1.0 APPROVAL:

This document has been approved by the following functional heads.

Department	Name	Signature / date
Quality Assurance		
Head of Production		
Head of Quality control		
Head of Engineering		
Head of Warehouse		
Head of QA		

2.0 TABLE OF CONTENTS:

3.0 PURPOSE:

This Risk Assessment is prepared for preventing the risk of cross contamination of products manufactured with the following purpose:

a. Identify and evaluate the risk associated with the cross contamination from process, products, equipment, facility and personnel.
b. Evaluate the technical and organizational measures available to control the risk of cross-contamination.
c. Identify any additional technical and organizational measures for controlling the risk of cross-contamination.

4.0 SCOPE:

This risk analysis is applicable for preventing the risk of contamination of products manufactured in Production area.

5.0 BACKGROUND INFORMATION:

This risk assessment study shall cover all the possible sources of contamination/ cross contamination and the available procedures to mitigate contamination / cross contamination. The risk assessment study shall also identify all the molecules which are manufactured in plant. A separate consideration shall be given for identifying the controls available for handling of molecules which require technical and organizational measures.

The risk assessment study shall focus on the following possible mechanisms for cross contamination:

a. Surface to Surface:

- Originating from contact with inadequately cleaned shared equipment/ tool surfaces through failures or inadequate design of cleaning process/equipment.
- Originating from contact with contaminated equipment
- Originating from personnel gowning.

b. Airborne to air/surface

- Originating from poorly controlled and unintended release of product into the environment due to inadequate control of powder particles during process after which the contamination settles on the product contact surface.
- From recirculation in AHU's between areas where filtration is inadequate.
- From inadequately controlled exhausts or return riser filters or filter integrity check.

c. Direct or indirect contamination from process or equipment failure:

- Back flow from waste or vacuum systems
- Technical failure of equipment.
- Spillage and leaks from equipment or handling during processing.

d. Originating from movement of personnel, materials or equipment or accessories from one location to other using processing area.

Mapping of stages with operations possible of generating particles leading to risk of contamination and cross contamination.

The mapping of stages where there is possible generation of particles with a risk to contamination/cross contamination shall identify the different stages where there is possibility of particles being generated of the active material.

The mapping is carried out based upon the amount of particles generated during a particular process. It is focused on processes which are more prone for generation of particles and processes which are less prone for generation of particles.

Below table represents the stages of particle generation and possible causes of particle generation.

STAGES		GENERATION OF PARTICLES	POSSIBLE CAUSES FOR GENERATION OF CONTAMINATION
Receipt of Raw materials		Low	Damaged containers containing the raw materials.
Sampling of raw material		High	Contamination during sampling if proper procedure is not followed.
Dispensing of raw material		High	Contamination during Weighing of raw materials in case spillage occurs
Bulk Preparation (Liquid Injection/ Ophthalmic)	Sampling	Medium	Contamination during sampling
	Stirring	Low	Stirring/ mixing of raw material ingredients carried out in closed equipment however there can be contamination during charging of material in equipment's.
	Filtration	Low	Filtration of prepared bulk solution carried out in closed filtration assembly and single time used filter for filtration of the product however there can be contamination during non dedicated filter used in filtration.
	Product transfer through transfer line	Low	Transfer of material through transfer line is carried out in close system.
	Filling of injection	Medium	Contamination can be happen during dosing of liquid in ampoule/ Vial due to time out of proxy sensor or not working properly to provide the signal for positioning of vial/ ampoule at the time of sterile liquid dosing.
Dry Powder Injection Filling	Sampling	Medium	Contamination during sampling
	Charging of container at Hopper	Low	Filtration of prepared bulk solution carried out in closed filtration assembly and single time used filter for filtration of the product however there can be contamination during non dedicated filter used in filtration.
	During In process verification of fill weight	Low	Contamination during In process verification of fill weight.
	Filling of Dry Powder injection	Medium	Contamination can be happen during dosing of powder and time out of star wheel, proxy sensor not working to provide the signal for positioning of vial holed by star wheel at the time of sterile powder dosing.
Ladling/ Visual Inspection/ Packing of Injection		Low	No any chances of contamination in Ladling/ Visual Inspection/ packing area because product is in packed condition
Dispatch of Finished goods		Low	No any chances as product in packed condition

This Risk Assessment has been initiated for evaluation of Technical and Organizational measures during manufacturing of hazardous as well as non-hazardous product and control measures available to mitigate contamination and cross contamination. The risk rating as High, medium and low have been assigned based on the risk control measures available.

6.0 TEAM INVOLVED FOR EVALUATION OF QUALITY RISK MANAGEMENT:

Risk Management team comprises of representative from Production, QA, QC, Warehouse and Engineering.

Name	Designation	Department
	Manager Compliance	Quality Assurance
	Deputy Manager	Quality Assurance
	Executive	Quality Assurance
	Deputy Manager	Quality Control
	Manager	Production

7.0 RISK ASSESSMENT:

Description of Risk identified	Risk Analysis and Evaluation				Current control measures	Risk classification based on control measures	Risk Acceptability (Yes/No)
	Potential Impact	Risk number	Failure mode	Risk classification based on risk identified			
Technical measures - Facility							
Inadequate containment of product within processing areas	There will be transfer of air borne contaminant to air /surface to corridor and adjacent processing areas. This will result in cross contamination of next product	R01	Failure in facility design with respect to pressure cascade so to confine potential airborne contaminant within a specified area	Medium	• The processing areas and corridor are having dedicated AHU systems for containment of air born particles and to prevent risk of cross contamination of products processing in different areas. • The corridor adjacent to the processing areas is having most negative as compared to the processing areas which prevents entry of air born particles to the processing areas and further to the adjacent areas. • The pressure zoning (cascade) and AHU zoning diagrams of all the areas at site has been reviewed and includes the controls are available for confine potential air born contaminant within processing areas. • Additionally, certain areas are having air locks separate for personnel entry and material entry • Magnahelic gauges are provided for indicating differential pressure across areas as follows ➢ processing area with respect to Corridor ➢ Corridor with respect to air lock (In certain areas) ➢ Corridor with respect to material entry (In certain areas) ➢ Air lock and material entry with respect to processing area (In certain areas) • Pressure differential is verified and documented before start of the critical activities such as dispensing, manufacturing and packing operations. • Doors provided for each processing areas are having door closures and ensures proper closing door so to prevent accidental conveying of air born particles if remains open. • In certain areas there are biometric interlocks which prevents simultaneous opening of doors of two adjacent areas & only authorized person will enter in processing area.	Low	Yes

7.0 RISK ASSESSMENT:

Description of Risk identified	Risk Analysis and Evaluation				Current control measures	Risk classification based on control measures	Risk Acceptability (Yes/No)
	Potential Impact	Risk number	Failure mode	Risk classification based on risk identified			
Technical measures -Facility (Contd.)							
Improper facility design with respect to surfaces of floor, walls and ceiling of processing area	There will be improper cleaning of surfaces leading to transfer of air borne contamination (that settles on the surfaces) to the air / surfaces in the area after product changeover is completed. This could result in cross-contamination of next product Product failure More Market complaint observed	R02	• Failure to clean surfaces of floor, walls and ceiling for removal of air born particles accumulated during processing • Failure to reach out all the location in processing areas for cleaning during routine product change over and in-between the same product.	Medium	• The surfaces of floor, walls and ceiling in processing areas are smooth which allows ease of cleaning or decontamination during routine product change over and in-between the same product. • The corners of floor, walls and ceiling are provided with coving so as to permit ease of cleaning. • All the locations in processing areas are easily assessable so as to allow cleaning and there are no collection points for powder that may be difficult to clean. • Procedures are available for cleaning of processing areas during routine product change over and in-between the same product. • All the personnel in production are trained on the respective procedures.	Low	Yes

7.0 RISK ASSESSMENT (CONTD.):

Description of Risk identified	Risk Analysis and Evaluation				Current control measures	Risk classification based on control measures	Risk Acceptability (Yes/No)
	Potential Impact	Risk number	Failure mode	Risk classification based on risk identified			
Technical measures -AHU design							
In-adequate controls on the re circulated air through AHU	There will be transfer of air borne contaminant to air / surface after product change over cleaning. This will result in cross contamination of next product	R03	• Failure to design AHU with respect to recirculation of air through inadequate controls in place for the filtration system • Recirculation of untreated or insufficiently filtered air to processing areas	Medium	• AHUs of processing areas are having series of filters as follows for air supplied to processing area so to ensure that airborne contamination is removed prior to recirculation. ➢ 10µ (Pre-filter) fresh air ➢ fine Filter: 5µ ➢ 0.3 HEPA exhaust filter ➢ Semi HEPA filter 3 µ ➢ Terminal: 0.3µ HEPA ➢ Return riser: 10µ • The filters are having gaskets at the sides which provides fitment in filter housing thereby preventing passing of unfiltered air to different filtration system and finally to the processing areas. • AHU qualification has been performed for all the AHUs in processing areas covering parameters which are impacting its performance of air supplied meeting Class A, B, C & D. • Air velocity measurement is verified Once in a 6 months ± 30 days • HEPA filter integrity is verified during revalidation of AHU once in a 12 months ± 30 days • Pressure Differential reading is recorded at every 4 hrs. Interval on daily basis. • Air flow pattern test (Smoke test) is verified once in a 12 months ± 30 days • Non-viable particulate counts measurement is verified Once in a 6 months ± 30 days (FOR ISO CLASS 5, 6,7) • Viable Particle count test is performed on daily basis. • HEPA filter integrity is verified during revalidation of all the AHUs once in a year as per SOP no. SOP, SOP titled" Qualification of Air Filtration System" • The change rooms are provided for entry and exit to the processing areas through a gowning procedure • All the personnel in production,QA and engineering are trained on the respective procedures.	**Low**	Yes

		R04	Failure to design AHU with respect to air changes for controlling the air born particles generated during processing	Medium	• AHUs of processing areas are having more than 20 air changes per hour for processes where there is high risk of air born particles generated as per SOP no. SOP, SOP titled ” Qualification of Air Filtration System” • The air changes are verified during revalidation of all the AHUs in processing areas once in a year, and air velocity once in 6 month for RLAF, LAF.	**Low**	Yes

7.0RISK ASSESSMENT (CONTD.):

Description of Risk identified	Risk Analysis and Evaluation				Current control measures	Risk classification based on control measures	Risk Acceptability (Yes/No)
	Potential Impact	Risk number	Failure mode	Risk classification based on risk identified			
Technical measures -AHU design(Contd.)							
In-adequate controls on the recalculated air through AHU (Contd.)	**Contd.**	R05	• Damage to filters of AHU resulting in recirculation of untreated or insufficiently filtered air to processing areas • Blockage of filters of AHU during routine operation which can impact the air changes supplied to processing areas	Medium	• Magnahelic gauges are provided across fine filters of AHUs so as to indicate the pressure differential across filter and there by guiding the personnel for taking decision of any filter that is damaged. • Terminal HEPA filters of AHUs of processing areas are also having port for measuring pressure differential across filter for taking decision of any filter that is damaged. • The differential pressure indicated on the gauge of 3µ fine filters of AHU is recorded at AHU switch on time. • Monthly verification of differential pressure is in place across terminal HEPA filter. • The differential pressure data recorded is used for taking decision of filter cleaning or replacement of filter if it does not meet the acceptance criteria as defined Refer following SOPs for differential pressure SOP No., SOP titled “SOP For Measuring Pressure Drop Across HEPA Filter”. ➢ SOP no., SOP titled ”SOP for Operation of Air Handling Unit. • Filter cleaning procedure is in place to clean the filters (20µ, 10µ, 5µ and 3µ) as per defined frequency in SOP no., titled “SOP for AHU Filter Cleaning” • Preventive maintenance of AHU is performed every 3 month Refer SOP No., SOP titled “SOP for Annual Preventive Maintenance Plan” • Refer SOP no., SOP titled “SOP for Preparation and implementation of preventive maintenance plan” for annual preventive maintenance schedule of HVAC Equipments. • Documentation details during preventive maintenance is as follows ◦ Details are recorded in checklist ◦ Preventive maintenance schedule is updated w.r.t. planed vs. Actual preventive maintenance date ◦ History card of respective equipment is updated after completion of preventive maintenance. ◦ After preventive maintenance AHU checked for its smooth operation. Refer SOP, SOP titled “SOP for Preventive Maintenance of HVAC Equipments”	Low	Yes

7.0RISK ASSESSMENT (CONTD.):

Description of Risk identified	Risk Analysis and Evaluation				Current control measures	Risk classification based on control measures	Risk Acceptability (Yes/No)
	Potential Impact	Risk number	Failure mode	Risk classification based on risk identified			
Technical measures -AHU design(Contd.)							
In-adequate controls on the recirculated air through AHU (Contd.)	**Contd.**	R05	**Contd,**	**Contd,**	• Filters of AHU are cleaned during routine operation as per SOP, SOP titled "SOP for filter cleaning". • Filters of AHU are replaced during routine operation if differential pressure does not meet acceptance criteria or any damage is observed as per SOP, titled "Procedure for integrity testing & replacement of vent filter of water system". • Return risers in processing areas are cleaned during every change over as per SOP, SOP titled "SOP for filter cleaning of ahu, return riser & duct cleaning " • Documentation details during filter cleaning is as follows ➢ Details are recorded in the operation logbook of filter cleaning station ➢ Visual inspection is done after completion of filter cleaning activity. • All the personnel in production and engineering are trained on the respective procedures.	Contd	Contd

7.0RISK ASSESSMENT (CONTD.):

Description of Risk identified	Risk Analysis and Evaluation				Current control measures	Risk classification based on control measures	Risk Acceptability (Yes/No)
	Potential Impact	Risk number	Failure mode	Risk classification based on risk identified			
Technical measures -AHU design(Contd.)							
Restart of AHU of corridor and processing area	There will be transfer of air borne particles to the adjacent areas such as corridor and other processing areas due to disturbance in pressure cascade resulting in cross contamination	R06	• Failure of AHU of corridor or processing areas • Failure to restart the AHU of corridor or processing areas after any AHU stoppage (fault) or switch off of AHU during out of hours and power failure, in a predefined sequence	Medium	• In case of AHU stoppage or power failure, the AHU of processing areas is restarted first and then corridor, so to prevent accidental conveying of air born particles from processing areas to corridor. • Procedures are available for handling AHU failure or powder failure. • Processing of product is stopped and intimated to Engineering • Procedures are defined to evaluate an impact on the processing conditions during power failure or AHU stoppage. • Assessment of the time needed to return to a clean status once power is switched ON after power OFF is performed as a part of AHU qualification and same is followed routinely in-case of any failure. • Recovery test has been performed as per AHU qualification Schedule. • Magnahelic gauge indicates pressure differential outside the acceptance criteria and same is used for identifying any failure of AHU.	Low	Yes
		R07	• Failure in controlling temperature / humidity supplied to area based on product requirement.	Medium	• The temperature / humidity monitoring devises are provided in processing areas to monitor conditions as the product requirement. • Processing of product is stopped in-case of any failure of conditions and intimated to Engineering. • Daily monitoring RH,Temperature and differential pressure from Radix as per SOP. SOP titled “OPERATION OF AIR HANDLING UNIT” • All the personnel in production, QA and engineering are trained on the respective procedures.	Low	Yes

7.0RISK ASSESSMENT (CONTD.):

Description of Risk identified	Risk Analysis and Evaluation				Current control measures	Risk classification based on control measures	Risk Acceptability (Yes/No)
	Potential Impact	Risk number	Failure mode	Risk classification based on risk identified			
Technical measures - Equipment Design							
In adequate equipment design	There will be inadequate cleaning of surfaces of shared equipment/ tool through inadequate design of equipment impacting cleaning process and resulting in surface to surface cross contamination of next product	R08	Failure in equipment design with respect to ease of cleaning	Medium	**Equipment Design Controls** • The product contact surfaces of equipment's are having smooth surfaces which facilitate ease of cleaning and assure confirmation of cleanliness to a predefined limit for left over residue of previous product. • Equipments are cleaned during every change over as per respective SOP of cleaning. • Based on review of product contact parts of equipment's following parts can be easily cleaned and confirm cleanliness through visual inspection swabbing and rinse. ➢ SS 316 L ➢ Silicon • Following product parts of equipment's has been identified as product dedicated ➢ Dispensing tools ➢ Manifold ➢ Piston ➢ Cartridge Filter Integrity ➢ Filling Nozzle ➢ Silicone tubing's used for spraying of solution • All the personnel in production & QA are trained on the respective procedures.	Low	Yes

7.0 RISK ASSESSMENT(CONTD.):

Description of Risk identified	Risk Analysis and Evaluation				Current control measures	Risk classification based on control measures	Risk Acceptability (Yes/No)
	Potential Impact	Risk number	Failure mode	Risk classification based on risk identified			
Technical measures - Equipment Design(Contd.)							
Inadequate containment of powder generated at source from different processes	There will power generation in processing areas resulting in blockage of return risers in area. This will in turn result in disturbance in pressure cascade and AHU performance with respect to Air changes thus resulting in cross contamination The personnel working in area will be exposed to the air born particles The air born particles will be transferred to the gowns worned by the personnel.	R09	• Failure to control the spread of powder generated at source during processes such as ➢ Sifting ➢ Mixing ➢ Granulation ➢ Drying ➢ Milling/grading ➢ Tablet inspection ➢ Compression ➢ Capsule filling ➢ Blister Packing	Medium	• Types of processes used during manufacturing of Tablet products have been reviewed with respect to release of powder to the environment during processing. These process have been grouped under following categories ➢ High risk processes includes: Dispensing, Sampling of raw materials, Sifting, Milling/ Grading of material, Racking of material during drying, Loading/unloading of material or granules or tablet, etc. ➢ Medium risk processes includes: Mixing/Granulation in Rapid Mixer Granulator, Blending, Compression, Coating, Packing of uncoated products (Blister Packing) etc. ➢ Low risk processes include: Inspection and packing of coated products (Blister Packing) • Certain parts of equipment's are having dust extraction so as to control the powder generated at source and prevents in release to environment in processing areas ➢ Compression zone at turret of compression Machine ➢ Feeding parts and Vibrator of Blister Packing Machine. ➢ Deduster of Compression Machine • Certain machines are having lifter type of arrangement for hopper which conveys granules to certain height and then feed it to the hopper of equipment. • In this case Bin Blender is used for transfer of dried granules to the hopper of equipment.	Low	Yes

7.0RISK ASSESSMENT(CONTD.):

Description of Risk identified	Risk Analysis and Evaluation				Current control measures	Risk classification based on control measures	Risk Acceptability (Yes/No)
	Potential Impact	Risk number	Failure mode	Risk classification based on risk identified			
Technical measures - Equipment Design(Contd.)							
Inadequate containment of powder generated at source from different processes **(Contd.)**	**Contd.**	R09 (Contd.)	Failure to control the spread of powder generated at source (Contd.)	Medium	• Gaskets are provided for certain parts such as lid of Mixing Tank, Holding Tank & Buffer vessel. This type of arrangement will provide air tight sealing. • Processes such have Dispensing and samplings are having Reverse Laminar Air Flow equipment's for controlling the powder generation in areas. • Enclosures are provided to certain parts of following equipment's to prevent release of powder to the environment in processing areas. ➢ Compression machine ➢ Blister Packing Machine • In-case of following equipment's charging ports are provided for feeding of powder or granules to the equipment which prevents entire opening of lid of equipment. This type of arrangement minimises the release of powder to environment in processing areas. ➢ Rapid Mixer Granulator ➢ Coating Machine ➢ Bin • Certain process which involves charging of powder / granules /tablets which involves powder generation, precautionary measures such as slow addition, direct charging from container or immediate closing of lid of hopper / equipment are followed by operating personnel.	Low	Yes

7.0 RISK ASSESSMENT(CONTD.):

Description of Risk identified	Risk Analysis and Evaluation				Current control measures	Risk classification based on control measures	Risk Acceptability (Yes/No)
	Potential Impact	Risk number	Failure mode	Risk classification based on risk identified			
Technical measures - Equipment Design(Contd.)							
Inadequate containment of powder generated at source from different processes **(Contd.)**	**Contd.**	R09 (Contd.)	Failure to control the spread of powder generated at source (Contd.)	Medium	• In following equipment's, precautionary measures are taken with respect time allowed for powder to settle in the equipment before opening ➢ After mixing in Rapid Mixer Granulator ➢ After Mixing in Bin Blender ➢ After drying in Fluid Bed Dryer ➢ After completion of milling process/sifting process etc. • During milling / sifting process,/ polybags are connected to the discharge which feeds the material/granules to bin. • All the personnel in production are trained on the respective procedures.	Low	Yes
Inadequate containment of purified water & water for injection generated at source from different processes	**Contd.**	R09 (Contd.)	• Failure to control the spread of water generated at source • Passivation sanitization was not peformed during qualication activity • PW & WFI Sampling plan is not prepared • PW & WFI sampling not performed according to sampling plan. • Conductivity failure • Circulation of water is not proper in loop line.	Medium	• In following instruments, precautionary measures are taken with respect time allowed for PW & WFI Genration. ➢ Passivation are completed after installation ➢ sanitization are performed on Monthly basis. ➢ Conductivity meter is installed in return loop line ➢ Automatic Actuated Valve ➢ valve & zero dedleg valve installed. ➢ pH meter installed. ➢ sampling plan available ➢ operation of PW & WFI process available. After completion of DQ, IQ & OQ of water system (PW & WFI), PQ was successfully performed. No any deviation has been observed & continue monitoring is running according to sampling plan. Refer SOP, SOP titled "Operation of Purified Water System" SOP titled "Operation of Purified Water Circulation Loop" SOP titled "Cleaning & Sanitization of Purified Water System" SOP titled "Qualification of Water system"	Low	Yes

Backflow or leakage of powders through the dust collector pipelines	• Backflow of powder will result in cross-contamination of next product if not cleaned or controlled • The leakage of powder though the pipelines will result in contamination of service areas	R10	Failure to exercise control back flow of powder from utilities such as pipe lines of dust collectors	Medium	• The pipelines connected to dust collectors and equipment's are having valves which prevent possibility of back flow of powder thereby controlling risk of cross-contamination. • The powder collected in the dust collectors is regularly cleaned which can affect its performance. • The filters of dust collector are cleaned as per the procedure. • The joints of pipelines of dust collectors are sealed so as to prevent release of powder in the area though which it is passed till the collection point. • Preventive maintenance of duct work or transfer line is performed which includes verification of any issues related to leaks which could contaminate other areas. • Documentation details during preventive maintenance follow & details are recorded in checklist • All the personnel in production are trained on the respective procedures.	Low	Yes

7.0RISK ASSESSMENT (CONTD.):

Description of Risk identified	Risk Analysis and Evaluation				Current control measures	Risk classification based on control measures	Risk Acceptability (Yes/No)
	Potential Impact	Risk number	Failure mode	Risk classification based on risk identified			
Technical measures - Equipment Design(Contd.)							
Inadequate containment within the dispensing and sampling area and In-adequate controls on the recirculated air through RLAF	There will be transfer of air borne contaminant to air / surfaces of adjacent areas. There will be transfer of air borne contaminant to air / surface after product change over cleaning. This will result in cross contamination of next product	R11	• Failure to exercise controls in areas on area where materials are sampled or dispensed with respect to cleaning between different products to prevent the spread of powder generated at source and cross contamination such as ➢ Sampling ➢ Dispensing • Failure to design Reverse Laminar Air Flow (RLAF) with respect to recirculation of air through inadequate controls in place for the filtration system • Recirculation of untreated or insufficiently filtered air to processing areas.	Medium	• Processes such as Dispensing and Sampling are having RLAF for controlling the powder generation in areas. • RLAFs are having series of filters as follows for air supplied to processing area so to ensure that airborne contamination is removed prior to recirculation. ➢ AHU plenum: 10µ and 5µ ➢ Supply: 0.3 µ HEPA ➢ Return riser: 3µ • The filters are having gaskets at the sides which provides fitment in filter housing thereby preventing passing of unfiltered air to different filtration system and finally to the material handling areas. • RLAF qualification has been performed covering parameters which are impacting its performance of supply air • Air velocity measurement is verified Once in a 6 months ± 30 days • HEPA filter integrity is verified during revalidation of RLAF once in a 12 months ± 30 days • Pressure Differential reading is recorded at every 4 hrs. Interval on daily basis. • Air flow pattern test (Smoke test) is verified once in a 12 months ± 30 days • Non-viable particulate counts measurement is verified Once in a 6 months ± 30 days (FOR ISO CLASS 5, 6,7) • Viable Particle count test is performed on daily basis. • All the personnel in production, QA and engineering are trained on the respective procedures Refer SOP, SOP titled" Qualification of Air Filtration System"	Low	Yes

7.0RISK ASSESSMENT (CONTD.):

Description of Risk identified	Risk Analysis and Evaluation				Current control measures	Risk classification based on control measures	Risk Acceptability (Yes/No)
	Potential Impact	Risk number	Failure mode	Risk classification based on risk identified			
Technical measures - Equipment Design(Contd.)							
Inadequate containment within the dispensing and sampling area and In-adequate controls on the re circulated air through RLAF**(Contd.)**	**Contd.**	R12	• Damage to filters of RLAF resulting in recirculation of untreated or insufficiently filtered air • Blockage of filters of RLAF during routine operation which can impact the air supplied to areas	Medium	• Magnahelic gauges are provided for following filters of RLAF so as to indicate the pressure differential across filter and there by guiding the personnel for taking decision of any filter that is damaged. • The differential pressure indicated on the gauge of filters of RLAF is recorded as per SOP • The differential pressure data recorded is used for taking decision of filter cleaning or replacement of filter if it does not meet the acceptance criteria as defined and same is intimated to production area. • Preventive maintenance of RLAF is performed as per SOP which includes verification of filters for any damage. • Documentation details during preventive maintenance is as follows ➢ Details are recorded in checklist ➢ Proper tightening of filter is verified after completion. ➢ Any damage to filter is verified • Return risers of RLAF are cleaned during every change over as per SOP titled" SOP for Dispensing Booth Filter Cleaning" • Documentation details during filter cleaning is as follows ➢ Details are recorded in the checklist ➢ Proper tightening of filter is verified after completion. • All the personnel in production, QA and engineering are trained on the respective procedures.	Low	Yes

7.0RISK ASSESSMENT (CONTD.):

Description of Risk identified	Risk Analysis and Evaluation				Current control measures	Risk classification based on control measures	Risk Acceptability (Yes/No)
	Potential Impact	Risk number	Failure mode	Risk classification based on risk identified			
Technical measures - Equipment Design(Contd.)							
Restart of RLAF during failure	There will transfer of air born particles to the containers in which materials are stored and materials that are dispensed / sampled	R13	Failure to exercise control during any stoppage of RLAF	Medium	• Procedures are available for handling of powder failure • Dispensing / sampling of material is stopped and intimated to Engineering as per SOP titled “Intimation, necessary action and documentation in-case of Breakdown of Machine and Systems”. • Procedures are defined to evaluate an impact on the processing conditions during power failure or RLAF stoppage. • Assessment of the time needed to return to a clean status once power is switched ON after power OFF is performed as a part of RLAF qualification and same is followed routinely in-case of any failure. • Magnahelic gauge indicates pressure differential outside the acceptance criteria and same is used for identifying any failure of RLAF. • All the personnel in production, QA and engineering are trained on the respective procedures.	Low	Yes

7.0RISK ASSESSMENT (CONTD.):

Description of Risk identified	Risk Analysis and Evaluation				Current control measures	Risk classification based on control measures	Risk Acceptability (Yes/No)
	Potential Impact	Risk number	Failure mode	Risk classification based on risk identified			
Technical measures - Equipment Design(Contd.)							
Inadequate monitoring of process parameters which controls cleaning process	There will failure to clean the equipment surfaces as per simulation during cleaning validation	**R14**	Failure to design cleaning process with respect to monitoring of critical parameters during cleaning process	Medium	• In certain areas High pressure jet machines which are used for cleaning of equipment's/parts are qualified with respect to assurance of cleaning procedures • Monitoring devices such as pressure gauges are available for indicating the pressure during cleaning process. • The High pressure jet machines are verified for its operation and shall be covered as a part of routine preventive maintenance.	Low	Yes
Malfunctioning of measuring instruments of AHU , RLAF and equipment's used for cleaning	There will be failure to clean the equipment surfaces as per simulation during cleaning validation There will impact on the performance on AHU/RLAF etc.	**R15**	Failure to exercise controls to identify malfunctioning of measuring instruments	Medium	• Calibration of measuring instruments is performed as per the schedule mentioned in the SOPs. SOP titled "calibration Policy" discontinue • The measuring instruments associated with processing equipment's and areas routinely checked for proper functioning. • The measuring instruments associated with equipment used for cleaning are checked for its proper functioning prior to start of cleaning process. • There is procedure available for handling any calibration failure or malfunctioning of measuring instruments which involves evaluation of potential impact on cross contamination and cleaning validation.	Low	Yes
Identification and cleaning of difficult to clean locations of equipment's	There will be inadequate cleaning of surfaces of shared equipment product contact parts Improper cleaning will result in surface to surface cross contamination of next product	**R16**	Failure to identify difficult to clean parts for confirming cleanliness after product change over cleaning	Medium	• The difficult to clean parts of equipment has been identified for each equipment with appropriate justification based on the following ➢ Material of construction of product contact parts ➢ Level of dismantling for cleaning ➢ Ease of access for cleaning ➢ Cleaning agent used for equipments cleaning. ➢ Check the light intensity. ➢ Time taking for cleaning ➢ Water pressure ➢ Water quantity • The difficult to clean parts are verified for visual cleanliness as a part of lines clearance during product change over. • The difficult to clean parts are covered for swab sampling or rinse sample during cleaning validation/ cleaning verification Refer SOP.	Low	Yes

7.0 RISK ASSESSMENT (CONTD.):

Description of Risk identified	Risk Analysis and Evaluation				Current control measures	Risk classification based on control measures	Risk Acceptability (Yes/No)
	Potential Impact	Risk number	Failure mode	Risk classification based on risk identified			
Technical measures - Equipment Design(Contd.)							
Inadequate control on air supplied for processing of equipment's	There will be contamination of product due to improper filtration of air supplied to equipment	**R17**	• Failure to design adequate filtration system which supplies filtered air to equipment that is coming in direct contact with product in-case of following equipment's ➢ Fluid Bed Dryer ➢ Coating machine • Supply of untreated or insufficiently filtered air to equipment.	Medium	• Processes such has Fluid Bed Dryer and Coating Machine are having filtration system with series of filters as follows for air supplied to equipment so to ensure that contamination is removed ➢ 20µ & 5µ or 10 µ (As per equipment suppliers design) ➢ 3 µ (As per equipment suppliers design) ➢ 0.3 µ HEPA • The filters are having gaskets at the sides which provides fitment in filter housing thereby preventing passing of unfiltered air equipment. • Qualification has been performed covering parameters which are impacting its performance of supply air • HEPA filter integrity is verified during revalidation as per SOP, SOP titled" Qualification of HVAC, LAF, RLAF, APU and Vacuum cleaning System" • All the personnel in production, QA and engineering are trained on the respective procedures.	Low	Yes

7.0RISK ASSESSMENT (CONTD.):

Description of Risk identified	Risk Analysis and Evaluation				Current control measures	Risk classification based on control measures	Risk Acceptability (Yes/No)
	Potential Impact	Risk number	Failure mode	Risk classification based on risk identified			
Technical measures - Equipment Design(Contd.)							

Inadequate control on air supplied for processing of equipment's**(Contd.)**	Contd.	**R17**	• Damage to filters of filtration system for equipment resulting in supply of untreated or insufficiently filtered air
			• Blockage of filters during routine operation which can impact the air supplied to equipment
				Medium	• HEPA filter integrity is verified during revalidation as per SOP titled" Qualification of HVAC, LAF, RLAF, APU and Vacuum cleaning System"
					• Preventive maintenance of filtration system of equipment is performed every month as per SOP titled "SOP for Preventive Maintenance of FBD, and SOP titled "SOP for Preventive Maintenance of Coating machine' as Per Schedules and Its Documentation" which includes verification of pre-filters for any damage.
					• Documentation details during preventive maintenance is as follows
					  • Details are recorded in checklist
					  • Proper tightening of filter is verified after completion.
					  • Any damage to filter is verified
					• Documentation details during filter cleaning is as follows
					  ➢ Details are recorded in the checklist
					  ➢ Proper tightening of filter is verified after completion.
					  ➢ Any damage to filter is verified before starting for routine operation.
					• All the personnel in production and engineering are trained on the respective procedures.
						Low	Yes

7.0RISK ASSESSMENT (CONTD.):

Description of Risk identified	Risk Analysis and Evaluation				Current control measures	Risk classification based on control measures	Risk Acceptability (Yes/No)
	Potential Impact	Risk number	Failure mode	Risk classification based on risk identified			
Technical measures - Equipment Design(Contd.)							
Inadequate control on air that is exhausted out from the equipment's	There will be contamination of environment in which the air is exhausted out.	**R18**	• Failure to design adequate filtration system for air that is exhausted out in-case of following equipment's ➢ Fluid Bed Dryer ➢ Coating machine	Medium	• Processes such has Fluid Bed Dryer and Coating machine are having HEPA filters for filtration system of air that is exhausted out from equipments to ensure that contamination is removed • The filters are having gaskets at the sides which provides proper fitment in filter housing thereby preventing passing of unfiltered air that is exhausted from equipment. • HEPA filter integrity is verified during revalidation of once in a year. • All the personnel in production and engineering are trained on the respective procedures.	Low	Yes

		R19	• Damage to HEPA filters of filtration system which will exhaust out untreated or insufficiently filtered air from equipment
			• Blockage of HEPA filters of during routine operation which can impact the air that is exhausted out from equipment
				Medium	• Filter cleaning procedure is in place to clean the filter as per cleaning frequency.
					• The differential pressure indicated on the gauge of filter is recorded
					• Preventive maintenance of filtration system of is performed as per SOP, titled "SOP for Filter cleaning, Replacement and Destruction of filters" which includes verification of filters for any damage as per SOP 'Replacement of Filter'.
					• Documentation details during preventive maintenance is as follows
					  • Details are recorded in checklist
					  • Proper tightening of filter is verified after completion.
					  • Any damage to filter is verified
					  • Differential pressure is verified before releasing for routine operation.
					• All the personnel in production and engineering are trained on the respective procedures.
						Low	Yes

7.0RISK ASSESSMENT (CONTD.):

Description of Risk identified	Risk Analysis and Evaluation				Current control measures	Risk classification based on control measures	Risk Acceptability (Yes/No)
	Potential Impact	Risk number	Failure mode	Risk classification based on risk identified			
Organizational Measures							
Movement of dirty mobile equipment's like Manifold, Nozzle filter housing & transfer line (silicon & SS) within the processing areas.	The contaminant of product from dirty equipment will fall into the corridor during movement. The product particles fallen could be conveyed to the adjacent areas resulting in cross contamination	R20	Failure to design procedure and routinely follow during movement of dirty Manifold, Nozzle, filter housing & transfer line (silicon & SS) within the processing areas	Medium	• The movement of Manifold, Nozzle filter housing & transfer line (silicon & SS) within the processing areas is controlled as follows to prevent risks of cross contamination of others products processed in adjacent areas. ➢ The external surfaces of like Manifold, Nozzle filter housing & transfer line (silicon & SS) are cleaned prior to movement to other areas. ➢ The equipment's like Manifold, Nozzle filter housing & transfer line (silicon & SS) are transferred in closed condition rapped with poly beg prior to movement to washing & sterilization area. • All the personnel in production, QA are trained on the respective procedures. Refer, SOP titled "Cleaning and storage of stainless steel container, scoops, mugs and other accessories used in manufacturing.'	Low	Yes

7.0RISK ASSESSMENT (CONTD.):

Description of Risk identified	Risk Analysis and Evaluation				Current control measures	Risk classification based on control measures	Risk Acceptability (Yes/No)
	Potential Impact	Risk number	Failure mode	Risk classification based on risk identified			
Organizational Measures (Contd.)							
Movement/ transfer of cleaned equipment's from storage areas to required processing areas	The air borne contamination will be settled on the surfaces of cleaned equipment's if not closed. The contaminant settled on the surfaces will result in cross contamination of next product	R21	Failure to design procedure and routinely follow during the movement/ transfer of cleaned mobile equipment's Manifold, Nozzle filter housing & transfer line (silicon & SS) from storage areas to the processing areas	Medium	• The movement of cleaned Manifold, Nozzle filter housing & transfer line (Located in different rooms) to the processing areas is controlled as follows to prevent risks of cross contamination of others products processed in adjacent areas. ➢ Open parts of equipment's are covered with poly bags prior to movement to other areas. • All the personnel in production are trained on the respective procedures Refer SOP no., SOP titled "Cleaning and storage of stainless steel container, scoops, mugs and other accessories used in manufacturing.'	Low	Yes
In adequate controls on the equipment that is un cleaned and cleaned in washing area Inadequate design of wash area	The air borne contamination generated in wash area during cleaning along with improper segregation identification and protection will results cross– contamination	R22	Failure to design procedure and routinely follow the control in wash rooms with respect to risk of cross-contamination or recontamination	Medium	• The wash rooms are designed in such a way that the residue of the previous product being cleaning from equipment's and accessories can be cleaned and removed through a drain provided • The AHU system is having return risers which allows control of air born particles release in area from the equipment being cleaned. • The washing is controlled in such a way that cleaned items are prevented for recontamination. • The cleaning of wash room is performed to ensure that there is no risk of cross-contamination or recontamination. • The status labels are affixed to equipment's and accessories for clear identification of cleared and cleaned items as per SOP titled " Status Labeling" • The cleaned equipment's and accessories are transferred to cleaned controlled area from washing & sterilization room after covering with polybag. • All the personnel in production are trained on the respective procedures.	Low	Yes

7.0RISK ASSESSMENT (CONTD.):

Description of Risk identified	Risk Analysis and Evaluation				Current control measures	Risk classification based on control measures	Risk Acceptability (Yes/No)
	Potential Impact	Risk number	Failure mode	Risk classification based on risk identified			
Organizational Measures(Contd.)							
Inadequate identification of previous product processed on the equipment	There will be cross contamination of next product processed on the equipment if identification of product processed is improper	**R23**	Failure to identify equipment's / product contact parts of equipment's for the product for which it was used for processing	Medium	• The equipment log books are used for documentation and identification for which the equipment was used for processing. • Status labeling is affixed on the movable or fixed equipment/ accessories/ product contact parts which provide identification for which the equipment was used for processing. to prevent mix up/ cross contamination. Refer SOP titled " Status Labeling"	Low	Yes
Inadequate identification of dedicated product contact part / dedicated equipment's	There will be cross contamination of next product processed on the equipment if identification is improper	**R24**	Failure to identify dedicated equipment's / dedicated product contact parts of equipment's	Medium	• Procedure is available for identification and controlling of dedicated equipment/parts. • The equipment log books are used for documentation and identification for which the equipment was used for processing. • The dedicated equipment/parts are having status label or engraving or marking, so as to prevent accidental use of parts for processing of different product other than for which it has been dedicated. Refer SOP titled " Status Labeling"	Low	Yes
Inadequate identification of products / materials stored in the storage area	There will be mix-up of products /materials due to improper identification	**R25**	Failure to identify and follow measures for handling of products / material during storage	Medium	• The status labels are affixed on the polybag or container used for storage of material/ product to prevent cross-contamination and / or mix-up from the material/ products having hazards. • The products / materials are handled with precautionary measures such as wearing gloves. • Rack wise product segregate & numbering system are allotted. • Approved materials are having under the green line with status labeled. • Under testing material are having under the yellow line with status labeled • Rejected materials are having under the red line with status labeled. Refer SOP titled " Status Labeling"	Low	Yes
Contamination of products stored in polybag/ container's	There will be cross contamination of product if it is not properly sealed to due transfer of air borne particles	**R26**	Failure to control cross contamination from the surfaces of containers / polybag after sampling or dispensing or unloading of processed product in containers / vessel	Medium	• The containers / poly bags are sealed and closed until used for processing. • The external surfaces of containers / polybag (e.g. after sampling or dispensing or unloading of processed product in containers / vessel) are cleaned before transfer to storage location for preventing risk from cross-contamination.	Low	Yes

7.0 RISK ASSESSMENT (CONTD.):

Description of Risk identified	Risk Analysis and Evaluation				Current control measures	Risk classification based on control measures	Risk Acceptability (Yes/No)
	Potential Impact	Risk number	Failure mode	Risk classification based on risk identified			
Organizational Measures(Contd.)							
Inadequate cleaning of Scoops used in sampling and dispensing Inadequate cleaning of sampling tools used during processing	There will be inadequate cleaning of surfaces of sampling tools/ dispensing tools Improper cleaning will result in surface to surface cross contamination of next product	**R27**	Failure to control contamination for Scoop used for sampling / dispensing and sampling equipment's used during processing	Medium	• The scoop used during sampling and dispensing are cleaned as per the respective cleaning procedures. • In-case of certain products dedicated scoops fare used for sampling / dispensing • Scoops used for sampling and dispensing are covered during cleaning validation. • Status labels are affixed on the tools to identify the details of product for which it is used. Refer following SOPs ➢ SOP titled "Cleaning and Storage of Dispensing Equipments"	Low	Yes
Spillage of product/ material in Store & Processing Area	There will be transfer of air borne contaminant to air / surfaces of adjacent areas such as corridor and other processing areas resulting in cross contamination The personnel in the processing areas will be exposed to the hazards of API due to air borne particles.	**R28**	Failure to exercise controls on the spillages during routine operation	Medium	• There is a requirement to remove spillages observed during processing and clean area. • The personnel involved in clearing the spillage and cleaning of area are trained with respect to procedure that needs to be followed for products along with precautions based on hazards involved with the material/product. • Impact assessment is performed if there is situation of spillages or other unusual events that could lead to cross-contamination of following in the close vicinity of area where incident occurred ➢ During clearing the spillages material proper covered the face, hand & other body part to prevent the any hazards. ➢ Equipment's/ parts of equipment' stored ➢ Containers / polybag of materials/ products stored. Refer following SOPs SOP titled "Handling of Spillage in Store " SOP titled "Spillage Handling"	Low	Yes

7.0 RISK ASSESSMENT (CONTD.):

Description of Risk identified	Risk Analysis and Evaluation				Current control measures	Risk classification based on control measures	Risk Acceptability (Yes/No)
	Potential Impact	Risk number	Failure mode	Risk classification based on risk identified			
Organizational Measures(Contd.)							
Entry / Exit procedure to Grade C Area & Aseptic processing areas	The personnel in the processing areas will be exposed to the hazards of product due to air borne particles. The air born particles on the gowns will lead to cross-contamination	**R29**	Failure to follow entry and exit procedure and precautionary measures as per hazards associated with the product	Medium	• Only authorized personnel are allowed to enter into the aseptic area. • The entry and exit to Grade C Area is though a change rooms after Remove slippers / shoes in Air lock-I and keep them systematically in SS Rack. Enter into the Air lock-II, by pushing the door with elbow. After that enter in garment room for wearing the cleaned cleaned garment. • The entry and exit to Aseptic processing areas is though a change rooms after removing the factory garment & enter to air lock I II & III in sequence. • The gowns are disposed for cleaning after exit from processing areas • Refer following SOPs ➢ SOP titled “Entry and Exit Procedure in Grade C Area” ➢ SOP titled “Entry and Exit Procedure in Aseptic Area”	Low	Yes
Organizational measures - Control through Campaign Manufacture							
Product change over cleaning procedures	There will be inadequate cleaning of surfaces of shared equipment through inadequate cleaning procedures resulting in surface to surface cross contamination of next product There will be transfer of air borne contaminant to air / surfaces from processing areas	**R30**	Failure to control carryover of product residues of previous products based on the hazards	Medium	• The products which requires manufacturing are identified based on toxicological assessment and PDE value so as to prevent cross contamination • There is requirement of reducing the contamination of equipment’s in the area where products having certain hazards are processed through following measures ➢ Removal of equipment from the area that is not required during campaign manufacturing of the product. These equipment’s are transferred with clean status. ➢ Equipment’s that are not required for production but cannot be removed from the area are covered. There equipment’s are also re-cleaned during product change over cleaning. • The controls are exercised for the movement of ancillary equipment (e.g. IPC test equipment) and materials between campaigns (of different products). • The procedure for campaign change over includes requirement of cleaning of product contact equipment, cleaning of non-product surfaces (Such as chairs, fire extinguishers, computer systems of equipment’s, return risers of AHU, exterior of equipment, walls, floors etc.	Low	Yes

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7.0 RISK ASSESSMENT(CONTD.):

Description of Risk identified	Risk Analysis and Evaluation				Current control measures	Risk classification based on control measures	Risk Acceptability (Yes/No)
	Potential Impact	Risk number	Failure mode	Risk classification based on risk identified			
Organizational measures - Equipment Cleaning and Inspection Controls							
Product change over cleaning procedures of equipment	There will be inadequate cleaning of surfaces of shared equipment through inadequate cleaning procedures resulting in surface to surface cross contamination of next product.	**R31**	Failure to design cleaning procedures based on product requirement	Medium	• The cleaning procedures of equipment's in different areas has been evaluated and covers the requirements of cleaning for all the products currently included in product matrix / equipment matrix that is maintained as a part of Cleaning Validation Master Plan. Refer SOP titled "Cleaning Validation" • The suitability of cleaning procedures for any new product introduced at site assessed as a part of cleaning validation evaluation as per respective CVMP.	Low	Yes
	There will be transfer of air borne contaminant to air / surfaces from processing areas	**R32**	Failure to exercise control on preventing re-contamination if cleaning of area is not performed in coordination with cleaning of equipment	Medium	During product changeover of the product there is coordination cleaning of area along with equipment cleaning so as to prevent re-contamination.	Low	Yes

7.0RISK ASSESSMENT (CONTD.):

Description of Risk identified	Risk Analysis and Evaluation				Current control measures	Risk classification based on control measures	Risk Acceptability (Yes/No)
	Potential Impact	Risk number	Failure mode	Risk classification based on risk identified			
Organizational measures - Equipment Cleaning and Inspection Controls (Contd.)							
Product change over cleaning procedures of equipment **(Contd.)**	There will be inadequate cleaning of surfaces of shared equipment through inadequate cleaning procedures resulting in surface to surface cross contamination of next product	R33	Failure to design cleaning procedures of equipment's covering detailed instruction that needs to be followed	Medium	• Cleaning procedures of equipment's in different areas has been evaluated and includes following as a part of **routine cleaning procedure** which needs to be followed during product change over cleaning ➢ Cleaning instructions are provided in cleaning procedures so as to control the hazard level ➢ Cleaning instructions are outlined based on design and complexity of equipment. ➢ Instructions for dismantling of different parts of equipment for assuring consistent cleaning process has been defined in the procedures ➢ Cleaning procedures includes instructions related to, ❖ Details of hard to clean areas which needs additional precautions during cleaning ❖ Requirement of scrubbing of parts, ❖ Details of LUX intensity of light for visual inspection. ❖ Details of volume of water ❖ Details of pressure of water which needs to applied. ❖ Details of cleaning agent which are used for cleaning. ❖ Details of equipments cleaning time. ➢ There is requirement defined for cleaning of equipment within the dirty hold time established based on dirty equipment hold time study. ➢ There is requirement defined for use of equipment's within cleaned hold time established. • Cleaning procedures of equipment's includes checklist covering above requirements. These checklists are used for documentation of cleaning process. • The details documented in the checklist are reviewed as a part of line clearance.	Low	Yes
Product change over cleaning procedures of vacuum transfer system	There will be inadequate cleaning of surfaces of shared accessories through inadequate cleaning procedures of vacuum cleaning system resulting cross contamination of next product	R34	Failure to exercise control contamination from Vacuum cleaning system used during cleaning	Medium	• Procedures are available for cleaning of vacuum transfer system to prevent such items from being a potential source of contamination. Refer SOP titled as 'Operation and Cleaning of Vacuum Cleaner.	Low	Yes

7.0RISK ASSESSMENT (CONTD.):

Description of Risk identified	Risk Analysis and Evaluation				Current control measures	Risk classification based on control measures	Risk Acceptability (Yes/No)
	Potential Impact	Risk number	Failure mode	Risk classification based on risk identified			
Organizational measures - Equipment Cleaning and Inspection Controls (Contd.)							
Product change over cleaning procedures of closed equipment and transfer pipelines	There will be inadequate cleaning of surfaces of shared equipment through inadequate cleaning procedures resulting in surface to surface cross contamination of next product	R35	Failure to design a procedure for assuring cleanliness of closed process equipment and transfer pipelines where visual inspection is not possible	Medium	Adequate justification is provided for selection of closed process equipment and transfer pipelines as a part of sampling for testing of left over carryover from product residue during cleaning validation where visual inspection is not possible. • In-case of certain closed process equipment and transfer pipelines where visual inspection is not conducted, there is a requirement defined for witnessing the cleaning. Equipment • After cleaning of closed process equipment & transfer pipeline where cleaning is not verified by visually. Cleaning can be justified by rinse sampling. • Refer following SOPs SOP titled “Procedure for Sampling of Rinse Water / Swab”	Low	Yes
Line clearance procedure during product change over cleaning	There will be failure to identify left over residues of previous product resulting in surface to surface cross contamination of next product	R36	Failure to design a line clearance procedure for equipment’s during product change over cleaning	Medium	• Cleaning procedures of equipment’s in different areas has been evaluated and includes following **visual inspection requirements** as a part of routine procedure which needs to be followed during line clearance of product change over. ➢ There is requirement for verification of cleanliness of equipment though visual inspection ➢ Visual inspection process defines requirement of inspection of difficult to clean product contact parts to assure detection of potential contaminants ➢ In-case of certain equipment’s there is requirement of visual inspection of parts after cleaning and before reassembly ➢ There is procedural requirement of use of SS mirror and/or torch to help for detection of residues on cleaned surfaces by visual inspection • The final visual inspection is independently performed by QA personnel as a part of line clearance during product change over cleaning. • During line clearance procedure any potential cross-contamination sources are identified prior to release of equipment • The personnel who perform the visual inspection are involved during cleaning validation and are trained by senior personnel through On Job training for assuring inspection in a consistent manner.	Low	Yes

7.0RISK ASSESSMENT (CONTD.):

Description of Risk identified	Risk Analysis and Evaluation				Current control measures	Risk classification based on control measures	Risk Acceptability (Yes/No)
	Potential Impact	Risk number	Failure mode	Risk classification based on risk identified			
Organizational measures - Equipment Cleaning and Inspection Controls (Contd.)							
Line clearance procedure during product change over cleaning **(Contd.)**	**Contd.**	R37	Failure to design a line clearance procedure for equipment's during product change over cleaning**(Contd.)**	Medium	• The personnel who conducts visual inspection are also trained on the requirements defined in SOP Refer following SOPs SOP titled "Procedure for Qualification of Visual Inspector • There is requirement for verify results of residual testing prior to release of equipment for next product after cleaning of equipment. Refer following SOPs SOP titled "Procedure for Sampling of Rinse Water / Swab" • There is a requirement to investigate the failure results for swab/rinse sample obtained during residual testing.	Low	Yes
Organizational measures - Cleaning Validation and Cleaning Verification							
Assurance of cleaning procedures	There will be inadequate cleaning of surfaces of shared equipment through inadequate cleaning procedures resulting in surface to surface cross contamination of next product	R38	Failure to exercise controls related to cleaning validation and verification of equipment's so as to prevent cross-contamination from the material/ products having certain hazards	Medium	• The products handled at site are identified for cleaning validation based on following ➢ Evaluation of toxicological assessment and PDE value ➢ Product characteristics such as solubility, lowest therapeutic dose and difficult to clean nature of product - • Identification of worst case product for cleaning is covered as a part of Cleaning Validation Master Plan and document title "Strategy for Managing Risks associated with Cross Contamination of Products in Shared Manufacturing Facility". • Product matrix and equipment matrix are maintained at site which indicates worst case product for cleaning validation. • Certain products having hazards which needs controls has been identified and cleaning verification is performed during every product changeover.	Low	Yes

7.0RISK ASSESSMENT (CONTD.):

Description of Risk identified	Risk Analysis and Evaluation				Current control measures	Risk classification based on control measures	Risk Acceptability (Yes/No)
	Potential Impact	Risk number	Failure mode	Risk classification based on risk identified			
Organizational measures - Cleaning Validation and Cleaning Verification(Contd.)							
Assurance of cleaning procedures	**Contd.**	R38	**Contd.**	Medium	• The MACO limits for the carryover of product residues are calculated based on PDE value, dose criteria & also visual inspection. The least value is considered for cleaning validation. • The swab and rinse sampling techniques are used for assurance of cleaning to an established MACO level. • In certain equipment where visual inspection of equipment or certain parts of equipment (e.g. closed systems or pipeline) is not possible, then rinse sampling technique is for assuring cleanliness. • The number and location (Such as difficult to clean locations) for swab samples during cleaning validation/ cleaning verification are identified based on evaluation of equipment design and hazard level of product, • The cleaning processes of all the equipment's are covered during cleaning validation so as to demonstrate that the cleaning process can be consistently followed by personnel. In certain cases, equipment's are grouped together based on identical design, cleaning procedures etc. • The cleaning procedures of equipment include checks covering all variables and opportunities that will represent the failure of manual cleaning. • Certain products identified as worst case based on evaluation of product characteristics as considered for periodic verification at a frequency of every three years. • There is procedure available for verification of equipment surfaces routinely, for ease of cleaning or any wear and tear after repeated use over a time since its installation and its potential impact on the validated cleaning procedures Refer Cleaning Validation Master Plan of respective areas and SOP titled "Cleaning Validation"	Low	Yes

7.0RISK ASSESSMENT (CONTD.):

Description of Risk identified	Risk Analysis and Evaluation				Current control measures	Risk classification based on control measures	Risk Acceptability (Yes/No)
	Potential Impact	Risk number	Failure mode	Risk classification based on risk identified			
Organizational measures - Cleaning Validation and Cleaning Verification(Contd.)							
Changes to validated cleaning procedures	There will be impact on validated cleaning procedures resulting in inadequate cleaning of surfaces of shared equipment and thus resulting in surface to surface cross contamination of next product	R39	Failure to exercise controls on changes to validated procedures	Medium	• The changes to any cleaning processes are evaluated through change control along with its impact on cleaning validation/verification. • The following changes are considered for evaluation of impact on cleaning validation ➢ Introduction of new product ➢ Change in formulation of existing product ➢ Introduction of new equipment in the train ➢ Shift of product to another equipment train ➢ Modification of product contact parts of equipment ➢ Revision of cleaning procedure • Revision in minimum batch size and maximum daily dose of next product which impact the MACO value of worst case product. AMV to be updated according to MACO value, If required. Refer Cleaning Validation Master Plan of respective areas and SOP titled “Cleaning Validation”	Low	Yes
Deviations observed during routine cleaning, line clearance and cleaning validation	There will be repeated failures resulting in cross contamination of next products	R40	Failure to identify procedures which can lead to potential failures or that needs improvement based on review of deviations observed during routine cleaning, line clearance and cleaning validation	Medium	• There is procedural requirement of initiating deviation to record failures observed during cleaning with respect to following: ➢ Any defined cleaning instructions in procedure that has failed to render the equipment clean ➢ Any equipment or its product contact part is found to be not cleaned during visual inspection by the independent person. • Failure in results for swab/rinse sample Refer SOP No. Cleaning Validation Master Plan of respective areas and SOP titled “Cleaning Validation”	Low	Yes

7.0RISK ASSESSMENT (CONTD.):

Description of Risk identified	Risk Analysis and Evaluation				Current control measures	Risk classification based on control measures	Risk Acceptability (Yes/No)
	Potential Impact	Risk number	Failure mode	Risk classification based on risk identified			
Organizational measures - Cleaning Validation and Cleaning Verification(Contd.)							
Inadequate training to personnel involved in sampling of product contact parts of equipment	There will be failure to collect the samples as per the validated procedures there by resulting in cross contamination of next products	R41	Failure to provide training to personnel involved in sampling of cleaning validation	Medium	• The personnel involved in collection of swab samples are trained in accordance with the procedure defined in cleaning validation protocol and details are documented in respective protocols.	Low	Yes
Analytical procedures used testing of samples	There will be failure to estimate left over residues from the swab/ rinse samples with accuracy and precision. This will result in cross contamination of next products	R42	Failure to demonstrate accuracy and precision of analytical procedures used for testing of samples collected for assurance of cleaning.	Medium	• Analytical method validation is performed with respect to identification of Limit of Detection (LOD) and Limit of Quantification (LOQ) so that method can quantify the residue that is established with accuracy and precision. • Recover of residue from the product contact parts of equipment's is performed for all the MOC's through use of swab and rinse sampling technique. • The results of testing are calculated taking into account of recovery value obtained during analytical method validation. Refer Cleaning Validation Master Plan of respective area Analytical Method Validation/ Verification	Low	Yes
Organizational measures - Personnel involved during processing							
Inadequate training of personnel	There will be non-uniformity and no reproducibility in following the procedures related to cleaning and processing of products during routine operation. This will result in cross contamination of next products	R43	Failure to follow the defined procedures during cleaning and processing during routine operation	Medium	• All the personnel (New recruit and existing) are provided training on the new procedures or retrained on the revised procedures related to cleaning and processing of products. • The operating personnel are communicated about the precautions related to gowning or respirators to be used during handling of any APIs that involves certain hazards.	Low	Yes

7.0 RISK ASSESSMENT (CONTD.):

Description of Risk identified	Risk Analysis and Evaluation				Current control measures	Risk classification based on control measures	Risk Acceptability (Yes/No)
	Potential Impact	Risk number	Failure mode	Risk classification based on risk identified			
Organizational measures - Personnel involved during processing (Contd.)							
Inadequate supervision of processes and procedures	There will be no identification and assurance that operation personnel always follow the procedures related to cleaning and processing of products during routine operation.	R44	Failure to follow the defined procedures during cleaning and processing during routine operation	Medium	• The routine operations (Processing and Cleaning) performed by operating personnel is supervised by Production Supervisor to ensure that the personnel follow the procedures defined along with their behaviours • There is also oversight from In-process Quality Assurance Personnel (IPQA) in processing areas	Low	Yes
Entry and Exit in manufacturing areas	There will safety hazard to personnel operating in processing areas There will be surface to surface transfer of particles from personnel gowning	R45	Failure to follow the defined procedures, movement and behaviours	Medium	• There is procedure available for Entry and Exit in manufacturing areas for all personnel though change rooms and following the clothing requirements adequate to prevent cross-contamination. • Precautions are followed by personnel after existing from processing areas to prevent cross contamination from gowning to other areas. • There are controls on movement of personnel (Production personnel and Support personnel such as QA,, QC, maintenance, engineers and contractors) between different processing areas	Low	Yes

8.0 SUMMARY AND CONCLUSION:

Based on the above risk assessment carried out it can be summarised that all the control measures are available preventing the risks of cross contamination from the identified risks.

During the QRM assessment following additional control measures have been identified for up gradation of procedures To verify the pressure differential across HEPA Filter of FBD and Coating Inlet.

a. Inclusion of requirements for following points in respective
   - Scale of CIP tank should be marked
   - Risers should be fitted properly with the duct, all bolt of riser duct should be tight.
   - Cleaning check list to be incorporate in all SOP of equipment cleaning
   - Product should be manufactured/ packed in a closed system, required to cover the packing and compression machine for implementation

Thus based on the above risk assessment and associated measures identified there is low risk with respect to contamination and cross contamination.