PHARMA DEVILS

QUALITY ASSURANCE DEPARTMENT

QUALITY RISK ASSESSEMENT AND MITIGATION PLAN

QRA No.:

Name of Facility/Equipment/Utility/System/Activity/Procedure **Unit Operation**: Eye Drop Filling Machine	**Date of Quality Risk Assessment:**

S. No.	Item/ Function	Potential Failure Mode (Failure Mode)	Potential Effect of Failure (Effect)	Potential Cause/ Mechanism of Failure	Current Control	Reference	S	O	D	Risk Priority Number (S*O*D)	Recommend-ended Actions (if any)	Post Risk			
												S	O	D	RPN S*O
1.	Filling Operation	➢ Improper filling and Capping	➢ Improper filling may result in volume variation. ➢ Lack of aseptic behavioral during filling and stoppering activity may leads to contamination and product failure.	➢ Lack of qualification procedure. ➢ Lack of cleaning and operational procedure. ➢ Unsterile parts or article may use I filling operation. ➢ Lack of environmental condition for filling. ➢ Improper handling of aseptic intervention may lead to product contamination. ➢ Operation handled by untrained and unqualified person. ➢ Due aseptic interventions ➢ during filling duration.	➢ Qualification of filling machine has been completed. ➢ SOP for filling machine cleaning and operation is in place. ➢ Sterilization procedure for machine parts loads is in place. ➢ Filling shall be carried out under class A condition (Unidirectional air flow area) ➢ Aseptic intervention shall be performed as per media fill protocol and BMR. ➢ Operational training has been done for all concerned persons for aseptic. ➢ Aseptic interventions has been established in media fill process simulation study. ➢ Filling duration has been validated in media fill .	Operation and Cleaning of Automatic High Speed Injectable Powder Filling and Stoppering Machine	4	2	1	8	Adequate procedure no recommendation required	NA	NA	NA	NA

QUALITY RISK ASSESSEMENT AND MITIGATION PLAN

QRA No.:

Name of Facility/Equipment/Utility/System/Activity/Procedure **Unit Operation**: Eye Drop Filling Machine	**Date of Quality Risk Assessment:**

S. No.	Item/ Function	Potential Failure Mode (Failure Mode)	Potential Effect of Failure (Effect)	Potential Cause/ Mechanism of Failure	Current Control	Reference	S	O	D	Risk Priority Number (S*O*D)	Recommend-ended Actions (if any)	Post Risk			
												S	O	D	RPN S*O
2.	Fill volume	➢ During filling operation there is volume variation of solution from set limit.	➢ There might be a problem of fill volume variation followed by impact on pharmacological action of drug.	➢ Unqualified filling machine used for filling operation. ➢ It might be due to piston setting/ dosing timing setting problem. ➢ Working personnel lack of adequate knowledge.	➢ Performance qualification of filling machine has been done as per its testing parameters. ➢ PLC Based Servo drive available for volume adjustment and product volume has been set accordingly. ➢ Only Trained persons authorized to access filling & sealing operations. ➢ Calibrated Measuring Cylinder used for in process checking.	Operation and Cleaning of Ampoule Filling And Sealing Machine	3	1	1	3	NA	NA	NA	NA	NA
3.	Filling & Capping Process.	➢ Machine is not running on variable speed i.e. 80, 130 & 150 Vials/min.	➢ The results at variable speed after filling will not be exactly assessed during filling. ➢ There might be a problem of rejection & product output.	➢ There might be problem with input-Output command by PLC. ➢ Unqualified filling machine used for filling operation. ➢ Working personnel lack of adequate knowledge	➢ Performance of the machine at different speed has been verified at the time of PQ. ➢ Performance qualification of filling machine has been done as per its testing parameters. ➢ Only Trained persons authorized to access filling & sealing operations.	Qualification Policy	3	1	2	6	NA	NA	NA	NA	NA

QUALITY RISK ASSESSEMENT AND MITIGATION PLAN

QRA No.:

Name of Facility/Equipment/Utility/System/Activity/Procedure **Unit Operation**: Eye Drop Filling Machine	**Date of Quality Risk Assessment:**

S. No.	Item/ Function	Potential Failure Mode (Failure Mode)	Potential Effect of Failure (Effect)	Potential Cause/ Mechanism of Failure	Current Control	Reference	S	O	D	Risk Priority Number (S*O*D)	Recommend-ended Actions (if any)	Post Risk			
												S	O	D	RPN S*O
4.	Nitrogen purging	➢ No Pre and Post nitrogen flushing during filling operation.	➢ During filling without nitrogen flushing will directly impact on the product Quality, safety& purity.	➢ Disconnection of nitrogen line from filling machine. ➢ In case of absence of nitrogen, filling will be automatically stopped followed by delay in operation.	➢ Nitrogen pressure is interlocked with operation of machine, whenever low pressure or no nitrogen available the filling machine will stop automatically. ➢ Low purging of Nitrogen Show red alarm and machine Stop challenge test has been done.	SOP for Operation of Nitrogen Gas Plant	4	1	1	4	NA	NA	NA	NA	NA
5.	Nitrogen filter	➢ Non-Sterile nitrogen is coming in aseptic area.	➢ There might be a chance of product contamination.	➢ Integrity failure of 0.2 µ filter.	➢ At the time of periodic validation all critical tests has been done to ensure the quality of nitrogen air in aseptic area as per the pre specified acceptance criteria. ➢ Before filling two dedicated 0.2 µ filters are in place. ➢ SOP of Integrity checking of Nitrogen filter in place.	Integrity Testing of Cartridge Filter	4	1	2	8	NA	NA	NA	NA	NA

QUALITY RISK ASSESSEMENT AND MITIGATION PLAN

QRA No.:

Name of Facility/Equipment/Utility/System/Activity/Procedure **Unit Operation**: Eye Drop Filling Machine	**Date of Quality Risk Assessment:**

S. No.	Item/ Function	Potential Failure Mode (Failure Mode)	Potential Effect of Failure (Effect)	Potential Cause/ Mechanism of Failure	Current Control	Reference	S	O	D	Risk Priority Number (S*O*D)	Recommend-ended Actions (if any)	Post Risk			
												S	O	D	RPN S*O
6.	Sensor Challenge test	➢ No nozzle no capping sensor ➢ No Vial no filling sensor not working. ➢ No vial no nozzle sensor not working. ➢ No Vial no screw capping sensor not working ➢ Compressed air pressure sensor not working ➢ Air velocity sensor not working ➢ Rejection sensor not working ➢ Safety door sensor (ORABS) not working	➢ Leakage of vial. ➢ It may leads to product loss. ➢ It can leads to sterility failure hence product failure. ➢ It can leads to product contamination. ➢ Lack of Isolation of class A grade ➢ Mixing of good vial with rejected vial leads to contamination. ➢ Controlled environment condition failure leads to product damage and contamination.	➢ Sensor not working when Compressed air pressure goes beyond set limit. ➢ Lack of Qualification ➢ Lack of challenge test ➢ Lack of Preventive maintenance	➢ Challenge test performed for the compressed air supply before the batch start and after any machine break down for air pressure and when goes beyond the set limit red alarm show and machine stop immediately. ➢ Performing challenge test for all the sensor by passing no nozzle no capping or no vial no filling or no vial no nozzle or no vial no screw capping or low air velocity or mixing rejected vial or safety doors opens before start and after any machine break down and in-built automatic alarm system available and when goes beyond set limit red alarm shows and immediately machine stop. ➢ During Performance Qualification all sensors has been verified. ➢ Training imparted to all the personnel working in filling area for the challenge test. ➢ Preventive maintenance has been done for all the sensors	Operation & cleaning of Filling, Dropper Fixing & Screw capping machine.	4	1	1	4	NA	NA	NA	NA	NA

QUALITY RISK ASSESSEMENT AND MITIGATION PLAN

QRA No.:

Name of Facility/Equipment/Utility/System/Activity/Procedure **Unit Operation**: Eye Drop Filling Machine	**Date of Quality Risk Assessment:**

S. No.	Item/ Function	Potential Failure Mode (Failure Mode)	Potential Effect of Failure (Effect)	Potential Cause/ Mechanism of Failure	Current Control	Reference	S	O	D	Risk Priority Number (S*O*D)	Recommend-ended Actions (if any)	Post Risk			
												S	O	D	RPN S*O
7.	LAF operation	➢ Failure of LAF during the filling operation. ➢ During filling power failure of LAF. ➢ Air velocity not in limit. ➢ HEPA filter may damage	➢ Filling during switch off condition of LAF will directly impact the sterility of the product. ➢ Filling during power failure condition of LAF will directly impact the sterility of the product and there might be a chance of contamination of product. ➢ Controlled environmental condition not achieved leads to contamination	➢ There might be failure of sensor & Problem in input-output command by PLC. ➢ Unqualified Laminar air flow unit used for filling operation. ➢ No preventive maintenance of LAF. ➢ No power supply in aseptic area. ➢ No UPS Backup of filling LAF. ➢ Air velocity sensor not working. ➢ Lack of awareness in the personnel	➢ During operational qualification air velocity sensors has been verified and set limit is controlled through PLC and when goes beyond the set limit, red alarm will show and immediately machine stop. ➢ Performance qualification of LAF operation has been verified. ➢ Preventive maintenance of LAF done as per schedule. ➢ During power failure of LAF all filling operation will stop. ➢ A proper training has been provided to concerned personnel that filling operations shall be done only under LAF and also background of LAF shall be maintained as per specific grade requirement. ➢ Area qualification done twice in year.	Operation and Cleaning of Laminar Air Flow Unit	4	1	1	4	NA	NA	NA	NA	NA

QUALITY RISK ASSESSEMENT AND MITIGATION PLAN

QRA No.:

Name of Facility/Equipment/Utility/System/Activity/Procedure **Unit Operation**: Eye Drop Filling Machine	**Date of Quality Risk Assessment:**

S. No.	Item/ Function	Potential Failure Mode (Failure Mode)	Potential Effect of Failure (Effect)	Potential Cause/ Mechanism of Failure	Current Control	Reference	S	O	D	Risk Priority Number (S*O*D)	Recommend-ended Actions (if any)	Post Risk			
												S	O	D	RPN S*O
8.	Filling & sealing process	➢ Filling line speed and volume variations.	➢ It can lead the unevenness of extractable volume from its specifications. ➢ It can be cause of batch failure.	➢ Filling line speed not verified. ➢ Wrong parameters set in the batch manufacturing record.	➢ Filling line speed of filling machine has been studied and verified during performance qualification of filling & sealing machine. ➢ Details of filling machine speed in Batch manufacturing record has been set as per PQ of m/c and checked & verified by production & QA personnel.	Cleaning and Sanitation of Aseptic/Manufacturing/Washing and Sterilization/Vial Sealing Area.	4	1	2	8	NA	NA	NA	NA	NA
9.	Filling & sealing process	➢ Filling room differential pressure is out of range during product filling. ➢ Filling room temperature & RH is out of range during product filling.	➢ Due to low DP there might be a risk of area contamination with respect to adjacent room followed by contamination in product. ➢ There might be an impact on in-process product.	➢ Due to insufficiency of AHU Performance. ➢ Non-qualified AHU used for operation. ➢ Due to inefficiency of chiller & heater of that particular AHU.	➢ Audio visual alarm system is provided in BMS System when pressure differential will go out of limit. ➢ At the time of PQ pressure differential has been verified. ➢ Audio visual alarm system is provided in BMS System when temperature & RH will go out of limit. ➢ At the time of PQ temperature & RH has been verified.	Monitoring of Differential Pressure Temperature & Relative Humidity in all Area	4	1	1	4	NA	NA	NA	NA	NA

QUALITY RISK ASSESSEMENT AND MITIGATION PLAN

QRA No.:

Name of Facility/Equipment/Utility/System/Activity/Procedure **Unit Operation**: Eye Drop Filling Machine	**Date of Quality Risk Assessment:**

S. No.	Item/ Function	Potential Failure Mode (Failure Mode)	Potential Effect of Failure (Effect)	Potential Cause/ Mechanism of Failure	Current Control	Reference	S	O	D	Risk Priority Number (S*O*D)	Recommend-ended Actions (if any)	Post Risk			
												S	O	D	RPN S*O
10.	Filling & sealing process	➢ Routine filling interventions occurs due to any mechanical problem.	➢ It can be a cause of producing a non sterile product. ➢ Product safety and quality problem occurs.	➢ Operators not qualified in each interventions and it can lead the chance of human error.	➢ Filling process is covered by media fill study and all operators has been involved & qualified in each intervention. ➢ Media fill report covers the container size and filling interventions.	Process simulation study	4	1	2	8	NA	NA	NA	NA	NA
11.	Filling machine safety door	➢ Safety Door (ORABS) opens	➢ Grading system failure which leads to product contamination	➢ Safety Door (ORABS) sensor Interlocking not working. ➢ Lack of awareness	➢ Challenge test perform before starting of operation. ➢ Training to be imparted to all the filling personnel about the Safety door interlocking system.	Operation & cleaning of Filling, Dropper Fixing & Screw capping machine.	4	1	1	4	NA	NA	NA	NA	NA
12.	Nozzle alignment	➢ Filling needle do not insert into LDPE Vial mouth more reliably	➢ It may leads to damage of LDPE vial which can cause product contamination.	➢ Machine setting was not proper	➢ Machine setting was done before the start of every batch. ➢ Operational SOP is in place		3	1	3	9	NA	NA	NA	NA	NA
13.	Dropping	➢ Dropping continue from bottom to top	➢ It may leads to variation in Fill volume which can cause batch failure.	➢ Machine setting was not proper	➢ Machine setting was done before the start of every batch. ➢ Operational SOP is in place		3	1	3	9	NA	NA	NA	NA	NA

QUALITY RISK ASSESSEMENT AND MITIGATION PLAN

QRA No.:

Name of Facility/Equipment/Utility/System/Activity/Procedure **Unit Operation**: Eye Drop Filling Machine	**Date of Quality Risk Assessment:**

S. No.	Item/ Function	Potential Failure Mode (Failure Mode)	Potential Effect of Failure (Effect)	Potential Cause/ Mechanism of Failure	Current Control	Reference	S	O	D	Risk Priority Number (S*O*D)	Recommend-ended Actions (if any)	Post Risk			
												S	O	D	RPN S*O
14.	Operation of Screw capping & Dropper fixing	➢ Failure of dropper fixing & screw capping	➢ It can leads to spillage of solution which can cause contamination	➢ Machine setting was not proper	➢ Machine setting was done before the start of every batch. ➢ Operational SOP is in place	Operation & cleaning of Filling, Dropper Fixing & Screw capping machine.	3	1	3	9	NA	NA	NA	NA	NA

Where: S=Severity; O=Occurrence Probability; D=Detection; Risk category 1-25 RPN is Low risk, 26-50 RPN is Medium Risk, 51-125 RPN is High Risk.

Name of Facility/Equipment/Utility/System/Activity/Procedure/Unit Operation : Eye Drop Filling machine	Date:

S. No.	Recommended Action	Responsible Person	Target Date of Completion
1.	NA	NA	NA
2.	NA	NA	NA

CAPA:
If required, mention CAPA No.:

QUALITY RISK ASSESSEMENT AND MITIGATION PLAN

QRA No.:

Name of Facility/Equipment/Utility/System/Activity/Procedure **Unit Operation**: Eye Drop Filling Machine	**Date of Quality Risk Assessment:**

Quality Risk Management Team			**Reviewed By** **Head Production** **Sign & Date**	**Approved By** **Head QA** **Sign & Date**
Name	**Department**	**Sign & Date**		

QUALITY RISK ASSESSEMENT AND MITIGATION SUMMARY REPORT

Name of Facility/Equipment/Utility/System/Activity/Procedure/Unit Operation : Media Fill Activity

Verification of Action Plan: NA

Remarks (if any): The entire above failure mode and their Severity, Occurrence, Detection rating done and RPN No. is found between 1-25. Hence Risk is detected as low which is acceptable.

Verified By
QA
Sign & Date

Approved By
Head QA
Sign & Date