechanical problem in autoclave. ➢ Working personnel lack of adequate knowledge. ➢ Impure steam provided by PSG.	➢ Autoclave qualification has been done and a validated load pattern is provided to production. ➢ Preventive maintenance is done as per schedule. ➢ Trained Person handles the all autoclave processes. ➢ PSG is qualified and produces a quality & pure steam for autoclaving process.	As Per SOP & Validation record	4	1	1	4 Low category & Risk Accepted	Adequate procedure no recommendation required.	NA	NA	NA	NA
32.	Machine parts & Filling Assembly	➢ Aseptically not handling after sterilization.	Product contamination	➢ Carry and kept without laminar air ➢ Use over the recommendation periods	➢ Machine parts carry in Mobile LAF and assembled under LAF, Which is operated through battery backup.	As Per SOP	4	1	1	4 Low category & Risk Accepted	Adequate procedure no recommendation required.	NA	NA	NA	NA
33.	Area monitoring by settle plate & active air sampling	➢ Irregular monitoring intervals. ➢ Inadequate detailing of test locations (sample points)	➢ Area monitoring effected and cannot record as per the time schedule. ➢ Critical locations can be left without monitoring.	➢ No schedule of area monitoring ➢ No justified and approved locations for area sampling. ➢ Working personnel lack of adequate knowledge.	➢ The area monitoring has been done as per the schedule for the different area. ➢ There are proper approved sampling locations for area monitoring. ➢ Trained personnel done the area monitoring.	As Per SOP	3	2	1	6 Low category & Risk Accepted	Adequate procedure no recommendation required.	NA	NA	NA	NA

QUALITY RISK ASSESSEMENT AND MITIGATION PLAN FOR CROSS CONTAMINATION

QRA No.:

Name of Facility/Equipment/Utility/System/Activity/Procedure **Unit Operation:** Cross Contamination	**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
34.	Cleaning validation	➢ Cross contamination	➢ Cross contamination	➢ Inadequate cleaning procedure ➢ Lack of training	➢ All products have been already considered in cleaning validation matrix and all manufacturing line have executed cleaning validation as per worst case. ➢ Cleaning validation has been performed as per the determined worst case. ➢ Training has been imparted to all concerned.	As Per SOP & Cleaning Validation Report	3	1	1	3 Low category & Risk Accepted	Adequate control in place. No recommendation required.	NA	NA	NA	NA
35.	Area Cleaning	➢ Area cleaning not done after batch completion.	➢ There is a high degree of chances to increase the chemical & microbial growth in the area that can lead product contamination also.	➢ Unawareness of operator and staff members. ➢ Working personnel lack of adequate knowledge.	➢ Only trained and authorized persons can enter & work in the aseptic area and they all are trained in their work. ➢ After completion of every batch the cleaning has been done in the presence of production and quality assurance personnel.	As Per SOP	4	1	1	4 Low category & Risk Accepted	Adequate procedure no recommendation required.	NA	NA	NA	NA
36.	Area Cleaning	➢ Area cleaning not done as per the schedule.	➢ High chances to increase the microbial growth in the area that can lead product contamination also.	➢ No schedule is there for area cleaning. ➢ SOP of area cleaning not followed. ➢ Working personnel lack of adequate knowledge.	➢ There is a proper schedule for cleaning of aseptic area and cleaning has been done as per the schedule by the trained personnel. ➢ SOP of area cleaning has been followed and log in the all details in respective log book.	As Per SOP	4	2	1	8 Low category & Risk Accepted	Adequate procedure no recommendation required.	NA	NA	NA	NA

QUALITY RISK ASSESSEMENT AND MITIGATION PLAN FOR CROSS CONTAMINATION

QRA No.:

Name of Facility/Equipment/Utility/System/Activity/Procedure **Unit Operation:** Cross Contamination	**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
37.	Area Cleaning	➢ Microbial growth increases in aseptic area.	➢ Product get contaminated ➢ Product failure.	➢ Disinfectant using area cleaning not validated. ➢ Effectiveness of disinfectant not up to the mark.	➢ Disinfectant validation has been done and only validated disinfectant has been used for cleaning of aseptic area.	As Per SOP & Validation record	4	2	1	8 Low category & Risk Accepted	Adequate procedure no recommendation required.	NA	NA	NA	NA
38.	AHU	➢ Cross contamination through AHU ➢ Poor AHUs and inadequate control of air recirculation system ➢ Improper cleaning of AHU filters.	➢ Area contamination followed by Product contamination	➢ No Dedicated Air handling units has been installed. ➢ AHU designed is not adequate. ➢ No procedure in place to clean AHU filters.	➢ Dedicated Air handling units with once through circulation has been installed. ➢ AHU designed with the filters off 10 micron, 5 micron followed by 0.3 micron HEPA filters at terminal. ➢ Approved procedure in place to clean AHU filters	DQ,IQ,OQ & PQ OF AHU	4	2	2	16 Low category & Risk Accepted	Adequate control in place. No recommendation required.	NA	NA	NA	NA

QUALITY RISK ASSESSEMENT AND MITIGATION PLAN FOR CROSS CONTAMINATION

QRA No.:

Name of Facility/Equipment/Utility/System/Activity/Procedure **Unit Operation:** Cross Contamination	**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
39.	Environment	➢ Improper airflow ➢ Improper area cleaning/sanitization ➢ Inadequate control of DP, temperature/humidity ➢ Inadequate control on environment monitoring (viable-non viable)	➢ Cross contamination ➢ Poor Product quality	➢ No interlocking system, Inadequate air flow ➢ Inadequate procedure on environment monitoring, area cleaning and sanitization ➢ Differential pressure, Temperature , RH controls are not maintained for clean rooms	➢ Dedicated Air handling units with once through circulation has been installed. ➢ Approved procedures are available for environment monitoring, area cleaning and sanitization and same has been followed. ➢ Airlock rooms, entry exit change rooms, are provided. Differential pressure, temperature and RH in clean rooms are maintained and monitored regularly ➢ Production area is designed with unidirectional air flow of men and material to avoid mix-up/cross contamination.	As Per SOP, RDS, AHU Validation	5	1	1	5 Low category & Risk Accepted	Adequate control in place. No recommendation required.	NA	NA	NA	NA
40.	Man & material entry in aseptic area	➢ Man & material entry not specified ➢ Cross Contamination ➢ Area contamination	➢ There are high chances of cross contamination. ➢ It can cause product failure. ➢ Inadequate Man movement in manufacturing area lead to cross contamination/ Area contamination.	➢ Man & material entry not properly segregated for entering in aseptic area. ➢ Entry & exit procedure for aseptic area not specified.	➢ There are separate entry procedures for man & material. ➢ All materials for aseptic area has been transferred through Dynamic pass box, and all personnel have been enter in the aseptic area through 03 change room system as per the entry & exit procedure for aseptic area. ➢ Training has been provided to concerned personnel.	As Per SOP & Validation record	3	1	1	3 Low category & Risk Accepted	Adequate procedure no recommendation required.	NA	NA	NA	NA

QUALITY RISK ASSESSEMENT AND MITIGATION PLAN FOR CROSS CONTAMINATION

QRA No.:

Name of Facility/Equipment/Utility/System/Activity/Procedure **Unit Operation:** Cross Contamination	**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
41.	Filling & sealing process	➢ Filling room differential pressure is out of range during product filling.	➢ Due to low DP there might be a risk of area contamination with respect to adjacent room followed by contamination in product.	➢ Due to insufficiency of AHU Performance. ➢ Non-qualified AHU used for operation.	➢ Audio visual alarm system is provided in BMS System when pressure differential will go out of limit. ➢ At the time of PQ pressure differential has been verified.	As Per SOP & Validation record	3	3	1	9 Low category & Risk Accepted	Adequate procedure no recommendation required.	NA	NA	NA	NA
42.	Filling & sealing process	➢ Filling room temperature & RH is out of range during product filling.	➢ There might be an impact on in-process product.	➢ Due to inefficiency of chiller & heater of that particular AHU.	➢ Audio visual alarm system is provided in BMS System when temperature & RH will go out of limit. ➢ At the time of PQ temperature & RH has been verified.	As Per SOP & Validation record	3	3	1	9 Low category & Risk Accepted	Adequate procedure no recommendation required.	NA	NA	NA	NA
43.	Filling & sealing process	➢ Routine filling interventions occurs due to any mechanical problem.	➢ It can be a cause of producing a non sterile product. ➢ Product safety and quality problem occurs.	➢ Operators not qualified in each interventions and it can lead the chance of human error.	➢ Filling process is covered by media fill study and all operators has been involved & qualified in each intervention. ➢ Media fill report covers the container size and filling interventions.	As Per SOP & Validation record	3	4	1	12 Low category & Risk Accepted	Adequate procedure no recommendation required.	NA	NA	NA	NA
44.	Line clearance and Labeling	➢ Inadequate verification of labeling of raw material as well as in process material	➢ Product Failure	➢ Inadequate training. ➢ Standard operating procedure is not defined	➢ Personnel are trained to follow line clearance procedure before to start any activity. ➢ Standard operating procedure for labeling at different stages is in place.	As Per SOP	4	1	2	8 Low category & Risk Accepted	Adequate procedure no recommendation required.	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.

QUALITY RISK ASSESSEMENT AND MITIGATION PLAN FOR CROSS CONTAMINATION

QRA No.:

Name of Facility/Equipment/Utility/System/Activity/Procedure **Unit Operation:** Cross Contamination	**Date of Quality Risk Assessment:**

Name of Facility/Equipment/Utility/System/Activity/Procedure/Unit Operation: Cross Contamination		**Date:** NA	
S. No.	**Recommended Action**	**Responsible Person**	**Target Date of Completion**
1.	NA	NA	NA
2.	NA	NA	NA

CAPA: Not required

If required, mention CAPA No.: NA

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 PLAN FOR CROSS CONTAMINATION

QRA No.:

Name of Facility/Equipment/Utility/System/Activity/Procedure **Unit Operation:** Cross Contamination	**Date of Quality Risk Assessment:**

QUALITY RISK ASSESSEMENT AND MITIGATION SUMMARY REPORT

Name of Equipment: Cross Contamination

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 3 to 12. Hence Risk is detected as low which is acceptable.

Verified By
QA
Sign & Date

Approved By
Head QA
Sign & Date