RISK ASSESSMENT FOR INTRODUCTION OF NEW PRODUCT IN FACILITY

Quality Risk Management (QRM) Table:

Utilities: HVAC, Water System, Electricity, Compressed air

Process step/input	Potential failure mode	Potential failure effect	Severity	Potential causes	Occurence	Current control	Detection	RPN	Actions recommended	Responsibility	Actions taken	Severity	Occurence	Detection	RPN
HVAC System	• Breakdown/ failure of HVAC system causing excursion of temperature, humidity and losing differential pressure between areas	• Cross contamination • Manufacturing disruption • Material and production failure • Increase in deviation situation	4	• Preventive maintenance plan implementation failure • HEPA filter integrity failure	3	• Annual HVAC requalification is done • BMS exists • Routine environmental monitoring plan exists and followed	3	36	Trend analysis of environmental data and critical review to be done Revalidation of HVAC to be done to include recovery time, alarm challenge, air visualization flow and air velocity.		--				
Purified Water System	• Breakdown/failure of purified water system	• Manufacturing disruption • Purified water quality failure	4	• Preventive maintenance plan implementation failure	3	• Preventive maintenance plan exists and followed • Periodic sanitization plan exists and followed • SCADA exists • Routine purified water system monitoring plan	3	36	Trend analysis of purified water system data and critical review to be done		--				

RISK ASSESSMENT FOR INTRODUCTION OF NEW PRODUCT IN FACILITY

						exists and followed									
Electricity	• Breakdown in power generation plant • Breakdown in electricity grid	• Manufacturing disruption • Material and production failure • Increase in power failure situation	4	• Natural gas supply failure in power plant • Preventive maintenance implementation plan failure	3	• In-house power generation plant exists • Preventive maintenance plan exists and followed • Govt power supply exists as alternative power source • Standard diesel generator exists • UPS exists	3	36	Annual preventive maintenance plan for the UPS to be made						
Compressed air	• Breakdown of air compressor • Compressed air line filter integrity failure	• Contamination of products	4	• Preventive maintenance implementation plan failure	3	• Preventive maintenance plan exists and followed • Routine monitoring of compressed air system done	3	36	Trend analysis of compressed air quality data and critical review to be done		--				
Faulty fabrics of plant	• Wear and tear of facility fabrics e.g., doors, wall, floor etc.	• Cross contamination • Regulatory observation	4	• Poor maintenance of facility fabrics e.g., doors, wall, floor etc	3	• Floor furnished with SLE • Sandwich panel wall to ensure non shedding surface • Automatic door closures exists	2	24	--		--				
Dispensing booth, dispensing, dispensing accessories															
Dispensing booth and people	• Breakdown of dispensing booth	• Cross contamination	4	• Preventive maintenance	3	• Biannual requalification	3	36	An additional disposable cap to be worn during each		--				

movement	• Uncontrolled material and people movement	• Regulatory observation •		plan failure • Non adherence to gowning procedure		plan for dispensing booth exists • Gowns/overalls changed after every batch dispensing • Chest and shoulder cover used on top of overall			material dispensing Personnel to wear additional shoe covers before entering dispensing booth and discard them when coming out. Zero adjustment of Magnehelic gauges and differential pressure sensors to be included as a part of calibration					
Weighing of materials	• Balance calibration failure • Human error in weighing and documenting	• Error in material weighing • Product test failure	4	• Balance calibration plan failure •	3	• Balance calibration plan exists and followed • Trained operators exist • Production and quality oversight	3	24	--		--			
Use of dispensing utensils and scoops	• Dispensing equipment/ scoops/balance cleaning failure	• Cross contamination	4	• Non validated cleaning procedure • Non adherence to SOPs	3	• Cleaning validation done • Hold time study of clean scoops, utensils done	3	36	Cleaning verification of dispensing booth to be done					
Sampling Booth, Sampling, Sampling Accessories														
Sampling booth and people movement	• Breakdown of sampling booth • Uncontrolled material and people movement	• Cross contamination • Regulatory observation •	4	• Preventive maintenance plan failure • Non adherence to gowning	3	• Biannual requalification plan for sampling booth exists • Gowns/overalls changed after	2	24	--		--			

RISK ASSESSMENT FOR INTRODUCTION OF NEW PRODUCT IN FACILITY

				procedure		every lot sampling									
Weighing of materials	• Balance calibration failure • Human error in sampling and documenting	• Error in material weighing •	4	• Balance calibration plan failure •	3	• Balance calibration plan exists and followed • Trained operators exist	2	24	--		--				
Use of sampling equipment and scoops	• Sampling equipment/ scoops/balance cleaning failure	• Cross contamination	4	• Non validated cleaning procedure • Non adherence to SOPs	3	• Cleaning validation of sampling equipment done •	3	36	Cleaning verification of sampling booth to be done		--				

RISK ASSESSMENT FOR INTRODUCTION OF NEW PRODUCT IN FACILITY

Granulation, granulation equipments and documentation

Process step/input	Potential failure mode	Potential failure effect	Severity	Potential causes	Occurence	Current control	Detection	RPN	Actions recommended	Responsibility	Actions taken	Severity	Occurence	Detection	RPN
Documentation	• Human error causing error in batch documentation	• Good documentation practice failure • Regulatory observation	4	• Lack/absence of supervision/quality oversight	3	• Manufacturing and QA oversight present • Trained operators exist	3	36	Refresher training on SOPs, GDP to be planned		--				
Material mixing	• Incompatibility of materials • Over mixing/under mixing • Mixing process failure	• Change in physical quality granules • Over mixing/under mixing	4	• Selection of wrong equipment • Inadequacy and absence of procedural details in SOPs/batch manufacturing instruction • Non adherence to mixing process	3	• Process validation done for products	3	36	Process validation to be done for new products		--				

	• Line clearance	• Cross contamination	4	• Inadequacy in line clearance checklist	3	• Line clearance SOP and checklist exist	3	36	Critically review line clearance SOP and update line clearance checklist to be updated Pictorial line clearance procedure to be displayed in the manufacturing cubicle		--				

RISK ASSESSMENT FOR INTRODUCTION OF NEW PRODUCT IN FACILITY

Process step/input	Potential failure mode	Potential failure effect	Severity	Potential causes	Occurence	Current control	Detection	RPN	Actions recommended	Responsibility	Actions taken	Severity	Occurence	Detection	RPN
Equipment usage and people movement	• Equipment cleaning failure • Uncontrolled people movement	Cross contamination	4	• Non validated cleaning procedure • Non adherence to SOPs	3	• Cleaning validation done • CIP system exists • Hold time study for equipment usage done • Close manufacturing equipment and dedicated transfer hose used • Dedicated staff entry to respective manufacturing cubicle • Gowns/overalls changed after every batch of product manufacturing	3	36	Cleaning validation/verification to be done for new molecule introduced Additional chest cover and cap to be worn and discard them before exiting the granulation room. Open ends of the hose / tubes to be kept closed while not in use.		--				
Granulation equipments	• Breakdown of granulation equipments	• Manufacturing disruption • Batch failure and rejection	4	• Preventive maintenance implementation plan failure	3	• Preventive maintenance plan exists • Equipment qualification done	3	36	Periodic equipment qualification to be done		--				

Access control	• Sharing password	Unauthorized access	4	Malicious intent	3	• Password protection, hence protected from unauthorized access • Computerized system validation done • Audit trial activated	3	36	Periodic computer system validation to be planned		--				

Drying, drying equipment and documentation

Process step/input	Potential failure mode	Potential failure effect	Severity	Potential causes	Occurence	Current control	Detection	RPN	Actions recommended	Responsibility	Actions taken	Severity	Occurence	Detection	RPN
Bulk material drying process	• Drying process failure	• Over drying /under drying of bulk materials • Capping of tablets	4	• Inadequacy and absence of procedural details in SOPs/batch manufacturing instruction • Selection of wrong equipment • Non adherence to drying process	3	• Process validation done for products	3	36	Process validation to be done for new products		--				

	• Line clearance	• Cross contamination	4	• Inadequacy in line clearance checklist	3	• Line clearance SOP and checklist exist	3	36	Critically review line clearance SOP and update line clearance checklist to be updated Pictorial line clearance procedure to be displayed in the manufacturing cubicle		--				
Document ation	• Human error causing error in batch documentation	• Good documentation practice failure • Regulatory observation	4	• Lack/absence of supervision/quality oversight	3	• Manufacturing and QA oversight present • Trained operators exist	3	36	Refresher training on SOPs, GDP to be planed		--				

Drying, drying equipment and documentation (Contd...)

RISK ASSESSMENT FOR INTRODUCTION OF NEW PRODUCT IN FACILITY

Process step/input	Potential failure mode	Potential failure effect	Severity	Potential causes	Occurence	Current control	Detection	RPN	Actions recommended	Responsibility	Actions taken	Severity	Occurence	Detection	RPN
Equipment usage and people movement	• Equipment cleaning failure • Uncontrolled people movement	Cross contamination	4	• Non validated cleaning procedure • Non adherence to SOPs	3	• Cleaning validation done • CIP system exists • Hold time study for equipment usage done • Dedicated staff entry to respective manufacturing cubicles • Closed manufacturing equipments and dedicated transfer hose exist • Gown/overall changed after every batch of product manufacturing	3	36	Cleaning validation/ verification to be done for new molecule introduced		--				

RISK ASSESSMENT FOR INTRODUCTION OF NEW PRODUCT IN FACILITY

Drying, drying equipment and documentation (Contd...)

Process step/input	Potential failure mode	Potential failure effect	Severity	Potential causes	Occurence	Current control	Detection	RPN	Actions recommended	Responsibility	Actions taken	Severity	Occurence	Detection	RPN
Drying equipments	• Malfunction	• Manufacturing disruption • Batch failure and rejection	4	• Breakdown of drying machine	3	• Preventive maintenance plan exists • Equipment qualification done	3	36	Periodic equipment qualification to be done		--				
Access control	• Sharing password	• Unauthorized access	4	• Malicious intent	3	• Password protection, hence protected from unauthorized access • Computerized system validation done • Audit trial activated	3	36	Periodic computer system validation to be planned		--				

RISK ASSESSMENT FOR INTRODUCTION OF NEW PRODUCT IN FACILITY

Milling, Milling equipment and documentation

Process step/input	Potential failure mode	Potential failure effect	Severity	Potential causes	Occurence	Current control	Detection	RPN	Actions recommended	Responsibility	Actions taken	Severity	Occurence	Detection	RPN
Bulk material milling process	• Milling process failure	• Oversize/ undersize of granules • Poor flow of granules • Compressibility failure	4	• Inadequacy and absence of procedural details in SOPs/batch manufacturing instruction • Selection of wrong sieve	3	• Process validation done for products • Each sieve with clearly marked ID and traceability with batch record	3	36	Process validation to be done for new products		--				
	• Line clearance	• Cross contamination	4	• Inadequacy in line clearance checklist	3	• Line clearance SOP and checklist exist	3	36	Critically review line clearance SOP and update line clearance checklist to be updated Pictorial line clearance procedure to be displayed in the manufacturing cubicle		--				

RISK ASSESSMENT FOR INTRODUCTION OF NEW PRODUCT IN FACILITY

Milling, Milling equipment and documentation (Contd...)

Process step/Input	Potential failure Mode	Potential failure effect	SEVERITY	Potential Causes	OCCURENCE	Current Control	DETECTION	RPN	Actions Recommended	RESPONSIBILITY	Actions Taken	SEVERITY	OCCURENCE	DETECTION	RPN
Documentation	• Human error causing error in batch documentation	• Good documentation practice failure • Regulatory observation	4	• Lack/absence of supervision/ quality oversight	3	• Manufacturing and QA oversight present • Trained operators exist	3	36	Refresher training on SOPs and GDP to be planed		--				
Equipment usage and people movement	• Equipment cleaning failure • Uncontrolled people movement	• Cross contamination	4	• Non validated cleaning procedure • Non adherence to SOPs	3	• Cleaning validation done • CIP system exists • Hold time study for equipment usage done • Dedicated staff entry to respective manufacturing cubicles • Closed manufacturing equipments and dedicated transfer hose exist • Gown/overall changed after every batch of product manufacturing	3	36	Cleaning validation/verification to be done for new molecule introduced		--				

RISK ASSESSMENT FOR INTRODUCTION OF NEW PRODUCT IN FACILITY

Milling, Milling equipment and documentation (Contd...)

Process step/input	Potential failure mode	Potential failure effect	Severity	Potential causes	Occurence	Current control	Detection	RPN	Actions recommended	Responsibility	Actions taken	Severity	Occurence	Detection	RPN
Milling equipments	• Malfunction	• Manufacturing disruption • Metal contamination • Batch failure and rejection	4	• Breakdown of milling machine/sieve	3	• Preventive maintenance plan exists • Equipment qualification done • Sieve integrity checked before and after milling	3	36	Periodic equipment qualification to be done		--				
Access control	• Sharing password	Unauthorized access	4	Malicious intent	3	• Password protection, hence protected from unauthorized access • Computerized system validation done • Audit trial activated	3	36	Periodic computer system validation to be planned		--				

RISK ASSESSMENT FOR INTRODUCTION OF NEW PRODUCT IN FACILITY

Blending, blending equipment and documentation

Process step/input	Potential failure mode	Potential failure effect	Severity	Potential causes	Occurence	Current control	Detection	RPN	Actions recommended	Responsibility	Actions taken	Severity	Occurence	Detection	RPN
Bulk material blending process	• Blending process failure	• Over/under blending • Blend uniformity test failure • Test failure on product batches	4	• Inadequacy and absence of procedural details in SOPs/batch manufacturing instruction • Selection of wrong blender	3	• Process validation done for products	3	36	Process validation to be done for new products		--				
	• Line clearance	• Cross contamination	4	• Inadequacy in line clearance checklist	3	• Line clearance SOP and checklist exist	3	36	Critically review line clearance SOP and update line clearance checklist to be updated Pictorial line clearance procedure to be displayed in the manufacturing cubicle		--				

RISK ASSESSMENT FOR INTRODUCTION OF NEW PRODUCT IN FACILITY

Blending, blending equipment and documentation (Contd...)

Process step/Input	Potential failure Mode	Potential failure effect	SEVERITY	Potential Causes	OCCURENCE	Current Control	DETECTION	RPN	Actions Recommended	RESPONSIBILITY	Actions Taken	SEVERITY	OCCURENCE	DETECTION	RPN
Documentation	• Human error causing error in batch documentation	• Good documentation practice failure • Regulatory observation	4	• Lack/absence of supervision/ quality oversight	3	• Manufacturing and QA oversight present • Trained operators exist	3	36	Refresher training on SOPs and GDP to be planed		--				
Equipment usage and people movement	• Equipment cleaning failure • Uncontrolled people movement	Cross contamination	4	• Non validated cleaning procedure • Non adherence to SOPs	3	• Cleaning validation done • CIP system exists • Hold time study for equipment usage done • Dedicated staff entry to respective manufacturing cubicles • Closed manufacturing equipments and dedicated transfer hose exist • Gown/overall changed after every batch of product manufacturing	3	36	Cleaning validation/verification to be done for new molecule introduced		--				

Blending, blending equipment and documentation (Contd...)

RISK ASSESSMENT FOR INTRODUCTION OF NEW PRODUCT IN FACILITY

Process step/input	Potential failure mode	Potential failure effect	Severity	Potential causes	Occurence	Current control	Detection	RPN	Actions recommended	Responsibility	Actions taken	Severity	Occurence	Detection	RPN
Blending equipments	• Malfunction	• Manufacturing disruption • Batch failure and rejection • Reworking of batch	4	• Breakdown of blender	3	• Preventive maintenance plan exists • Equipment qualification done	3	36	Periodic equipment qualification to be done		--				
Access control	• Sharing password	• Unauthorized access	4	• Malicious intent	3	• Password protection, hence protected from unauthorized access • Computerized system validation done • Audit trial activated	3	36	Periodic computer system validation to be planned		--				

RISK ASSESSMENT FOR INTRODUCTION OF NEW PRODUCT IN FACILITY

Compression, tablet press and documentation

Process step/input	Potential failure mode	Potential failure effect	Severity	Potential causes	Occurence	Current control	Detection	RPN	Actions recommended	Responsibility	Actions taken	Severity	Occurence	Detection	RPN
Tablet compression process	• Poor flow of granules • Die hole filling variability	• Weight variation of tablets • Low/high hardness of tablets • High friability	4	• Low/high bulk density of granules • High equipment speed	3	• Process validation done for products • Particle size controlled	3	36	Process validation to be done for new products		--				
	• Granules contamination with metal	• Metal contamination	4	• Abrasion of metal parts • Breakage of sieve	3	• Metal detector installed in each tablet press • Metal detection challenge test done at the start and end of batch	2	24	–		--				

	• Line clearance	• Cross contamination	4	• Inadequacy in line clearance checklist	3	• Line clearance SOP and checklist exist	3	36	Critically review line clearance SOP and update line clearance checklist to be updated Pictorial line clearance procedure to be displayed in the manufacturing cubicle		--				

Compression, tablet press and documentation (Contd...)

Process step/Input	Potential failure Mode	Potential failure effect	SEVERITY	Potential Causes	OCCURENCE	Current Control	DETECTION	RPN	Actions Recommended	RESPONSIBILITY	Actions Taken	SEVERITY	OCCURENCE	DETECTION	RPN
Document ation	• Human error causing error in batch documentation	• Good documentation practice failure • Regulatory observation	4	• Lack/absence of supervision/ quality oversight	3	• Manufacturing and QA oversight present • Trained operators exist	3	36	Refresher training on SOPs and GDP to be planed		--				

RISK ASSESSMENT FOR INTRODUCTION OF NEW PRODUCT IN FACILITY

Equipment usage and people movement	• Equipment cleaning failure • Uncontrolled people movement	• Cross contamination	4	• Non validated cleaning procedure • Non adherence to SOPs	3	• Cleaning validation done • Hold time study for equipment usage done • Dedicated staff entry to respective manufacturing cubicles • Closed manufacturing equipments and dedicated transfer hose exist • Gown/overall changed after every batch manufacturing	3	36	Cleaning validation/verification to be done for new molecule introduced		--			

Compression, tablet press and documentation (Contd...)

RISK ASSESSMENT FOR INTRODUCTION OF NEW PRODUCT IN FACILITY

Process step/input	Potential failure mode	Potential failure effect	Severity	Potential causes	Occurence	Current control	Detection	RPN	Actions recommended	Responsibility	Actions taken	Severity	Occurence	Detection	RPN
Tablet press	• Malfunction	• Manufacturing disruption • Batch failure and rejection	4	• Breakdown of tablet press	3	• Preventive maintenance plan exists • Equipment qualification done	3	36	Periodic equipment qualification to be done		--				
Access control	• Sharing password	• Unauthorized access	4	• Malicious intent	3	• Password protection, hence protected from unauthorized access • Computerized system validation done • Audit trial activated	3	36	Periodic computer system validation to be planned		--				

RISK ASSESSMENT FOR INTRODUCTION OF NEW PRODUCT IN FACILITY

Coating, tablet coater and documentation

Process step/input	Potential failure mode	Potential failure effect	Severity	Potential causes	Occurence	Current control	Detection	RPN	Actions recommended	Responsibility	Actions taken	Severity	Occurence	Detection	RPN
Tablet coating	• Friction causing abrasion of tablets	• Breakdown of tablets	4	• Low hardness of tablets	3	• Process validation done for products • Particle hardness controlled	3	36	Process validation to be done for new products		--				
	• Line clearance	• Cross contamination	4	• Inadequacy in line clearance checklist	3	• Line clearance SOP and checklist exist	3	36	Critically review line clearance SOP and update line clearance checklist to be updated Pictorial line clearance procedure to be displayed in the manufacturing cubicle		--				
Coating suspension preparation	• Spraying system failure	• Mottling/orange peel effect on tablets	4	• Spray nozzle blocking	3	• Coating suspension preparation procedure explicitly outlined in BMR	2	24	--		--				
Documentation	• Human error causing error in batch documentation	• Good documentation practice failure • Regulatory observation	4	• Lack/absence of supervision/ quality oversight	3	• Manufacturing and QA oversight present • Trained operators exist	3	36	Refresher training on SOPs and GDP to be planned		--				

RISK ASSESSMENT FOR INTRODUCTION OF NEW PRODUCT IN FACILITY

Coating, tablet coater and documentation (Contd...)

Process step/Input	Potential failure Mode	Potential failure effect	SEVERITY	Potential Causes	OCCURENCE	Current Control	DETECTION	RPN	Actions Recommended	RESPONSIBILITY	Actions Taken	SEVERITY	OCCURENCE	DETECTION	RPN
Equipment usage and people movement	• Equipment cleaning failure • Uncontrolled people movement	Cross contamination	4	• Non validated cleaning procedure • Non adherence to SOPs	3	• Cleaning validation done • Hold time study for equipment usage done • Dedicated staff entry to respective manufacturing cubicles • Closed manufacturing equipments and dedicated transfer hose exist • Gown/overall changed after every batch manufacturing	3	36	Cleaning validation/verification to be done for new molecule introduced		--				
Inspection	Inadequacy in tablet inspection.	• Defective tablets passing for packing • Dust generation • Customer complaint • Batch failure	4	• Manual Tablet inspection	2	• Inspection belt qualified. • Skilled stuff exist. • Eye check-up of relevant employee is performed at a regular frequency. • AQL being implemented	3	36	Tablet inspection tray to be connected to a dust collector.						

RISK ASSESSMENT FOR INTRODUCTION OF NEW PRODUCT IN FACILITY

Coating, tablet coater and documentation (Contd...)

Process step/Input	Potential failure Mode	Potential failure effect	SEVERITY	Potential Causes	OCCURENCE	Current Control	DETECTION	RPN	Actions Recommended	RESPONSIBILITY	Actions Taken	SEVERITY	OCCURENCE	DETECTION	RPN
Tablet coater	• Malfunction	• Manufacturing disruption • Batch failure and rejection	4	• Breakdown of tablet coater	3	• Preventive maintenance plan exists • Equipment qualification done	3	36	Periodic equipment qualification to be done		--				
Access control	• Sharing password	• Unauthorized access	4	• Malicious intent	3	• Password protection, hence protected from unauthorized access • Computerized system validation done • Audit trial activated	3	36	Periodic computer system validation to be planned		--				

RISK ASSESSMENT FOR INTRODUCTION OF NEW PRODUCT IN FACILITY

Campaign production, equipment usage and documentation

Process step/input	Potential failure mode	Potential failure effect	Severity	Potential causes	Occurence	Current control	Detection	RPN	Actions recommended	Responsibility	Actions taken	Severity	Occurence	Detection	RPN
Campaign production	• Degradation of products and microbial proliferation • Equipment cleaning failure	• Contamination of products	4	• High impurity from degradation • High .... load • Non validated cleaning procedure • Non adherence to SOPs	3	• Hold time study done for equipment usage • Cleaning validation done	3	36	Cleaning validation/verification to be done when new molecule is introduced		--				
	• Line clearance	• Cross contamination	4	• Inadequacy in line clearance checklist	3	• Line clearance SOP and checklist exist	3	36	Critically review line clearance SOP and update line clearance checklist to be updated Pictorial line clearance procedure to be displayed in the manufacturing cubicle		--				
Documentation	• Human error causing error in batch documentation	• Good documentation practice failure • Regulatory observation	4	• Lack/absence of supervision/ quality oversight	3	• Manufacturing and QA oversight present • Trained operators exist	3	36	Refresher training on SOPs and GDP to be planed		--				

RISK ASSESSMENT FOR INTRODUCTION OF NEW PRODUCT IN FACILITY

Campaign production, equipment usage and documentation (Contd...)

Process step/Input	Potential failure Mode	Potential failure effect	SEVERITY	Potential Causes	OCCURENCE	Current Control	DETECTION	RPN	Actions Recommended	RESPONSIBILITY	Actions Taken	SEVERITY	OCCURENCE	DETECTION	RPN
Equipment usage	• Wrong batch quantity • Wrong size of equipment compared to product bulk	• Insufficient equipment performance • Poor product quality	4	• Wrong selection of equipment	3	• Preventive maintenance plan exists • Qualified equipment used	2	24	--		--				
Access control	• Sharing password	Unauthorized access	4	Malicious intent	3	• Password protection, hence protected from unauthorized access • Computerized system validation done • Audit trial activated	3	36	Periodic computer system validation to be planned		--				

RISK ASSESSMENT FOR INTRODUCTION OF NEW PRODUCT IN FACILITY

Bottling, bottling equipment, documentation

Process step/input	Potential failure mode	Potential failure effect	Severity	Potential causes	Occurence	Current control	Detection	RPN	Actions recommended	Responsibility	Actions taken	Severity	Occurence	Detection	RPN
Bottling of tablets	• Line clearance	• Cross contamination	4	• Inadequacy in line clearance checklist	3	• Line clearance SOP and checklist exist	3	36	Critically review line clearance SOP and update line clearance checklist to be updated Pictorial line clearance procedure to be displayed in the manufacturing cubicle		--				
Documentation	• Human error causing error in batch documentation	• Good documentation practice failure • Regulatory observation	4	• Lack/absence of supervision/ quality oversight	3	• Manufacturing and QA oversight present • Trained operators exist	3	36	Refresher training on SOPs and GDP to be planed		--				
Bottle unscrambling	• Emptying the hopper	• Insufficient performance	4	• Not enough bottle	3	• Hopper can be refilled without stopping machine	2	24	--		--				
Bottle cleaning station	• Poor cleaning caused by malfunctioning of air compressor	Product contamination by particles	4	Residue from bottle production	3	• Bottle cleaning process with compressed air validated	2	24	--		--				

RISK ASSESSMENT FOR INTRODUCTION OF NEW PRODUCT IN FACILITY

Slide rails	• Wrong adjustment of parts	Bottle might fall and interrupt packaging operation	4	Wrong guidance for that size of bottles	3	• Guidance and heights are continuously adjustable	2	24	--		--				
Bottling, bottling equipment, documentation (Contd...)															
Machine speed	• Malfunction	Low output	4	Belt too slow for packaging	3	• Speed validation done • Speed can be adjusted	2	24	--		--				
Product (tablet) filling	• Malfunction	Spillage of tablets	4	No bottle in place	3	• No bottle/no fill function in place	2	24	--		--				
	• Equipment qualification failure	Wrong quantity of tablets filled	4	Malfunction in control panel	3	• Periodic IPQC done • Online check weigher exists	2	24	--		--				
Equipment cleaning	• Unable to reach hard to clean area	• Contamination	4	• Insufficient cleaning	3	• Critical parts can be easily dismantled for cleaning • Cleaning validation done	3	36	Cleaning validation/ verification to be planned for each new product introduced		--				
Induction sealing	• Malfunction of induction sealer	Leak test failure	4	Wrong pressure and sealing temperature	3	• Packaging process validated • Preventive maintenance plan exists	2	24	--		--				

RISK ASSESSMENT FOR INTRODUCTION OF NEW PRODUCT IN FACILITY

Bottling, bottling equipment, documentation (Contd...)

Process step/input	Potential failure mode	Potential failure effect	Severity	Potential causes	Occurence	Current control	Detection	RPN	Actions recommended	Responsibility	Actions taken	Severity	Occurence	Detection	RPN
Bottle torque	• Equipment malfunction	Cap not tightly closed	4	Bad crimp quality	3	• Torque tester exists	2	24	--		--				
Machine speed	• Malfunction	Low output	4	Belt too slow for packaging	3	• Speed validation done • Speed can be adjusted	2	24	--		--				
Final packaging with outsert	• Uncontrolled inventory management	• Market complaint • Product recall • Rework	4	Mix up of different product outserts	3	• Segregated storage with lock and key facility	2	24	--		--				

RISK ASSESSMENT FOR INTRODUCTION OF NEW PRODUCT IN FACILITY

Blister packing machine, blister packaging, documentation

Process step/input	Potential failure mode	Potential failure effect	Severity	Potential causes	Occurence	Current control	Detection	RPN	Actions recommended	Responsibility	Actions taken	Severity	Occurence	Detection	RPN
Bottling of tablets	• Line clearance	• Cross contamination	4	• Inadequacy in line clearance checklist	3	• Line clearance SOP and checklist exist	3	36	Critically review line clearance SOP and update line clearance checklist to be updated Pictorial line clearance procedure to be displayed in the manufacturing cubicle		--				
Documentation	• Human error causing error in batch documentation	• Good documentation practice failure • Regulatory observation	4	• Lack/absence of supervision/ quality oversight	3	• Manufacturing and QA oversight present • Trained operators exist	3	36	Refresher training on SOPs and GDP to be planed		--				

RISK ASSESSMENT FOR INTRODUCTION OF NEW PRODUCT IN FACILITY

Tablet filling in to blister packaging line	• Malfunctioning of inlet sensors	• Filling disruption • Empty blister	4	• Not enough tablet in the hopper	3	• Controlled by inlet sensor	2	24	--		--				

Blister packing machine, blister packaging, documentation (Contd...)

Process step/input	Potential failure mode	Potential failure effect	Severity	Potential causes	Occurence	Current control	Detection	RPN	Actions recommended	Responsibility	Actions taken	Severity	Occurence	Detection	RPN
Slide rails	• Wrong adjustment of parts	Bottle might fall and interrupt blister packaging	4	Wrong guidance for that product packaging	3	• Guidance are adjustable • Spares suiting product packaging exists	2	24	--		--				
Machine speed	• Malfunction	Low output	4	Belt too slow for packaging	3	• Speed validation done • Speed can be adjusted	2	24	--		--				
Tablet filling in blister pocket	• Malfunction	Partially filled blister	4	No tablets in blister pocket	3	• Non fill detector camera exists • Non fill detection challenge test done at the start and end of batch	2	24	--		--				

RISK ASSESSMENT FOR INTRODUCTION OF NEW PRODUCT IN FACILITY

Equipment cleaning	• Unable to reach hard to clean area	• Contamination	4	• Insufficient cleaning	3	• Critical parts can be easily dismantled for cleaning • Cleaning validation done	3	36	Cleaning validation/ verification to be planned for each new product introduced		--			

RISK ASSESSMENT FOR INTRODUCTION OF NEW PRODUCT IN FACILITY

Blister packing machine, blister packaging, documentation (Contd...)

Process step/input	Potential failure mode	Potential failure effect	Severity	Potential causes	Occurence	Current control	Detection	RPN	Actions recommended	Responsibility	Actions taken	Severity	Occurence	Detection	RPN
Blister sealing	• Malfunction of the sealing system	• Leak test failure	4	• Wrong pressure and sealing temperature	3	• Packaging process validated • Preventive maintenance plan exists	2	24	--		--				
Access control	• Sharing password	• Unauthorized access	4	• Malicious intent	3	• Password protection, hence protected from unauthorized access • Computerized system validation done • Audit trial activated	3	36	Periodic computer system validation to be planned		--				
Secondary packaging	• Malfunction	• Market complaint • Product recall • Rework	4	• Uncontrolled inventory management	3	• Segregated storage under lock and key facility	2	24	--		--				

RISK ASSESSMENT FOR INTRODUCTION OF NEW PRODUCT IN FACILITY

Process step/input	Potential failure mode	Potential failure effect	Severity	Potential causes	Occurence	Current control	Detection	RPN	Actions recommended	Responsibility	Actions taken	Severity	Occurence	Detection	RPN
Plant Layout	• Faulty facility design	• Zigzag in man material movement • Cross contamination • Regulatory observation	4	• Design verification and qualification not done	3	• Facility has been designed by reputed pharmaceutical consultancy firm	2	24	--		--				
	• Uncontrolled people and material movement	• Cross contamination • Regulatory observation	4	• Short cutting while movement from one place to another • Non adherence to SOPs	3	• Dedicated man and material movement route exists • Air lock exists between areas of different air quality • Change room with gowning facilities exists	2	24	--		--				

RISK ASSESSMENT FOR INTRODUCTION OF NEW PRODUCT IN FACILITY

Manufacturing of new product: Product manufacturing, equipment usage, stability study, documentation

Process step/input	Potential failure mode	Potential failure effect	Severity	Potential causes	Occurence	Current control	Detection	RPN	Actions recommended	Responsibility	Actions taken	Severity	Occurence	Detection	RPN
Product manufacturing	• Critical quality attributes failing to meet product specifications	• Batch failure • Batch rejection	4	• Wrong selection of equipment (e.g., mixer/tablet coater etc. not of suitable size)	3	• Qualified equipments are in use	3	36	Optimization batch to be manufactured to determine right equipment size and manufacturing parameters		--				
Equipment cleaning	• Uncontrolled material and people movement • Non adherence to SOPs	• Cross contamination	4	• Insufficient cleaning • Limited access to cleaning • Poor cleaning caused by insufficient CIP • Uneven equipment surface	3	• Enough space inside machine to facilitate cleaning • 316L electro polished equipment surface	3	36	Cleaning validation to be done for introducing new product		--				
Control: PLC, Software	• Uncontrolled use of equipment	• Malfunction	4	• Error in recipe set in PLC • Breakdown of software	3	• Recipe setting done from optimization batch data • Skilled operators exist	3	36	Process validation batches to be manufactured to validate process recipe		--				

RISK ASSESSMENT FOR INTRODUCTION OF NEW PRODUCT IN FACILITY

Manufacturing of new product: Product manufacturing, equipment usage, stability study, documentation

Process step/input	Potential failure mode	Potential failure effect	Severity	Potential causes	Occurence	Current control	Detection	RPN	Actions recommended	Responsibility	Actions taken	Severity	Occurence	Detection	RPN
Batch manufacturing	• Insufficient optimization batch data	• Inconsistency in batch testing results • Validation failure	4	• Wrong selection of critical process parameters • Wrong selection of batch size	3	• Critical process parameters are available from optimization batch	3	36	Process validation batches to be manufactured to optimize critical process parameters		--				
Product stability	• Incompatibility • Thermal degradation	• Stability study failure	4	• Degradation of products over time	3	• Stability chambers exist	3	36	Stability study protocol to be prepared Stability study to be conducted		--				

RISK ASSESSMENT FOR INTRODUCTION OF NEW PRODUCT IN FACILITY

Warehousing

Process step/input	Potential failure mode	Potential failure effect	Severity	Potential causes	Occurence	Current control	Detection	RPN	Actions recommended	Responsibility	Actions taken	Severity	Occurence	Detection	RPN
Material receipt	• Approved supplier list not followed	• Material may come from unapproved supplier/ unapproved site • Received lot may contain damaged containers	4	• Approved supplier list not followed	3	• Approved supplier list exists • Checklist used	2	24	--		--				
Material issuance to production	• Exposure to outside environment	• Damage	4	• Lack of adequate transportation facility • Lack of supervision	3	• Own covered van used for transferring RM/PM from warehouse to production	2	24	--		--				
Material storage	• Uncontrolled storage	• Mix up	4	• Lack of storage capacity	3	• Segregated storage of items with 1 lot 1 pellet 1 item.	2	24	--		--				

RISK ASSESSMENT FOR INTRODUCTION OF NEW PRODUCT IN FACILITY

Warehousing (contd..)

Process step/input	Potential failure mode	Potential failure effect	Severity	Potential causes	Occurence	Current control	Detection	RPN	Actions recommended	Responsibility	Actions taken	Severity	Occurence	Detection	RPN
Material store	• Creeping of pest from outside	• Infestation • Degradation	4	• Non eradication of pest • Excursion of temp.	3	• Pest control done • Temperature controlled in warehouse • Storage for cold chain items exist	2	24	--		--				
Material store	• Lack of RM/PM monitoring	• Material expiry	4	• Short shelf life items • Slow moving finished products	3	• Validated inventory management system exists and it alerts before expiry • Product planning module takes care of consumption of materials • Reject material store exists	2	24	--		--				

5.1 Discussion on the QRM Table:

The oral solid dosages facility of …… is a multiproduct manufacturing facility with three dispensing booths, four blending rooms, five granulation suites, five compression and six coating rooms. The packing area has five blister lines and one bottle filling line, each connected to a secondary packaging line.

The manufacturing block is serviced by 20 Air handling units and 8 Dehumidifier units. These along with dampeners help in maintaining the specified temperature, relative humidity and differential pressure in the manufacturing and packaging area.

Ground water is the source for the potable and purified water lines in the manufacturing facility, where water is circulated and delivered at a speed of 1000 litres / hour.

A review of the discussion included in the QRM table suggests that the existing control measures are capable of ensuring the safety to the patient as well as the product.

The plant layout is planned and executed to ensure ample space for material storage, manufacturing and packaging operations, and separate entry for man and material. Material integrity is accorded the maximum priority by ensuring transportation of material between warehouse and manufacturing block in a covered, locked and sealed van, with a confirmation for dispatch and receipt of the van at both ends in place.

All the utilities like, HVAC, Water, Electricity and Compressed air required for the manufacturing and packaging operations are being monitored round the clock for their performance, with periodic performance maintenance and requalification/ calibration programs. Critical storage areas like the warehouse are mapped for the temperature and relative humidity. The critical environmental conditions, viz, temperature, relative humidity and differential pressure are monitored during every operation and recorded in relevant log books, registers or documents. There is a program for conducting environmental monitoring for viable bacterial/ fungal/ microbial growth.

The filters of the HVAC system are periodically cleaned and their efficiency is evaluated on a recurring basis. Preventive maintenance programs are available for all the utilities used in the manufacturing operation, including compressed air, water system and HVAC systems.

These ensure that the manufacturing and packaging areas are free of contamination from other material or particulate matter that can be present in the water system, or compressed air.

SOPs exist for all major activities and training has been provided to all relevant employees of the specific areas on these SOP’s. These guide individuals about the procedure to be followed for performing a particular activity.

All employees are provided training on the basic good manufacturing practices (GMP) and refresher trainings on the cGMP requirements as per the various guidelines across the globe.

These measures ensure that all relevant areas are free of any contamination due to human intervention.

Balances and other machinery used are qualified and calibrated periodically to ensure error free operation. There is a requirement to check the balance before every weighing and ensure its levelling. Areas are earmarked for the positioning of the material

container, personnel performing the weighing and placement of the balance in the dispensing booths.

All the manufacturing and packaging areas require proper gowning including a cover for the chest and shoulder in the dispensing area. Every area has a restriction for the personnel entry and dedicated staff are deployed for the different areas of manufacturing and packaging. The gowning procedure requires employees to change their dress, after every batch dispensing or batch processing, thereby ensuring a clear environment and avoiding any remote chances for cross contamination.

Entry and exist procedures for employees to the manufacturing and packaging areas are well defined. All employees require to wash and sanitize their hands before and after a visit to the manufacturing / packaging areas.

A doer- checker system is followed for steps like potency calculation, weighing, cleaning and cleanliness check, recording of critical parameters like temperature, relative humidity differential pressure, etc. at every stage of the manufacturing operation, be it dispensing, milling, blending, granulation, compression or coating. There is always a presence of the production and quality personnel during the dispensing activity to ensure no human error creeps in due to negligence.

The batch production records used to document the manufacturing as well as the packaging operations are prepared in a simple and lucid language and these explicitly instruct the operators and supervisors about the process steps to be followed in a sequence.

All the manufacturing and packaging operations are validated and are performed by well trained personnel following the instructions provided in batch production records.

An effective labelling procedure is available to ensure the correct equipment/ instrument is used for a specific activity. For example, the sieves used in the milling operation are all appropriately labelled for ready identification.

The cleaning operation is validated and hold time reports are available for keeping the equipments in a clean or dirty state without any operation. Multiple types of cleanings are available like product to product cleaning, batch to batch cleaning and cleaning after a preventive or a breakdown maintenance.

An experienced team of formulation scientists are available with the research and development department, who ensure that products are transferred to the manufacturing facility only after successful pilot scale batches are manufactured and their stability has been conducted and confirmed.

Material storage is provided the highest importance and there is a clear segregation of approved, quarantine and rejected material, both for raw materials as well as for packaging material. There exists three storage areas in the warehouse, namely, general area, cold room and cool rooms. The general area is maintained at a temperature below 25°C and a relative humidity below 60 %. The cool room is maintained at a temperature between 8°C and 15°C, while the cold room is maintained at 5°C ± 3°C. This ensure the storage of materials at the conditions as recommended by the respective material supplier.

Similarly, the storage of raw and packaging material in the intermediate storage area in the manufacturing area is also maintained as per the manufacture recommendation. Material is usually stored in the original container and if transferred, there is a procedure to transcribe the details on to a fresh label.

Appropriate tests are performed by the production and quality personnel to ensure a check at every stage during the manufacturing and packaging operation.

The stability of the product is conducted using qualified stability chambers that maintain the temperature and relative humidity as per the requirements of the protocol that is approved for conducting the study. Stand by chamber, which is qualified and calibrated for all the possible storage conditions is also available for an emergency breakdown so as to protect the interest of the manufactured product. The stability studies are protocol based and are governed by appropriate management SOPs.

An access control exists on all the computerised systems and the PLCs, ensuring that there is not unauthorized access into them. Each user has been allotted an individual user id and password for accessing the computerized systems. All the current applications and software are validated by the respective vendors before they have been used for the relevant activity. Audit trail exists in all computerized systems and PLCs to identify the activities done and actions taken thereof.

The personnel in the maintenance section are capable and well trained to overcome any breakdown situation to minimize the down time of various equipments.

All visitors intending to visit the facility are always accompanied by technical staff of the respective section of the manufacturing and packaging areas.

The additional control measures that are recommended to be executed would only reinforce the stringent controls that are already in place for the manufacturing and packaging of multiple pharmaceutical drug products in the same facility using shared equipments and areas.

6. QRM Review Plan:

On review of the QRM table and the discussion above, it is clear that there exists no risk to the products manufactured at the manufacturing facility. Appropriate controls are demonstrated for manufacturing different products in the same facility.

The progress of the actions recommended and actions taken for a new product that is introduced in the product portfolio of the facility shall be reviewed annually and reported appropriately.

7. Conclusion:

It can be concluded that with the existing control measures and the actions recommended when new products shall be added to the product basket of the organization, there will be no risk to the patient as well as the quality and supply of the products manufactured at the facility.