# QUALITY RISK ASSESSEMENT AND MITIGATION PLAN

**QRA No.:**

| **Name of Facility/Equipment/Utility/System/Activity/Procedure**<br>**Unit Operation**: Liquid vial Filling and Stoppering 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 | | | |
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| | | | | | | | | | | | | S | O | D | RPN S*O*D |
| **1.** | Vial Size | ➢ Equipment is not suitable for different size of Vials | ➢ Filling process will be interrupted and filling process cannot continue further. | ➢ Different Vial sizes may not be processed with same equipment. | ➢ Filling machine is suitable for filling of different sizes of Vials by changing format (change) parts<br>➢ Change parts for different Vial size with marking provided by vendor, along with the equipment, as per requirement.<br>➢ Machine has been qualified with different Vial size. | OQ& PQ of Filling And Stoppering machine | 4 | 2 | 1 | 8 | Adequate procedure no recommend ation required. Hence risk is accepted. | NA | NA | NA | NA |
| **2.** | Vial transport | ➢ Overturned/ fallen Vials on the infeed conveyor belt. | ➢ Vial jamming, Vial damage or breakage may take place.<br>➢ Continuous filling operation will effected. | ➢ Design of the system is not adequate to the Vials.<br>➢ Positioning of Vials on infeed conveyor belt is not up to the point.<br>➢ Functioning of the system not verified properly. | ➢ The design of the system is adequate to positioning and transfer of Vials via a conveyor belt with SS side guides.<br>➢ Overturned Vials not enter in the conveyor.<br>➢ Functionality has been verified during qualification activities. | OQ& PQ of Filling Stoppering machine | 3 | 1 | 1 | 3 | Adequate procedure no recommend ation required. Hence risk is accepted. | NA | NA | NA | NA |
| **3.** | Transfer of Vials from tunnel to filling station. | ➢ Depyrogenated Vials travel through unclean (unclassified) environment | ➢ Particle contamination of Vial.<br>➢ Micro-biological contamination possible. | ➢ The transfer of Vials to filling & stoppering is performed under the non classified area.<br>➢ Classification level hasn't verified. | ➢ The transfer of Vials, filling & stoppering is performed under unidirectional air flow unit (Grade A).<br>➢ Classification level has been verified during the qualification study. | OQ& PQ of Filling And Stoppering machine | 4 | 1 | 1 | 4 | Adequate procedure no recommend ation required. Hence risk is accepted. | NA | NA | NA | NA |

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| | | | | | | | | | | | | S | O | D | RPN S*O*D |
| **4.** | Transfer of Vials | ➢ Improper positioning of Vials during transfer to filling station. | ➢ Filling shall not be proper<br>➢ Product spillage may occur. | ➢ Design of the system is not adequate to the Vials.<br>➢ Positioning of Vials on to filling station is not up to the point.<br>➢ Functioning of the system not verified properly. | ➢ The design of the system is adequate that individual Vials are transferred and positioned properly below the filling needles at filling station.<br>➢ Functionality has been checked during qualification activities | OQ of Filling And Stoppering machine. | 3 | 1 | 2 | 6 | Adequate procedure no recommend ation required. Hence risk is accepted. | NA | NA | NA | NA |
| **5.** | Transfer of product | ➢ Contamination of product while transfer from holding vessel. | ➢ Product failure | ➢ No proper & safe transfer line available for transfer the product to filling & stoppering machine.<br>➢ The product transfer system not properly sterilized. | ➢ The product transferred through a closed system wherein sterile product has been transferred through Nitrogen gas pressure, from holding vessel to buffer tank (placed on filling machine), through sterilizable grade filter (0.2 µm), whenever applicable.<br>➢ The complete transfer system has been sterilized routinely through SIP, before every batch, as per SOP. | SOP for CIP& SIP of Vessels. | 4 | 1 | 1 | 4 | Adequate procedure no recommend ation required. Hence risk is accepted. | NA | NA | NA | NA |

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| | | | | | | | | | | | | S | O | D | RPN S*O*D |
| **6.** | Transfer of Vials | ➢ Vials minimum load on the infeed conveyor table. | ➢ No Vials supplied to the Vial filling machine.<br>➢ Product spillage may occur. | ➢ No provision for detecting the low amount of Vials in the infeed conveyor table.<br>➢ Machine continuously runs even if there is no Vial on infeed conveyor table. | ➢ Vials minimum load detection sensor is installed on the infeed conveyor table to detect the low accumulation of Vials along with alarm provision.<br>➢ Machine automatically goes into standby mode in case of low Vials at infeed conveyor table. | OQ& PQ of Filling And Stoppering machine. | 4 | 1 | 1 | 4 | Adequate procedure no recommend ation required. Hence risk is accepted. | NA | NA | NA | NA |
| **7.** | Transfer of product from holding vessel to buffer tank (on filling machine) | ➢ Connection of transfer line to buffer tank not in Grade A environment. | ➢ Particle contamination of product.<br>➢ Micro-biological contamination possible | ➢ No proper & safe transfer connections are there for the product transfer to buffer tank.<br>➢ The product transfer system not classified. | ➢ All the connections to the buffer tank are performed under Grade A conditions.<br>➢ Classification level shall be verified and qualified during qualification. | SOP for bulk filtration & transfer. | 4 | 1 | 1 | 4 | Adequate procedure no recommend ation required. Hence risk is accepted. | NA | NA | NA | NA |
| **8.** | Filling & stoppering | ➢ Filling & stoppering carried out under unclean environment | ➢ Particle contamination of product.<br>➢ Micro-biological contamination possible. | ➢ Grade A and unidirectional airflow is not available for performing aseptic filling & stoppering process. | ➢ Unidirectional Air Flow system (Grade A) is provided over complete filling & stoppering machine.<br>➢ Classification level has been verified and qualified during the qualification study. | OQ & PQ of Filling LAF | 4 | 1 | 1 | 4 | Adequate procedure no recommend ation required. Hence risk is accepted. | NA | NA | NA | NA |

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| | | | | | | | | | | | | S | O | D | RPN S*O*D |
| **9.** | Ceramic Piston pump and needles | ➢ Material reacts with the products. | ➢ Contamination of sterile product.<br>➢ Product failure. | ➢ Piston pumps and needles are not suitable and upto the mark for product filling. | ➢ Ceramic piston pumps & needles used for filling machine.<br>➢ The suitability of the materials has been verified by certificate/ manufacturers declarations. | IQ of filling machine | 4 | 1 | 1 | 4 | Adequate procedure no recommend ation required. Hence risk is accepted. | NA | NA | NA | NA |
| **10.** | Dosing pumps | ➢ Incorrect product dosing in Vials. | ➢ Inefficient filling of Vials may leads to wrong dosage.<br>➢ Vial with incorrect product dose shall be rejected from market. | ➢ Design of the rotary piston pump and peristaltic pump design is not appropriate.<br>➢ There is no synchronized movement of Rotary piston pump & peristaltic pump. | ➢ The rotary piston pump designing is adequate for required amount of product is filled inside the Vials.<br>➢ Rotary piston pump movement has been synchronized with the transport movement before filling. | Operation and Cleaning of Laminar Air Flow Unit | 4 | 1 | 1 | 4 | Adequate procedure no recommend ation required. Hence risk is accepted. | NA | NA | NA | NA |
| **11.** | Product transfer line from buffer tank to filling needle | ➢ Product contact parts of equipment cannot be sterilized. | ➢ Contamination of sterile product may possible.<br>➢ Product failure. | ➢ There is no provision to remove the contact parts of the equipment. | ➢ Product contact parts of equipment are removable and sterilizable grade and sustain steam sterilizable for validated time.<br>➢ Machine part load has been validated & same incorporate in SOP. | SOP of Filling & Stoppering machine | 4 | 1 | 1 | 4 | Adequate procedure no recommend ation required. Hence risk is accepted. | NA | NA | NA | NA |

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| | | | | | | | | | | | | S | O | D | RPN S*O*D |
| **12.** | Product Dosing | ➢ Different range of filling volume could not be achieved. | ➢ Incorrect dosage may leads to market recall. | ➢ No provision for different range of filling volume<br>➢ Fill volume set point adjustment not possible. | ➢ Different rotary piston pump sets are provided by vendor for different range of filling volume, to ensure accurate volume.<br>➢ PLC Based Servo drive available for volume adjustment and product volume has been set accordingly. | Operation of filling machine. | 3 | 2 | 1 | 6 | Adequate procedure no recommend ation required. Hence risk is accepted. | NA | NA | NA | NA |
| **13.** | Filling processes | Presence of headspace oxygen | ➢ Chance of product degradation.<br>➢ Microbial contamination due to presence of air. | ➢ No provision of nitrogen flushing. | ➢ Provision for Pre and post nitrogen purging is available in machine.<br>➢ Control system available to set the pre and post nitrogen purging time and the pressure for the same. | Cleaning and Sanitation of Aseptic/Vial Stoppering Area. | 4 | 1 | 1 | 4 | Adequate procedure no recommend ation required. Hence risk is accepted. | NA | NA | NA | NA |
| **14.** | Nitrogen Gas Purging | ➢ Purging pressure too high/ cannot be adjusted. | ➢ Chances of product spillage in case of too high pressure. | ➢ Nitrogen flow can't be monitored.<br>➢ No provision is there of alarm in case of High pressure. | ➢ Flow regulator has been installed on nitrogen gas flow line for regulate the purging gas flow.<br>➢ High purging of Nitrogen Show red alarm and machine Stop challenge test has been done. | SOP for Operation of Nitrogen Gas Plan | 4 | 1 | 2 | 8 | Adequate procedure no recommend ation required. Hence risk is accepted. | NA | NA | NA | NA |

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| | | | | | | | | | | | | S | O | D | RPN S*O*D |
| **15.** | Nitrogen Gas Purging | ➢ Low Flow of nitrogen | ➢ Purging of Vials cannot be performed. | ➢ Nitrogen flow can't be monitored.<br>➢ No provision is there of alarm in case of low pressure. | ➢ Flow meters for monitoring the gas flow along with alarm system are available.<br>➢ Nitrogen pressure is interlocked with operation of machine, whenever low pressure or no nitrogen available the filling machine will stop automatically.<br>➢ Low purging of Nitrogen Show red alarm and machine Stop challenge test has been done. | SOP for Operation of Nitrogen Gas Plan | 4 | 1 | 1 | 4 | Adequate procedure no recommend ation required. Hence risk is accepted. | NA | NA | NA | NA |
| **16.** | Nitrogen Gas Purging | ➢ Nitrogen gas quality failure. | ➢ Particle and microbial contamination of Vials may leads to product failure | ➢ No provision to filter the nitrogen gas before use.<br>➢ Purity of nitrogen is not identified.<br>➢ Nitrogen gas generator didn't qualified. | ➢ Before pre-purging and post purging station two dedicated 0.2 µ filters are in place.<br>➢ SOP of Integrity checking of Nitrogen filter in place.<br>➢ Nitrogen gas supply to the equipment has been qualified & COA available for purity. | | 4 | 1 | 1 | 4 | Adequate procedure no recommend ation required. Hence risk is accepted. | NA | NA | NA | NA |

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| | | | | | | | | | | | | S | O | D | RPN S*O*D |
| **17.** | Filling | ➢ Product level in the buffer tank could not be monitored | ➢ Low level or no product inside buffer tank may produce wrong fill in Vials. | ➢ Level sensor is not provided.<br>➢ No provision for alarm in case of low level of product. | ➢ Product level sensor is Available to monitor the product level inside the buffer tank.<br>➢ In case of low level of product inside buffer tank, alarm will be generated and filling will be stopped. | Operation & Cleaning of Filling & Stoppering | 3 | 1 | 1 | 3 | Adequate procedure no recommend ation required. Hence risk is accepted. | NA | NA | NA | NA |
| **18.** | Filling | ➢ Filling speed could not be adjusted or maintained. | ➢ Variation in output | ➢ No provision for counting the Vials from filling machine.<br>➢ No provision for adjust & maintain the rate of Vial filling. | ➢ Counters are placed at infeed and out feed to count number of filled Vials.<br>➢ The equipment control system is suitable to adjust & maintain the rate of Vial filling (number of Vials/ minute). | | 3 | 1 | 1 | 3 | Adequate procedure no recommend ation required. Hence risk is accepted. | NA | NA | NA | NA |
| **19.** | Filling | ➢ Position of the filling needles could not be adjusted. | ➢ Spillage of product may possible.<br>➢ Generation of air bubbles due to gap between needle and Vial surface, which might lead to product contamination**.** | ➢ Nozzle alignment & Dropping test not performed.<br>➢ Machine is not suitable for filling of different sizes of Vials.<br>➢ Filling needle height can't adjustable based on different format parts. | ➢ Nozzle alignment & Dropping test has been performed during PQ.<br>➢ Machine is suitable for filling of different sizes of Vials by adjusting height of the filling needle automatically as per different Vial size with different set of dosing pump & needle.<br>➢ Filling needle height shall be adjustable based on different format parts, so as to be close to the Vial mouth. | OQ &PQ of Filling & Stoppering machine | 3 | 2 | 1 | 6 | Adequate procedure no recommend ation required. Hence risk is accepted. | NA | NA | NA | NA |

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| | | | | | | | | | | | | S | O | D | RPN S*O*D |
| **20.** | Filling | ➢ Filling starts without Vial at filling station | ➢ Possible contamination of clean room, filling machine and product due to spillage | ➢ No provision for detecting the presence of Vials.<br>➢ Sensor not working when Compressed air pressure goes beyond set limit. | ➢ No Vial no filling sensor has been installed before filling station & Performing challenge test for sensor and when goes beyond set limit red alarm shows and immediately machine stop.<br>➢ 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. | SOP of Filling & Stoppering machine | 3 | 1 | 1 | 3 | Adequate procedure no recommend ation required. Hence risk is accepted. | NA | NA | NA | NA |
| **21.** | Filling | ➢ Dripping of products from filling needles. | ➢ Contamination of filling machine and product loss. | ➢ No provision to ensure that no dripping takes place after filling.<br>➢ No provision provided for filling needles in the control system to prevent dripping. | ➢ The design viz., the SS rotary piston pumps and needles movement has been verified during PQ and that no dripping takes place after filling.<br>➢ Back suction provision for filling needles is available in the control system to prevent dripping.<br>➢ Functionality has been verified during execution of qualification studies. | OQ & PQ of Filling & Stoppering machine | 3 | 1 | 2 | 6 | Adequate procedure no recommend ation required. Hence risk is accepted. | NA | NA | NA | NA |

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| | | | | | | | | | | | | S | O | D | RPN S*O*D |
| **22.** | Stoppering | ➢ Sterility failure of stoppers | ➢ Contamination of filled product | ➢ Classification is not as per the expected level.<br>➢ There is no procedure for transfer of sterile stoppers. | ➢ Classification level has been verified during qualification.<br>➢ SOP is applicable for transfer of sterile stoppers. | IQ & PQ of Filling & Stoppering machine | 3 | 1 | 1 | 3 | Adequate procedure no recommend ation required. Hence risk is accepted. | NA | NA | NA | NA |
| **23.** | Stoppering | ➢ No stopper in bowl | ➢ Vial will not be stoppered.<br>➢ Product contamination may occur. | ➢ Qualification of stoppering machine is not done during qualification activities. | ➢ Functionality has been checked during the execution of qualification studies. | | 3 | 2 | 1 | 6 | Adequate procedure no recommend ation required. Hence risk is accepted. | NA | NA | NA | NA |
| **24.** | Stoppering | ➢ Low level of stopper at chute/ track | ➢ Vial will not be stoppered.<br>➢ Product contamination may occur. | ➢ Qualification of stoppering machine is not done during qualification activities. | ➢ Functionality has been checked during the execution of qualification studies. | | 3 | 2 | 1 | 6 | Adequate procedure no recommend ation required. Hence risk is accepted. | NA | NA | NA | NA |
| **25.** | Stoppering | ➢ No vial at stoppering station | ➢ Stoppers shall be spilled inside the filling area. | ➢ Qualification of stoppering machine is not done during qualification activities. | ➢ Functionality has been checked during execution of qualification studies. | | 3 | 1 | 1 | 3 | Adequate procedure no recommend ation required. Hence risk is accepted. | NA | NA | NA | NA |

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| **26.** | Stoppering | ➢ Stoppering station height not adjustable. | ➢ Improper bunging for different size of vials. | ➢ Qualification of stoppering machine is not done during qualification activities. | ➢ Functionality has been checked during execution of qualification studies. | IQ & PQ of Filling & Stoppering machine | 3 | 2 | 1 | 6 | Adequate procedure no recommend ation required. Hence risk is accepted. | NA | NA | NA | NA |
| **27.** | Transfer to downstream equipment | ➢ Filled & stoppered vials are exposed to environmental air during transfer to stoppering machine | ➢ Contamination of product filled vials may occur. | ➢ Area Classification is not as per the expected level and not qualified also. | ➢ Classification level has been verified and qualified during qualification. | IQ & PQ of Filling & Stoppering machine | 3 | 1 | 1 | 3 | Adequate procedure no recommend ation required. Hence risk is accepted. | NA | NA | NA | NA |
| **28.** | Transfer of filled and stoppered vials | ➢ Vials get stuck in the discharge guide. | ➢ Damage of vials<br>➢ Product loss due to damage of filled vials. | ➢ There is no alarming system available for rectification. | ➢ Vial jamming lead to an alarm, leading to immediate stopping of machine. | IQ & OQ of Filling & Stoppering machine | 3 | 2 | 1 | 6 | Adequate procedure no recommend ation required. Hence risk is accepted. | NA | NA | NA | NA |
| **29.** | Filling and Transfer to downstream equipment | ➢ Unidirectional air flow/ Laminarity not maintained under LAF during filling. | ➢ Turbulent flow may increase particulate count and contaminate the product. | ➢ Air flow study not performed during the qualification study. | ➢ Air flow study has been conducted to demonstrate laminarity. | PQ of Filling & Stoppering machine | 4 | 1 | 1 | 4 | Adequate procedure no recommend ation required. Hence risk is accepted. | NA | NA | NA | NA |

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| | | | | | | | | | | | | S | O | D | RPN S*O*D |
| **30.** | Star wheels & Main drive | ➢ Star wheels & main drive overload | ➢ Filling process may be affected | ➢ Preventive maintenance schedule is not up to the mark. | ➢ Preventive maintenance of star wheels and motors has been carried out at regular intervals. | SOP for annual Preventive Maintenance plan | 3 | 2 | 1 | 6 | Adequate procedure no recommend ation required. Hence risk is accepted. | NA | NA | NA | NA |
| **31.** | Out feed | ➢ Maximum accumulation at out feed | ➢ Vial filing machine operation may continue leading to accumulation of Vials, which may lead to Vial breakage. | ➢ No occupancy sensor is provided.<br>➢ No provision to stop filling machine in case of full capacity. | ➢ Out feed occupancy sensor is provided.<br>➢ Vial filling & stoppering machine will stop in case of full capacity at out feed.<br>➢ Functionality has been verified during execution of qualification studies. | OQ & PQ of Filling & Stoppering Machine. | 3 | 2 | 1 | 6 | Adequate procedure no recommend ation required. Hence risk is accepted. | NA | NA | NA | NA |
| **32.** | Filter (Nitrogen gas line) | ➢ No provision for sterile filtration of nitrogen gas.<br>➢ Filter leakage. | ➢ Basic requirement.<br>➢ Product contamination possible<br>➢ Filter leakage may lead to product contamination. | ➢ Integrity failure of 0.2 µ filter | ➢ Before filling two dedicated 0.2 µ Hydrophobic, Sterilizable grade filters are in place.<br>➢ Filter integrity testing has been performed at regular intervals as per SOP. | SOP for Operation of Nitrogen Gas Plant | 4 | 1 | 1 | 4 | Adequate procedure no recommend ation required. Hence risk is accepted. | NA | NA | NA | NA |

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| **33.** | Metallic components in direct contact with Vials/ filling media/ compressed air | ➢ The material may not be suitable.<br>➢ May contaminate the product. | ➢ MOC not resistant - Interaction with product & media possible | ➢ DQ & IQ not verified. | ➢ Metallic critical contact surfaces is constructed of 316 grade stainless steel or better, electro polished, orbitally welded.<br>➢ Supporting structure and non-contact parts has been made up of SS 304 or better.<br>➢ The suitability of the materials has been proven by certificate. | DQ & IQ of Filling & Stoppering Machine. | 3 | 1 | 1 | 3 | Adequate procedure no recommend ation required. Hence risk is accepted. | NA | NA | NA | NA |
| **34.** | Polymeric materials | ➢ Polymeric materials are not compatible and are not replaceable. | ➢ Shall lead to contamination of Vials. | ➢ Not using the food grade polymeric materials.<br>➢ There is no certification/declaratio n provided by vendor.<br>➢ Not possible to change the polymeric parts easily. | ➢ Gaskets and O-rings coming in direct/ indirect contact surfaces is made up of food grade polymeric materials only and has been high temperature and pressure resistant.<br>➢ Food grade polymeric material certificate/ declaration have been provided by vendor.<br>➢ The easy change of gaskets is possible. | DQ & IQ of Filling & Stoppering Machine | 3 | 1 | 1 | 3 | Adequate procedure no recommend ation required. Hence risk is accepted. | NA | NA | NA | NA |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | S | O | D | RPN S*O*D |
| **35.** | Process automation | ➢ Process parameters are not controlled automatically. | ➢ Possibility of human error leads to a process which is not validated | ➢ PLC System is not there for automatic control.<br>➢ There is no automatic failure mode detection. | ➢ The System is PLC based and fully automatic.<br>➢ The equipment can control & detect failure mode automatically. | IQ of Filling & Stoppering Machine | 3 | 2 | 1 | 6 | Adequate procedure no recommend ation required. Hence risk is accepted. | NA | NA | NA | NA |
| **36.** | Man-machine Interface | ➢ Process / process status not visible for operating personnel. | ➢ Possibility of human error leads to a process which is not validated.<br>➢ Process can be interrupted. | ➢ There is no adequate display for operating the process parameters. | ➢ MMI is provided with adequate display and clean room suitable Touch screen for operation and entering process parameters. | DQ & IQ of Filling & Stoppering Machine | 3 | 2 | 1 | 6 | Adequate procedure no recommend ation required. Hence risk is accepted. | NA | NA | NA | NA |
| **37.** | PLC/ Control system | ➢ Control system does not detect failures and generate alarms. | ➢ Process optimization and validation is not possible. | ➢ No alarming system is there for detecting the critical conditions.<br>➢ There is no automatic failure mode detection. | ➢ Alarm is provided in case of any critical instrument/ sensor not working properly, loss of communication.<br>➢ Failure of set parameters got indicated as alarms and necessary interlocks are in place. | DQ & IQ of Filling & Stoppering Machine | 2 | 1 | 1 | 2 | Adequate procedure no recommend ation required. Hence risk is accepted. | NA | NA | NA | NA |

# QUALITY RISK ASSESSEMENT AND MITIGATION PLAN

**QRA No.:**

| **Name of Facility/Equipment/Utility/System/Activity/Procedure**<br>**Unit Operation**: Liquid vial Filling and Stoppering 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*D |
| **38.** | PLC / Control system | ➢ Power failure/ emergency stop | ➢ Process out of specification.<br>➢ Unsafe if start automatically on restoration of power. | ➢ There is no alarming system.<br>➢ Machine becomes start automatically.<br>➢ There is no provision of UPS for power back up in case of power failure. | ➢ Alarm message is provided.<br>➢ On power failure equipment comes to rest to protect operator, equipment itself & the articles also.<br>➢ Machine is not start automatically without operator intervention after incident.<br>➢ Provision of UPS is also there to the control the system in case of power failure. | DQ & IQ of Filling & Stoppering Machine | 3 | 2 | 2 | 12 | Adequate procedure no recommend ation required. Hence risk is accepted. | NA | NA | NA | NA |
| **39.** | PLC / Control system | ➢ No protection of PLC against manipulation & changes. | ➢ Process data can be manipulated easily.<br>➢ Product process details can be affected. | ➢ No password protection has been provided.<br>➢ All users have been provided with same passwords.<br>➢ There is no access security system. | ➢ Minimum 3 level password protections are provided for the system.<br>➢ **Level 1:** Operator<br>➢ **Level 2:** Supervisor<br>➢ **Level 3:** Admin/ Manager<br>➢ All users have been provided with unique passwords.<br>➢ System is allowing only authorized users to access system and change parameters. | DQ & IQ of Filling & Stoppering Machine | 3 | 2 | 1 | 6 | Adequate procedure no recommend ation required. Hence risk is accepted. | NA | NA | NA | NA |

# QUALITY RISK ASSESSEMENT AND MITIGATION PLAN

**QRA No.:**

| **Name of Facility/Equipment/Utility/System/Activity/Procedure**<br>**Unit Operation**: Liquid vial Filling and Stoppering 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*D |
| **40.** | LAF (Over Filling & discharge conveyor) | ➢ The air flow from LAF is not uniform or is turbulent. | ➢ Turbulent or insufficient flow may lead to particulate contamination of the product inside Vials. | ➢ Uniform unidirectional flow not maintained from the LAF.<br>➢ Air velocity is not maintained at the working level.<br>➢ Air velocity and filter integrity didn't carry out during qualification. | ➢ Uniform unidirectional flow maintained from the LAF up to the working area inside oRABs.<br>➢ A uniform air velocity of 90 fpm ± 20% has been maintained at the working level inside oRABs.<br>➢ Air velocity and smoke study has been carried out during qualification for verification of the same. | IQ ,OQ & PQ of Filling & Stoppering Machine | 4 | 2 | 1 | 8 | Adequate procedure no recommend ation required. Hence risk is accepted. | NA | NA | NA | NA |
| **41.** | LAF (over Filling & discharge conveyor) | ➢ LAF fails / Stops | ➢ Contamination of product is possible if machine is in operation. | ➢ No interlocking system is available with LAF Operation.<br>➢ Machine running continuously in case of any LAF failure.<br>➢ There is no alarm provision if in case LAF fails/Stops. | ➢ Machine operation is interlocked with LAF's operation, which are mounted on top of the entire filling & Stoppering machine and on its infeed and discharge side.<br>➢ Machine stops in case of any LAF failure.<br>➢ Alarm provision has been provided in case of LAF fails/ stops. | IQ ,OQ & PQ of Filling & Stoppering Machine | 4 | 2 | 1 | 8 | Adequate procedure no recommend ation required. Hence risk is accepted. | NA | NA | NA | NA |

# QUALITY RISK ASSESSEMENT AND MITIGATION PLAN

**QRA No.:**

| **Name of Facility/Equipment/Utility/System/Activity/Procedure**<br>**Unit Operation**: Liquid vial Filling and Stoppering 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*D |
| **42.** | LAF (over Filling & discharge conveyor) | ➢ HEPA Filter leakage/ Choking | ➢ In case of leakage may lead to product contamination. | ➢ There is no extra precaution in case of HAPA choking/leakage to prevent direct load of particles on HEPA filter.<br>➢ There is no provision to monitor pressure across all HEPA filters of LAF.<br>➢ Filter integrity test of HEPA filters didn't carry out during qualification. | ➢ Pre-filter is installed at the upstream of HEPA filters to prevent direct load of particles on HEPA filter<br>➢ Differential pressure switch/ transmitter are provided to monitor pressure across all HEPA filters of LAF, along with alarm in case of high or low DP.<br>➢ Integrity test of HEPA filters shall be performed during qualification and routinely as per SOP. | IQ ,OQ & PQ of Filling & Stoppering Machine | 4 | 2 | 2 | 16 | Adequate procedure no recommend ation required. Hence risk is accepted. | NA | NA | NA | NA |
| **43.** | LAF (over Filling & discharge conveyor) | ➢ Choking/ Damage of Pre-filter | ➢ Particulate matter load directly on the HEPA filter, may lead to frequent replacement of HEPA filter. | ➢ There is no provision for indicating choking or leakage of pre-filters.<br>➢ In case of low or high DP there is no provision for alarm system.<br>➢ Cleaning frequency of pre filers is not defined. | ➢ Differential pressure switch/ gauge are provided for indicating choking or leakage of pre-filters with alarm provision in case of high or low DP.<br>➢ Pre-filters are also be cleaned regularly as per SOP. | IQ ,OQ & PQ of Filling & Stoppering Machine | 3 | 2 | 1 | 6 | Adequate procedure no recommend ation required. Hence risk is accepted. | NA | NA | NA | NA |

# QUALITY RISK ASSESSEMENT AND MITIGATION PLAN

**QRA No.:**

| **Name of Facility/Equipment/Utility/System/Activity/Procedure**<br>**Unit Operation**: Liquid vial Filling and Stoppering 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*D |
| **44.** | oRABs access doors | ➢ oRABs access door may be opened during process. | ➢ Chances of product contamination by direct handling of operators. | ➢ There is no provision for access the door with the interlocking system.<br>➢ There is no alarm provision provided. | ➢ Security switches/ sensors are provided at the access doors with interlock feature with the operation of machine i.e. machine stops immediately if oRABs access doors are opened.<br>➢ Alarm provision has been also provided for the same. | DQ, IQ & OQ of Filling & Stoppering Machine | 3 | 2 | 2 | 12 | Adequate procedure no recommend ation required. Hence risk is accepted. | NA | NA | NA | NA |
| **45.** | Compressed air | ➢ Insufficient pressure | ➢ Equipment operation will be disturbed. | ➢ There is no pressure gauge and pressure limits are provided.<br>➢ No alarming system is there in case of low air pressure.<br>➢ No qualification activity has been performed. | ➢ Pressure gauge/ Pressure switch is provided at compressed air inlet to monitor & control compressed air pressure along with alarm provision in case of low pressure.<br>➢ Verification has been performed at the time of qualification studies. | DQ & IQ of Filling & Stoppering Machine | 2 | 3 | 1 | 6 | Adequate procedure no recommend ation required. Hence risk is accepted. | NA | NA | NA | NA |
| **46.** | User | ➢ Operation SOP does not contain proper information and user may operate system | ➢ User may make a wrong decision. | ➢ System operation SOP's didn't reviewed through concerned personnel.<br>➢ There is no technical support to the user. | ➢ System operation SOP has been reviewed with all aspects and approved.<br>➢ Vendor provided execution support to the user for completion all stages of the qualification report. | DQ,IQ & OQ of Filling & Stoppering Machine | 3 | 1 | 1 | 3 | Adequate procedure no recommend ation required. Hence risk is accepted. | NA | NA | NA | NA |

# QUALITY RISK ASSESSEMENT AND MITIGATION PLAN

## QRA No.:

| **Name of Facility/Equipment/Utility/System/Activity/Procedure**<br>**Unit Operation**: Liquid vial Filling and Stoppering 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*D |
| | | ➢ Unauthorized person tries to start/stop the system. | ➢ Untrained persons may damage the system or product quality may be affected. | ➢ There is no security access system for running the machine. | ➢ System is not start without password | DQ, IQ & OQ of Filling & Stoppering Machine | 3 | 1 | 1 | 3 | Adequate procedure no recommend ation required. Hence risk is accepted. | 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 :** Liquid vial Filling and Stoppering 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.:** NA

# QUALITY RISK ASSESSEMENT AND MITIGATION PLAN

**QRA No.:**

| **Name of Facility/Equipment/Utility/System/Activity/Procedure**<br>**Unit Operation**: Liquid vial Filling and Stoppering machine | **Date Of Quality Risk Assessment:** |
|---|---|

| **Quality Risk Management Team** | | | **Reviewed By**<br>**Head Production**<br>**Sign & Date** | **Approved By**<br>**Head QA**<br>**Sign & Date** |
|---|---|---|---|---|
| **Name** | **Department** | **Sign & Date** | | |
| | | | | |
| | | | | |

## QUALITY RISK ASSESSEMENT AND MITIGATION SUMMARY REPORT

**Name of Facility/Equipment/Utility/System/Activity/Procedure/Unit Operation :** Liquid vial Filling and Stoppering machine

**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**