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| **Risk Assessment Document Dispensing, Sieving & Blending Isolator**  **Equipment ID:**  **Revision index**   |  |  |  | | --- | --- | --- | | **Revision** | **Date** | **Reason for revision** | | 00 |  | First issue | |  |  |  | |  |  |  | |  |  |  | |

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| **1.0 Approval**  This document is prepared by the validation team of ……………for the project ‘OSD Formulations Facility’ of …………………..under the authority of their Project Manager. Hence, this document before being effective shall be approved by the QA team of ……………..and authorized by the appropriate Project Authority. |

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| **2.0 Introduction**  According to the definition, given in Annex 15, 20 to the EU-GMP-Guide, a risk assessment is a method to assess and characterize the critical parameters in the functionality of an equipment or process. Therefore, risk assessment is a key element in the qualification and validation approach.  In the project context, risk assessment is performed as basic GMP/EHS-Risk assessment, which shall help to identify important GMP/EHS-requirements.  **3.0 Aim of the Risk Assessment**  At the very basic stage of design the risk assessment is carried out to verify that all features are taken into consideration to avoid the risk of failure of critical GMP and EHS parameter in the equipment.  During study, all GMP, EHS and operational parameters will be identified and assessed for the risk, appropriate mitigation will be proposed and verification point will be identified and defined.  The Risk assessment report is produced to provide the documented evidence that design concepts or requirement are complete in considering all GMP, EHS and operational risks.  **4.0 Reference Documents**   |  |  |  | | --- | --- | --- | | **S.No.** | **Document Title** | **Document Number** | | 1. | Validation master plan |  | | 2. | Project validation plan |  | |

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| **5.0 Equipment Description:**  Dispensing, Sieving & Blending Isolator is designed for dispensing, sampling & sieving of active potent ingredients which needs high containment transfer. Dispensing, Sieving & Blending Isolator is having a negative pressure w.r.t. room and air leakage rate not more than 5% of isolator volume  Dispensing, Sieving & Blending Isolator consists of two sections i.e. a Dispensing and blending section and a sieving section. There is no physical barrier between the two sections, but the Blending section is double height to accommodate the blender. The chamber has provided HEPA filters supported by fine filter. Wash nozzle and hose is used for manual cleaning of chamber. There is drain outlet in the base of chamber. Sieving section has series of glove ports, weighing balance, Spray gun for wash in place (WIP). IBC with RTP passive at charging & discharging are docked to an active at the base of the Isolator using a fixed jacking hoist to ensure valve integrity.  **6.0 Participants**   |  |  |  | | --- | --- | --- | | **Name (block letters)** | **Function** | **Signature** | |  |  |  | |  |  |  | |  |  |  | |  |  |  | |  |  |  |  * 1. **Risk Management Process**   A typical Risk management process consists of following steps:   * + - Risk Assessment:       * Risk Identification       * Risk Analysis       * Risk Evaluation     - Risk Control       * Risk Reduction       * Risk Acceptance |

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| * Result of Risk management processes * Risk Review * Risk Assessment consists of the identification of hazards and the analysis and evaluation of risks associated with exposure to those hazards.   Risk identification is a systematic use of information to identify hazards referring to the risk question or problem description.  Risk analysis is the estimation of the risk associated with the identified hazards. It is the qualitative or quantitative process of linking the likelihood of occurrence and severity of harm.  Risk evaluation compares the identified and analyzed risk against given risk criteria. Risk evaluation considers the strength of evidence for all three of the fundamental questions.  The output of a risk assessment is either a quantitative estimate of risk or a qualitative description of range of risk. In case of qualitative description the risk is expressed using descriptors such as “high”, “medium” or “low”.   * Risk control includes decision making to reduce and/ or accept risks. The purpose of risk control is to reduce the risk to an acceptable level. The amount of effort used of risk control should be proportional to the significance of the risk.   Risk reduction focuses on processes for mitigation or avoidance of quality risk when it exceeds a specified (acceptable) level. Risk reduction might include actions taken to mitigate the severity and probability of harm.  Risk acceptance is a decision to accept risk. Risk acceptance can be a formal decision to accept the residual risk or it can be a passive decision in which residual risks are not specified.   * The output/ result of the quality risk management process should be appropriately communicated and documented. * Risk management should be an ongoing part of the quality management process. A mechanism to review or monitor events should be implemented.   The output/ results of the risk management process should be reviewed to take into account new knowledge and experience.  This document applies the risk management principles to identify the risks associated with the design, construction and operational features of any equipment, which is going to be procured and installed in the facility.  **7.1 Identifying GMP risk**  Identification of Risk associated with the equipment, is generally based on prior experience and the concerns of the participants of risk assessment document.  The risks identified are categorized as “GMP risk” or “Non-GMP risk”.  GMP is defined as “the practices which ensures that products are consistently produced and controlled to the quality standards appropriate to their intended use and as required by the marketing authorization.” Thus, GMP covers all aspects of the manufacturing process: defined manufacturing process; validated critical manufacturing steps; suitable premises, storage, transport; qualified and trained production and |

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| quality control personnel; adequate laboratory facilities; approved written procedures and instructions; records to show all steps of defined procedures have been taken; full traceability of a product through batch records and distribution records; and systems for recall and investigation of complaints.  Thus those risks which might have a direct or indirect impact on the quality of the product are classified as “GMP risk”. Also, those risks which might result in regulatory guidelines non-compliance are also classified as “GMP risk”.  For example: The MOC of the product contact part has a direct impact on the quality of the product. Thus, it is classified as GMP risk.  The “Non GMP” risks include risks related to EHS, operational and other non-critical hazards.  Following types of risks are mainly identified during risk assessment process:   * Risk related to product contact materials for equipment and containers (eg. Selection of SS grade, gaskets, lubricants etc.) * Risks related to appropriate utilities and their control (eg. Steam, gases, power source, compressed air etc.) * Risks related to calibration/ preventive maintenance * Risks related to protection the environment and health & safety of personnel. * Risks related to cleaning & sterilization * Risks related to control system of the equipment * Risks related to product loss   **7.2 Risk Analysis & Evaluation**  The risk analysis is performed using a qualitative basis of approach.  Qualitative analysis uses word form or descriptive scales to describe the magnitude of potential consequences/ impact and the likelihood that those consequences will occur.  The qualitative measures of likelihood includes descriptors like “Unlikely”, “Possible” and “Likely”, whereas the qualitative measures of consequence/ impact includes descriptors like “Minor”, “Moderate” and “Major”.  **Qualitative measures of likelihood**   |  |  |  | | --- | --- | --- | | **Level** | **Descriptor** | **Example detail description** | | 1 | Unlikely | May occur at some time | | 2 | Possible | Might occur at some time | | 3 | Likely | Will probably occur in most circumstances |   **Qualitative measures of consequence/ impact\***   |  |  |  | | --- | --- | --- | | **Level** | **Descriptor** | **Example detail description** | | 1 | Minor | * No impact on the product quality or outcome of the equipment. * Features required for easing equipment operation. | | 2 | Moderate | * No direct impact on product quality/ outcome of equipment. however may indirectly affect the product quality. * Minor effect on personnel health | |

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| |  |  |  | | --- | --- | --- | | **Level** | **Descriptor** | **Example detail description** | |  |  | * Used in the initial stage of operation, however it may affect the final output but those are not used for final release of output. * Effect on environment such as clean room. | | 3 | Major | * Features having direct impact on product quality/ outcome of equipment like contact parts MOC, Surface finish, Control system, Process air quality etc. * Failure could lead to regulatory non-compliance. * Loss/ damage to equipment or its critical sub-components * Critical instruments not calibrated or not of desired range or accuracy. * Proper supporting documentation not provided. * Major effect on personnel health |   Based on the above parameters of likelihood and consequence a qualitative risk analysis matrix is prepared to identify the overall Level of Risk, as mentioned in table below.  **Qualitative risk analysis matrix – level of risk\***   |  |  |  |  | | --- | --- | --- | --- | | **Likelihood** | **Consequences/ Impact** | | | | **1 – Minor** | **2 – Moderate** | **3 – Major** | | **1 (Unlikely)** | Low | Medium | High | | **2 (Possible)** | Low | Medium | High | | **3 (Likely)** | Medium | High | High |   The final Risk level shall thus be described using descriptors such as “Low”, “Medium” & “High”, where each descriptor implies the following meaning:  **Low –** Risk can be accepted or ignored. These do not affect the final quality of the equipment/ system and it can be managed by routine procedures and are unlikely to need specific application of resources.  **Medium** – Risk required ongoing monitoring and review, to ensure level of risk does not increase.  Otherwise managed by routine procedures.  **High** – Action plans must be developed, with clear assignments of individual responsibilities and timeframes. |

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| **8.0 Risk Assessment**  In the following section a table is produced for the risk assessment. The significance or instruction for each column is described in the following paragraph.  Column 1: **Serial number** of Risk assessment item  Column 2: **Process step/Component**: Identify the process step or component associated with the risk.  Column 3: **Risks**: Identify the type of risk associated with the process or component. Column 4: Verify that whether there is **GMP risk.**  Column 5: **Justification**: Provide justification for declaring both yes/no for GMP Impact in column 3.  Column 6: For the risk **other than of GMP risk,** write what is the other type of risks  e.g. EHS, Operational.  Column 7: **Justification**: Provide justification for considering any risk.  Column 8: **Risk level** Determine the Risk level as High, Medium or low based on the impact.  Column 9: **Risk Control:** It is further divided into following three sections  Column 9a: **Mitigation Method**: Write the risk mitigation strategy as considered in design. Column 9b: **Residual risk level**: After the risk mitigation what is the residual risk level,  whether it is acceptable, low or Medium  Column 9c: **Verification**: Write the test point where the risk mitigation strategy will be verified. |

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| **S. No** | **Process steps/component** | **Risk** | **GMP**  **Risk Yes/No** | **Justification** | **Other Risk type** | **Justification** | **Risk Level** | **Risk Control** | | |
| **Mitigation Method** | **Residual risk level** | **Verificatio n** |
| **Charging** | | | | | | | | | | |
| 1. | Charging of raw material container is not possible. | Provision not available for placing the raw material container in isolator | Yes | Basic requirement | No | NA | High | Proper transferring system shall be considered in the design .transfer hatch / liner shall be used for  transfer of material | Acceptable | IQ/OQ |
| 2. | Transfer of API containers from warehouse to dispensing room | Wrong container is transferred with respect to material identification, container integrity and material receipt  number for FIFO. | Yes | Basic GMP requirement | EHS | In case the container is not integral | Medium | SOP: material storage and dispensing manufacturing instructions: checklist | Acceptable | SOP |
| 3. | Lighting | Light is not suitable | Yes | Basic GMP requirement | No | NA | High | Proper lighting (min 500 lux)shall be provided | Acceptable | IQ/OQ |
| 4. | Weighing  platform | Weighing platform is  not shockproof | Yes | Inaccurate  weighing possible | No | NA | High | Anti-vibration platform is  included | Acceptable | IQ |
| 5. | Visibility in the chamber | Visibility in the chamber is poor | Yes | Readability of weight is critical  process requirement | No | NA | High | Transparent material shall be used to ensure visibility. | Acceptable | IQ |

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| **Mitigation Method** | **Residual risk level** | **Verificatio n** |
| 6. | Height of isolator | Isolator height is not suitable to dock the material collection bin | Yes | Basic requirement | No | NA | Medium | Working height is considered to  accommodate a vessel of specified height | Acceptable | OQ |
| 7. | Docking not gastight | Docking not gastight | No | Does not have any impact on product quality | EHS | Contaminati on of air with high potent drug | High | Supplier to ensure the gastight closure of isolator. Regular leak test schedule for door gasket replacement SOP: Preventive maintenance to include schedule of leak  test and gasket replacement. | Acceptable | IQ/OQ |
| 8. | Size of isolator and container | Docking cannot be done due to mismatched aperture diameter between isolator and container | Yes | Basic requirement | EHS | Contaminati on of external/ room with high potent  drug | High | Aperture on isolator, container and split valve will be kept same for correct interfacing | Acceptable | IQ |
| 9. | Chamber space of isolator | Isolator chamber space is not suitable to keep  the material container | Yes | Design adequacy | No | NA | Medium | Design considered with all operational requirements | Acceptable | IQ |

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| **Mitigation Method** | **Residual risk level** | **Verificatio n** |
| 10. | Size of sleeve | Sleeve port size is not suitable to transfer minimum 5 kg powder materials, HEPA filter  and waste material. | Yes | Design adequacy | No | NA | Medium | Design considered a size of minimum 200 mm sleeve port | Acceptable | IQ |
| 11. | Opening of Isolator doors | The opening of isolator door is not warned | No | Does not have any impact on the quality of the product | EHS | Contaminati on of external/ room with high potent drug.  Operator safety | Medium | The opening of isolator door should be alarmed and equipment should come to rest with exhaust running. | Acceptable | OQ |
| 12. | Weighing and weighing balance | Balance is not suitable for weighing in  required range of quantity | Yes | Affect weighing accuracy | No | NA | High | Design considered the range and accuracy | Acceptable | IQ / OQ |
| 13. | Balance readings | Balance readings are not visible | Yes | Critical requirement for  weighing accuracy | No | NA | Medium | Reading should be visible | Acceptable | OQ |
| 14. | Balance level | Balance could not be leveled properly | Yes | Affect weighing accuracy | No | Na | High | Balance base to be provided with level adjustment screw and spirit level. | Acceptable | IQ |

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| **Mitigation Method** | **Residual risk level** | **Verification** |
| 15. | Printer interface | Print of weight cannot be taken | Yes | Documentation requirement; however can be manually recorded | No | NA | Medium | In case printout is not available, weight will be recorded in batch manufacturing record  manually. | Acceptable | IQ/SOP for weighing |
| 16. | Hand gloves | Uncomforted operation with hand gloves, chances of material  spillage. | No | No impact on weighed quantity | Operational | Loss of material | High | SOP: Dispensing of active ingredient in Isolator Training of operators for  the operations in isolator | Acceptable | IQ/OQ |
| **Vibro Sifter** | | | | | | | | | | |
| 17. | Charging of material | Spillage during charging of material | Yes | Loss of quantity of the materials, result in disturbed proportion of the same, area  contamination | No | NA | High | charging chute will be designed wide enough for appropriate feeding method of input materials | Acceptable | IQ / PQ |
| 18. | Charging vent | Material spreads out from the charging vent | Yes | Loss of quantity of the materials, result in disturbed proportion of the  same, area contamination | No | NA | High | Lid/Cover will be provided to stop powder to spreading out | Acceptable | IQ / PQ |

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| **Mitigation Method** | **Residual risk level** | **Verificatio n** |
| 19. | Sifting | Dead spots formed | Yes | Material will remain non-sifted | No | NA | Medium | * Equipment should be designed so that there would not be any dead spot * Sieve shall be located within the isolator with outlet connected directly to the outlet port * Alarm shall be provisioned for   malfunction /start | Acceptable | OQ |
| 20. | Frame and sieve assembly | Frame and sieve assembly get loosen during operation | Yes | Malfunctioning of the sifting process | EHS | Accident due to detachment of parts.  Product exposure. | High | Secure locking of the frame, gasket and sieve assembly will be considered so that it will  remain tighten during entire sifting operation | Acceptable | IQ / OQ |
| 21. | Discharge chute | Powder spreads out during transferring | Yes | Product loss | EHS | Product exposure | High | Discharge chute shall be designed to avoid the spillage using silica latex  sleeve | Acceptable | IQ / PQ |

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| 22. | Product discharge | Incomplete discharge of the product | Yes | Uniformity of content of product may get disturbed | No | NA | Medium | Vibrosifter will be designed to facilitate complete discharge of the product. Tangential slope  will be provisioned at the discharge. | Acceptable | IQ / PQ |
| **Blender** | | | | | | | | | | |
| 23. | RPM of blender | With respect to process requirement desired RPM cannot be set and  monitored. | Yes | Process requirement for effective mixing. | No | NA | High | RPM should be set and controlled from control panel. | Acceptable | OQ |
| 24. | Timer | Blending time cannot be set | Yes | Basic requirement | No | NA | High | Timer should be set and controlled from the control  panel. | Acceptable | OQ |
| 25. | Timer | Blending time gets reset before completion of blending cycle. | Yes | Correct Blending time cannot be achieved which will lead to improper mixing. | No | NA | High | Provision to be provided to continue the blending from where it was stopped due to breakdown or any other reason. Memory backup  should be facilitated. | Acceptable | IQ / OQ |
| 26. | Blending | Upon completion of blending operation  blender stops in undesired direction | No | Does not have any impact on the  quality of the product | Operational | Difficulty in unloading | Medium | After completion of the blending time, the  discharge valve should rest at bottom side | Acceptable | OQ |

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| 27. | Sampling | Sampling is not possible from the blender | Yes | Sampling is required for validation study and routine  assessment sample. | No | NA | High | Provision for manhole should be provided to assist sampling. | Acceptable | IQ / OQ |
| **Controlling system** | | | | | | | | | | |
| 28. | Control system | Control system do not detect failures | Yes | Basic requirement | No | NA | Medium | Failure mode detection is considered | Acceptable | OQ |
| 29. | Machine operation | Operator and staff is not trained | Yes | Untrained operators may not operate equipment properly | Operational/ EHS | Chances of accidents | High | Proper training to be imparted with operator and staff by the vendor | Acceptable | OQ |
| **Discharge** | | | | | | | | | | |
| 30. | Discharge of dispensed material | Discharge of dispensed material in closed condition in IBC not possible | No | Does not have any impact on the quality of the product | EHS | Staff protection | High | * Rapid transport port shall be provided * RTP active and passive shall be provided for IBC * Jacking hoist shall be provided to support easy lifting of IBC | Acceptable | IQ/OQ |

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| **Cleaning and material of construction** | | | | | | | | | | |
| 31. | Material of chamber | Material of chamber not suitable | Yes | May lead contamination | No | NA | High | * SS316 or better grade shall be provided for the contact parts with   0.4 Ra mirror finish   * Non contact parts shall be SS304 or better * All bolts, nuts on the exterior part of the equipment will be * MOC certificate shall be provided | Acceptable | IQ |
| 32. | Transfer of material | Isolator is not in cleaned condition | Yes | Cross contamination | No | NA | High | SOP: Operation & cleaning of dispensing sieving & Blending Isolator | Acceptable | To record in checklist of batch mfg records/  SOP |

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| 33. | Cleaning of chamber | Chamber is not cleanable | Yes | May cause cross contamination of product | No | NA | High | Design of equipment should enhance cleaning feasibility by providing minimum sharp corners, minimum crevices &  smooth finished weld joints | Acceptable | IQ |
| 34. | Isolator surface | Isolator surface is not compatible with  decontaminating agents | Yes | Contamination | No | NA | High | MOC selection is considered with decontaminating agents | Acceptable | IQ |
| 35. | Draining of water | During cleaning water is not drained from the surface | Yes | Chances of microbial growth if water is not drained  completely | No | NA | High | A suitable slope towards drain port is considered | Acceptable | IQ |
| 36. | Isolator surface | Isolator surface is not dried | Yes | Require dryness for operation. Chances of microbial growth if surface is not  dried | No | NA | High | Isolator should be suitable to connect with compressed air | Acceptable | IQ |

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| 37. | Connection of utility to chamber | Chamber cannot be connected with clean media (potable water, purified water,  compressed air) for cleaning | Yes | Contamination | No | NA | Medium | Nozzle and hose for connecting clean media shall be provided for manual cleaning | Acceptable | IQ |
| 38. | Cleaning of balance | Balance base is not cleanable and not compatible with  decontamination agent | Yes | Contamination | No | NA | High | MOC of balance base should be compatible with decontaminating agent | Acceptable | IQ |
| **Safety:** | | | | | | | | | | |
| 39. | Weighing chamber | Chamber is gastight | No | Equipment is installed in clean area | EHS | Emission of high potent drug | Medium | * Supplier to ensure the gastight closure of isolator * Regular leak test * Schedule for door gasket replacement * SOP: Preventive maintenance to include schedule of leak test   and gasket replacement | Acceptable | IQ/OQ |

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| 40. | HEPA filters and electrical sockets | During cleaning weighing balance, HEPA filter and electrical sockets are not protected from water | No | This is a special requirement for these components to protect from water | Operational | Components or component performance is not  compatible with water | High | * SOP: Precaution to be taken during cleaning * Alarm shall be generated in case of filter blockage | Acceptable | OQ/SOP |
| 41. | Wash water | Wash water pass  through the plastic sleeve port | Yes | If not detected  dispensed material may get wet | No | NA | High | A suitable cover over sleeve port is considered | Acceptable | IQ |
| 42. | Maintenance | Chamber is not accessible during breakdown  maintenance | Yes | GMP requirement | No | NA | High | Isolator will be provided with access door | Acceptable | IQ |
| 43. | Joint gaskets | Joint gaskets are not replaceable | Yes | Maintenance requirement | EHS | If damaged there is chance of product  leakage | Medium | Gasket will be replaceable | Acceptable | IQ |
| 44. | Gaskets | Gaskets are not compatible with material handled in isolator | Yes | Contamination | EHS | If damaged, there is a chance of  product leakage | High | Gaskets should be food grade selected gaskets should be compatible with  decontaminating and cleaning agent | Acceptable | IQ |

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| 45. | Hand gloves | Hand gloves are not replaceable | Yes | Contamination in case of damage | EHS | Product leakage | High | Hand gloves should be replaceable  SOP: Preventive maintenance (for visual  checking and replacement) | Acceptable | IQ |
| 46. | Hand gloves | Pinhole leaks in hand gloves are not detectable | No | Does not have any impact on product | EHS | Product leakage | High | Hand gloves should be suitable for in place integrity test | Acceptable | OQ |
| 47. | Hand gloves | Hand glove material is not compatible with material to weigh | Yes | Material contamination | No | NA | Medium | * Hand gloves should be inert to product * Doubled layer glove shall be considered | Acceptable | IQ |
| 48. | Hand gloves | Hand glove material is not compatible with  decontaminating agent | Yes | Material contamination | No | NA | Medium | Hand gloves should be inert to decontaminating  agent | Acceptable | IQ |
| 49. | Balance body | Balance body is not compatible with decontaminating agent | Yes | Material contamination | No | NA | Medium | SOP: During cleaning, balance body will be wrapped and taken out | Acceptable | OQ/ SOP |
| 50. | Balance cable | Balance cable is not  compatible with decontaminating agent | Yes | Material contamination | No | NA | Medium | SOP: During cleaning,  balance cable will be wrapped and taken out | Acceptable | OQ/ SOP |

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| **S. No** | **Process steps/component** | **Risk** | **GMP**  **Risk Yes/No** | **Justification** | **Other Risk type** | **Justification** | **Risk Level** | **Risk Control** | | |
| **Mitigation Method** | **Residual risk level** | **Verification** |
| 51. | Lubrication | Lubricants quality not good | No | May leads to contamination of product | No | NA | High | * Lubricants must be food grade and non – toxic * Food grade certificate shall be available | Acceptable | IQ |
| 52. | Air handling system | Design does not prevent leakage of powder in the environment/ System does not work properly | Yes | Chances of cross contamination | EHS | Emission of powder | High | * All ducting must be leak proof Outlet and exhaust supported with HEPA filter * Blower shall be able to generate required CFM of supplied air * Speed shall be controlled by VFD * Alarm shall be generated in case of Blower VFD   not working properly | Acceptable | IQ, OQ |
| 53. | Waste water drainage | Rinse water drain in wrong drain | No | Does not have any impact on the quality of the  product | EHS | Will not be properly treated | Low | Isolator drain line will be directed towards the correct drain | Acceptable | Facility Qualification |
| 54. | Air break | No air break maintained | Yes | Back suction of waste water | No | NA | Low | All drain points will have air break | Acceptable | Facility Qualification |
| **Measuring Instruments:** | | | | | | | | | | |

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| **S. No** | **Process steps/component** | **Risk** | **GMP**  **Risk Yes/No** | **Justification** | **Other Risk type** | **Justification** | **Risk Level** | **Risk Control** | | |
| **Mitigation Method** | **Residual risk level** | **Verification** |
| 55. | Measuring Instruments | Measuring instruments  are not in defined range | Yes | Instruments are  not suitable for use. | No | NA | High | Measuring ranges shall be defined | Acceptable | IQ / OQ |
| 56. | Measuring Instruments | Measuring instruments could not be calibrated | Yes | Instruments are not suitable for use as it may produce false results | No | NA | High | * Must be calibrated and suitable for recalibration * Suitable calibration   certificate shall be provided | Acceptable | IQ / OQ |
| 57. | Pressure of chamber | Pressure of chamber cannot be measured | Yes | GMP requirement | No | NA | Medium | * Provision for measurement of differential pressure * Magnehelic gauge shall be installed to monitor the pressure of chamber * There should be alarm in case pressure reaches   out of specification | Acceptable | IQ / OQ |

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| **S. No** | **Process steps/component** | **Risk** | **GMP**  **Risk Yes/No** | **Justification** | **Other Risk type** | **Justification** | **Risk Level** | **Risk Control** | | |
| **Mitigation Method** | **Residual risk level** | **Verification** |
| 58. | Differential pressure across the HEPA filter | Differential pressure across the HEPA filter cannot be measured | Yes | GMP requirement | No | NA | Medium | * Differential pressure gauge / magnehelic gauge shall be provisioned to monitor differential pressure across the HEPA * Alarm for pressure out of specification | Acceptable | IQ / OQ |
| **Air filteration** | | | | | | | | | | |
| 59. | Air filtration | Air is not filtered / contaminated | Yes | Cross contamination possible , product may get  contaminated | No | NA | High | In the supply and exhaust air double HEPA shall be provisioned to ensure pure air | Acceptable | IQ / OQ |
| 60. | HEPA filter | Integrity of HEPA  filter cannot be tested | Yes | Basic GMP  requirement | No | NA | High | There should be POA/DOP  port for integrity testing | Acceptable | IQ / OQ |
| 61. | Coarse filter | Air not filtered from coarse particle | Yes | HEPA filter could  functioned properly | No | NA | High | Coarse filter shall be  installed before the HEPA filter | Acceptable | IQ / OQ |
| **Environment** | | | | | | | | | | |

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| **S. No** | **Process steps/component** | **Risk** | **GMP**  **Risk Yes/No** | **Justification** | **Other Risk type** | **Justification** | **Risk Level** | **Risk Control** | | |
| **Mitigation Method** | **Residual risk level** | **Verification** |
| 62. | Power failure | Equipment start after recovery without human intervention | No | Does not have any impact on the quality of the product | EHS | Machine function may get disturbed, may lead to accident | Medium | * On power failure equipment shall come to rest, to protect equipment itself * Power restart must not be automatic and human intervention must be required | Acceptable | IQ / OQ |
| 63. | Closer for rotating parts | Closer not provided to equipment | No | Does not have any impact on the  quality of the product | EHS | May leads to accident | High | Appropriate closer for all rating parts in the  equipment shall be provided | Acceptable | IQ |
| 64. | Noise level | Too much noise generated by equipment | No | Does not have any impact on the quality of the product | EHS | May cause deafness to the operator/  staff | Medium | Noise level below 80 db at a distance of 1 m from the equipment | Acceptable | OQ |
| **Documentation:** | | | | | | | | | | |
| 65. | Documentation | Critical surfaces are not tested for material of construction and test reports are not provided | Yes | Lack of documented evidence leads to question on the quality of MOC | No | NA | High | MOC description and certification of critical parts to be provided | Acceptable | IQ / OQ |

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| **Mitigation Method** | **Residual risk level** | **Verification** |
| 66. | Documentation | Instruments are not provided with calibration certificate | Yes | Calibration cannot be assured due to lack of documented  evidence | No | NA | High | Critical instrumentation shall be supported with calibration certificates. | Acceptable | IQ / OQ |
| 67. | Documentation | Equipment is not provided with design and functional  specification | Yes | Design qualification is not possible | No | NA | High | Design and functional specification should be supplied as per URS | Acceptable | IQ / OQ |
| 68. | Documentation | Equipment is not provided with Operation &  maintenance manual | Yes | Correct operation is not ensured and Qualification  requirement | No | NA | High | O & M manual should be supplied per URS | Acceptable | IQ / OQ |
| 69. | Standard Operating procedure | Standard operating procedures are not available. | Yes | Procedures critical operations cannot be carried out successfully resulting process  failure. | Operational | Productivity will get decrease to unavailabilit y of  procedure. | High | SOPs for Operation, Cleaning and maintenance shall be prepared in line with operational and maintenance manual and  finalized. | Acceptable | IQ / OQ |

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| * 1. **Summary and Conclusion:**      + The risk assessment is performed to establish the design parameters of the equipment so as to meet the desired performance of the equipment i.e. Dispensing, Sieving & Blending isolator.      + The critical risks pertaining to GMP and other than GMP were analyzed with justification and mitigation procedures.      + For each recognized GMP-risk and other than GMP risks necessary measures are defined. Organizational measures, like SOPs, are also possible measures for special GMP-risks. The availability of these SOPs will be checked at the time of accomplishment of OQ of the machine.      + To control the risk, various mitigation methods shall be verified through SOPs ,operation & maintenance manuals, and calibration certificates at respective verification points      + Based on Risk assessment, the URS shall be prepared.   *“It is concluded that the* ***Risk Assessment*** *performed for the equipment will mitigate the risk of failures of critical parameters during design, commissioning, installation, operation and performance of the equipment”.* |

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| **10.0 Abbreviation:**   |  |  | | --- | --- | | **Acronym** | **Definition** | | cGMP | Current Good Manufacturing Practice | | db | Decibel | | EU-GMP | European –Good Manufacturing Practice | | GA | General Arrangement | | GMP | Good Manufacturing Practices | | HEPA | High efficiency particulate air | | HMI | Human Machine Interface | | IQ | Installation Qualification | | MOC | Material Of Construction | | OQ | Operational Qualification | | O & M | Operation and Maintenance Manual | | PQ | Performance Qualification | | PLC | Programable logic controller | | RH | Relative humidity | | SOP | Standard Operating Procedures | | SS | Stainless steel | | URS | User Requirement Specification | | w.r.t. | With respect to | |