Risk Assessment related to Cross Contamination Control in Manufacturing Area

1. Risk Assessment:

A.	Risk Identification				Risk Analysis/ Evaluation				
S.No.	**Item or Process Step**	**Potential risk and/or Failure mode**	**Probable impact of potential risk and/or failure mode**	**Current control measures**	**S**	**O**	**D**	**RPN**	**Risk Level**
1.	Facility design	- Facility design qualification is not qualified. - Improper design of building / facilities - Dedicated manufacturing area not available for particular medicinal products. - In process storage area is not dedicated. - Hazardous contamination with highly sanitizing materials and biological preparation. - Dedicated air lock not design for each processing cubical.	- Cross contamination of products. - Product failure - Contamination of product through air	- Interior surfaces e.g. walls, floors, ceiling are • Smooth • Free from cracks and open joints • Should not shed particulate matter • Should permit easy and effective cleaning. - Pipe work, ventilation and light points and other services are designed in such to avoid creation of recesses which are not difficult to clean. - Facility qualification was done - Maximum protection against the entry of insects, birds or other pests. - Pest control and effective monitoring system is in place. - Dedicated and self contained facility should be available for manufacturing of general categories solid oral dosage form (tablet and capsule). - Appropriately designed air locks provided to all processing area except blending, compression and coating area. - Pressure differentials, air supply and	4	3	3	36	Medium risk .

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				extraction system are provided. - Adequate in process storage area to minimize risk of mix up between different products or their components. Orderly placing and logical positioning of equipment and materials.					
2	HVAC system	- HVAC system is not qualified. - Contamination caused by re-circulation or re-entry of untreated or insufficiently treated air.	- Cross contamination of products. - Product failure	- Appropriately designed air locks, pressure differential, air supply and extraction system is provided. - Using a 'closed system' in production. - Periodically validate the HVAC system. - Differential pressure has been daily monitored as per SOP.	4	2	2	16	Low risk
3	Men movement	- Good gowning practices not implemented - Men-material movement is not controlled.	- Cross contamination of products. - Product failure	- In manufacturing area each employee wear the Secondary uniform (Overgown) over the primary factory uniform before enter in manufacturing area as per SOP. - Training given to all concern for good gowning procedure. - Good gowning procedure is appropriate for process and followed by each employee. - Man material procedure is defined and layout is in place. - Training given to concern for men material movement.	4	2	1	8	Low risk

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4	Material movement	- Line clearance procedure not fully implemented. - Common dispensing area for active and excipients. - Material air locks not design. - Lack of written procedure for de-dusting of bulk container. - Accessories used in manufacturing (FBD bag, Filter, Transfer pipe, hose pipe etc.) are not dedicated. - Lack of standard procedure for dispensing of raw materials. - Reverse laminar air flow performance is not validated. - Ineffective cleaning procedure.	- Product failure - Contamination of starting materials or of a product by another material.	- Before any processing/ operation start, line clearance step should be taken to ensure that the work area and equipment are clean and free from any starting material, previous products, product residues, labels or documents not required for the current operation. - Line clearance procedure followed as per SOP. - Dedicated dispensing area is defined for dispensing of active and excipients. - Entry of materials through separate air lock. - De-dusting of materials containers before receiving in store quarantine as per SOP. - Accessories used in manufacturing (FBD bag, Transfer pipe, hose pipe etc.) should be dedicated - Weighing of material one at a time under reverse laminar air flow. - Procedure for dispensing of raw material are in place. - Reverse laminar air flow are periodically validated for performance. - Material movement is in closed container and in controlled process. - Validated cleaning procedure for cleaning of	4	2	2	16	Low risk

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				sampling booth and utensil. - Trained and dedicated responsible technical person for each process.					
5	Manufacturing	- Ineffective provision for dust control. - Uncontrolled release of dust, gases, vapour and sprays. - Manufacturing activity is done in open inlet equipment. - Line clearance procedure is not fully implemented. - Uncontrolled movement of materials and man. - Product handling SOP not available in manufacturing area	- Cross contamination arises from product in-process - Mix up between different products and their components. - Product contamination.	- Installed dust extractor system where dust is generated (granulation, compression and filling area). - Manufacturing activity is performed in closed condition/ equipment. - Close the machine hopper like compression machine, capsule filling machine with lid during operation. - In-process container is closed with lid after material take in and takeout. - Dedicated vacuum cleaner with HEPA filter is used in granulation, compression and capsule filling area. - Line clearance done at each stage as per SOP. - Intermediate materials movement done in well closed container in presence of production staff. - Documented in-process material movement in quarantine logbook. - Adequate & dedicated in-process checks area. - Procedure for handling of intermediates / in-process material is defined in SOP.	4	2	1	8	Low risk

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6	Equipment / Area Cleaning	- Equipment cleaning procedure is not validated. - Ineffective cleaning procedure. - Cleaned equipment is not with proper status label. - Written cleaning procedure for equipment is not available in production area. - Line clearance procedure is not fully implemented. - Ineffective cleaning and decontamination procedure.	- Residues on equipment - Product contamination.	- Testing of residues by performing rinse / wash water analysis. - Clean common equipment according to validated cleaning procedure during production of different products. - Using cleanliness status label on cleaned equipment with validity date & time. - Clean production equipment thoroughly on scheduled basis as per SOP and wrap with fresh polythene bags until use. - Before any processing operation is started, line clearance step should be taken to ensure that the work area and equipment are clean and free from any starting material, products, product residues, labels or documents not required for the current operation. - Line clearance procedure followed as per SOP. - Clean common equipment according to validated cleaning procedure during production of different products. - After use, production equipment should be cleaned without delay according to detailed written procedure and stored under clean and dry condition in a separate area or in a	4	2	2	16	Low risk

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				manner that will prevent contamination. - Time limits for storage of equipment after cleaning and before use should be stated in SOP and implemented in practice.					
7	Environmental condition	- Environmental monitoring is not performing as per standard operating procedure. - Settle plate not properly exposed. - Environmental monitoring is not recorded. - HVAC system not qualified.	- Cross contamination	- Measure the environmental monitoring control and their effectiveness periodically according to standard operating procedure. - Procedure for Settled plate method is defined in SOP. - Environment monitoring performed as per SOP. - Daily temperature and humidity is monitored and recorded in log book. - HVAC system is periodically validated. - Training given to concern person.	3	2	2	12	Low risk

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8	Contamination arises from accessories / pipelines	- Equipment seals, gaskets directly contact to products. - Common accessories (e.g, finger bag, suspension hose, hose pipe, filters etc) are used for different products. - Water pipeline coupling is not proper.	- Product failure - Product contamination	- Equipment seals, on rotating shafts e.g. agitators, pumps, compressors should not come in contacts with products. If unavoidable then seal lubricant should be of food grade. - Dust cup is used during compression. - Used dedicated accessories which are difficult to clean e.g, finger bag, silicon pipe, vent filters etc) - Water distribution pipelines should have sanitary couplings, slope for drainage, and positive pressure at point of use to avoid suck back of air.	3	2	1	6	Low risk
9	From operator clothing	- Protective gowning is deficient. - Standard written gowning procedure is available. - Man movement is not controlled in production area.	- Product failure - Product contamination	- Wearing protective clothing (overgrown, mask, gloves) where products or material are handled. - Dedicated dress code for each processing area. - Standard written procedure for proper gowning are in place. - Training given all concern people for proper implementation.	3	2	2	12	Low risk
10	Human errors	- Health examination not performed for all personnel. - Lack of written procedure for	- Product contamination / Cross contamination	- All personnel, prior to and during employment as appropriate, should undergo health examination as per SOP.	4	2	2	16	Low risk

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		personal hygiene. - All personnel are not trained for hygiene.		- A high level personal hygiene should be maintained. - All personnel should be aware of the principle of GMP that affects them. - Receive initial and continuing training, including hygiene instructions. - Direct contact should be avoided between the operator's hands and starting materials, primary packaging materials and intermediate or bulk product.					

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B.	Risk Reduction/ Acceptance					Risk Review					
S.No.	Potential risk and/or Failure mode	Risk level	Risk Acceptance Yes / No	Justification	Any action/ Mitigation plan for reduction	S	O	D	RPN	Final Risk Level	Residual Risk
1	Probability of process area air to mix with corridor air may lead to cross contamination	Medium	Yes	The above mentioned control measure are adequate and additionally to improve more assurance to prevent the cross contamination mitigation plan is required.	- A electromagnetic lock to be installed for blending, compression and coating room's door so that the door will always be magnetically locked apart from the existing door closure. In case of door closure failure, electromagnetic lock will act as secondary control to keep the door close always. - Interlocking access control system to be installed in all airlock to control door opening discipline (one door at one time). if the employees fail to follow door opening discipline, interlock will act as a secondary control. - To prevent unauthorized personnel entry in manufacturing area, biometric access control system to be installed at door of critical areas like warehouse entry / exit door, production entry / exit door and microbiology lab entry door.	3	2	1	6	Low	Proposed CAPA plan for mitigation of failure mode is adequate to control the potential risk.

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S.No.	Potential risk and/or Failure mode	Risk level	Risk Acceptance Yes / No	Justification	Any action/ Mitigation plan for reduction	S	O	D	RPN	Final Risk Level	Residual Risk
					- Interlocking access control system, electromagnetic locks functions, biometric access control system to be qualified after installation to challenge the door locking and unauthorized entry in manufacturing area.						

Conclusion:

1. Risk Assessment carried out related to cross contamination in production area. Through proper brainstorming work carried out by the cross functional team for assessment the risk and evaluation the risk.
2. A change control has been raised to installed door interlocking system, electromagnetic locks and biometric access control system.
3. The above mentioned current control measures and practices has been followed in manufacturing area. The processing room i.e. Granulation, compression, coating, encapsulation and packing cubical air contaminating positively pressure corridor is remote.

   Hence cross contamination possibility is minimize with the proposed action and mitigation plan for installation of electromagnetic lock provision on door, airlock door interlocking system and control of unauthorized person entry in production are through biometric access control system.

4. Risk Review and Approval:

S.No.	Name	Designation	Department	Sign/Date
1.				
2.				
3.				
4.				
5.				
6.				
7.				