RISK ASSESSMENT DOCUMENT
FOR
HVAC SYSTEM

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1 Introduction

According to the definition, given in Annex 15 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 for the equipment is performed as basic GMP/ EHS-Risk Assessment, which shall help to identify important GMP/ EHS-requirements.

2 Aim of 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.

3 Reference Documents/ Drawings

S. No.	Document Title	Document Number
1.	Validation master plan	

4 Equipment/ System Description

This risk assessment is conducted for the HVAC System of the Sterile Formulations Facility and consists of the air handling units for manufacturing areas.

The HVAC system for this Sterile Formulations Facility has been designed for obtaining and maintaining the required working conditions by means of providing specified Temperature, RH & Differential pressure in the rooms and by controlling the non-viable & viable particle count inside the clean room areas catered.

The HVAC System shall be designed to achieve the desired indoor environment conditions as per defined Hygiene Zones required for various activities of pharmaceutical drugs. The system shall be designed in conformance to all International cGMP standards for HVAC systems.

The requirements of all the classes are given below.

Double HDPE wire mesh shall be provided at the fresh air inlet before the pre filters for preventing entry of insects and dust particles

Inside conditions shall be as per AHU zoning as below.

Class	Type of System	Inside Condition		AHU			Terminal HEPA Filter
		Temp.	RH	Pre Filter	Fine Filter	Semi HEPA Filter	Final
		(ºC)	(%)	G4	F7	F9	H14
B	Recirculation	19-25	30-55	Y	Y	Y	Y
C	Recirculation*	19-25	30-60	Y	Y	Y	Y
D	Recirculation*	19-25	30-60	Y	Y	Y	Y
CNC	Recirculation*	NMT 27	NA	Y	Y	NA	NA

*Return air from wash areas, janitor room and housekeeping area will not be recirculated into the system. The return air from these areas will be completely exhausted using inline fans.

Sr. No.	Description	Efficiency
1.	Pre filter	EU4 as per EN 779
2.	Fine filter	EU5 as per EN 779
3.	Fine filters in AHU	EU7 & EU9 as per EN 779
4.	Terminal HEPA filters	H-14 as per EN 1822

Airborne Particles Related To Environmental Grades

Sr. No.	EU GMP Grade Classification	ISO Classification		American Federal Standards 209D Class	Maximum Permitted number of Particle/m3 equal to or above	
					0.5 µm (d)	5 µm (d)
1.	Grade A	At rest	ISO – 5	100	3,520	20
		In operation	ISO – 5	100	3,520	20
2.	Grade B	At Rest	ISO -5	100	3,520	29
		In operation	ISO -7	10000	352,000	2930
3.	Grade C	At rest	ISO – 7	10,000	352,000	2930
		In operation	ISO – 8	100,000	3,520,000	29300
4.	Grade D	At rest	ISO – 8	100,000	3,520,000	29300
		In operation	Not Applicable	Not Applicable	Not Applicable	Not Applicable

Most of the possible risk concerning the handling/ operation of the HVAC System has been considered in this RA document**.**

5 Participants

Name	Designation/ Department	Signature/ Date

6 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

- 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.

- 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 the proposed sterile formulation facility.

The objectives of this risk assessment are to:

- Review the design around a structured methodology
- Identify the failure modes and associated risks
- Check if the proposed control measures are adequate
- Identify recommendations to obtain a more acceptable risk level if required

6.1 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 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 Hygiene level of the manufacturing areas 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 hygiene level of the manufacturing and supporting areas
- Risks related to appropriate utilities and their control (eg. 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 unidirectional flow of the material
- Risks related to cross contamination of the products
- Risks related to entry and exit of personnel and material.
- Risks related to all the environment features of the manufacturing areas.
- Risks related to requirement of particular rooms for different activities.
- Risks related to environment health and safety of personnel.

6.2 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 • 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.

7 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 the 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 risk have **GMP impact** in terms of Yes/ No.

Column 5 : **Justification:** Provide justification for declaring both Yes/ No for GMP impact in column 4.

Column 6 : For the risk **other than of GMP impact**, write that what is/ are the type of risks e.g. EHS, operational, etc.

Column 7 : **Justification:** Provide justification for considering the 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 the following three sections:

Column 9a : **Mitigation Method:** Write the risk mitigation strategy as considered in the 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 : **Test document:** Write the test point where the risk mitigation strategy will be verified.

Column 10 : **Status of RA:** Mention the status of the Risk assessment point i.e. whether it is ‘Closed” or “Open”, after the execution/ approval of the Test document.

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Supply											
1.	Supply air fans	• Required amount of air is not sucked • Improper functioning of the blower (low/high flow/static pressure) • MOC of the blower is not compatible.	Yes	If the blower doesn't meet the required specifications then the required CFM and specified room conditions cannot be achieved.	No	NA	High	• Fan of desired CFM is selected and installed in the AHU. • Controller shall be provided for the ON/OFF status of the supply air fan. • Room conditions within process rooms are to be monitored. • VFD shall be provided to control the blower according to designed CFM. • The MOC of the blower shall be selected accordingly. MS with galvanised coating is recommended • SOP: preventive maintenance of AHUs is to be developed	Acceptable	IQ, OQ & SOP	
Cooling / Heating coils											

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2.	Cooling coils	Insufficient performance, breakdown & choking of coils.	Yes	Room Temperature/ RH may deviate from specifications.	Operational	Loss of energy	Medium	• Pipelines and coils are pressure tested. • Auto controlling shall be provided w.r.t room temperature/RH & duct temperature. • Room temperature and RH will be monitored and alarm will be display in EMS. • The strainer shall be provisioned at inlet of cooling coils. • MOC: Cooling coils Copper tube with aluminium fins.	Acceptable	IQ & OQ	
3.	Air	Suction of polluted air from condensate drain	No	Downstream filter will take care	Operational	The filter shall be choked frequently leading to extra maintenance.	Low	• Condensate drain should be provided with suitable arrangement • Air break /Siphon/U-bend should be provided in the drain line to trap the air.	Acceptable	IQ	
3 way Valves											

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4.	3 way Valves	Improper function	Yes	May deviate from Temperature/ RH specifications	No	NA	Medium	• Proper valve function is to be verified during qualification. • Chilled water should be bypass in case of room conditions are within specified limits. • Temperature RH excursions for the Room/Return will be alarmed in the BMS/EMS.	Acceptable	IQ & OQ	
Drain											
5.	**Drain**	Improper draining of the condensate and excess supplies	Yes	Stagnant water may lead to microbial growth in AHU.	No	NA	Low	Proper slope / pitch shall be provided towards the pan drain outlet.	Acceptable	IQ	
Filters For CNC Areas											
6.	**Pre- Filter**	Filter doesn't fit tight in frame, filter damaged	No	• Proper filtration from pre-filter cannot be achieved. • No effect on final air quality.	Operational	Overload on the downstream filter shall lead to frequent maintenance	Low	• Routine check and preventive maintenance is to be done. • Design of pre filter shall ensure easy handling of pre- filter. • SOP to be developed for DP monitoring & cleaning of Pre filter on the basis on their DP.	Acceptable	IQ & SOP	

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7.	**Pre- Filter**	Filter not provided	No	Pre- filter is supported by downstream fine filter.	Operational	• Overload on fine filter, • Maintenance for fine filter will be frequent.	Medium	• Approved EU- 4/G-4 grade pre-filter should be installed. • Certificate of EU-4/G-4 shall be available.	Acceptable	IQ	
8.	Pre-Filters	Filter choking/ damage	Yes	Desired quantity of air will not be supplied and thus differential pressure and air changes could not be achieved	Operational	Over load on the Blower and high energy consumption.	High	• The pre filters shall be non-metallic, non-particle shedding, and Synthetic washable (HDPE) type. • Fixing frame of filter should be made up of Aluminium. • Differential pressure across the filter shall be measured by differential pressure gauge/ switch. • SOP to be developed for DP monitoring & cleaning of Pre filter on the basis on their DP.	Acceptable	IQ, OQ & SOP	
9.	Pre-Filters	• Washing not possible • Washing in unclean room.	Yes	Could result in choking of filters.	Operational	Frequent changing of filters	High	• Pre-filters (G-4) should be washable. • Washing of Pre filters shall be performed in the Clean room areas/in filter cleaning Station. • .	Acceptable	IQ	
10.	Filters	Sufficient space not available for filter removal for cleaning or replacement.	Yes	Cleaning of filters is a GMP requirement.	Operational / EHS	Difficulty in removing the filter and cleaning.	Medium	Sufficient space should be provided in the AHU plenum for filter removal for cleaning or replacement.	Acceptable	IQ	

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11.	**Fine filter (F7)**	Filter doesn't fit tight in frame, filter damaged	No	Proper filtration from fine filter cannot be achieved. No effect on final air quality.	Operational	Overload on the downstream filter shall lead to frequent maintenance	Medium	• Design of fine filter shall ensure the easy handling of filter. • Routine check and preventive maintenance procedure to be done for verification of Gaskets for the Filters.	Acceptable	IQ & SOP	
Filters For Classified Areas											
12.	**Fine filter (F9)**	Fine filter not provided before HEPA filter	No	Fine filter is supported by the HEPA filter. So, downstream flow will be filtered through HEPA filter	Operational	• Overload on HEPA filter. • Frequent changing of HEPA filter.	Medium	• Fine filter (EU-9) grade filter shall be provisioned in the design. • Certificate of fine filter shall be available.	Acceptable	IQ	
13.	Fine filter (F9)	Fine filter choking/ damage	Yes	Desired quantity of air will not be supplied and thus differential pressure and air changes could not be achieved	Operational	Over load on the Blower and high energy consumption.	High	• The fine filters shall be non-metallic, non-particle shedding, and Synthetic (HDPE) type. • Differential pressure across the fine filter shall be measured by differential pressure gauge/ switch.. .	Acceptable	IQ & OQ	

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14.	HEPA filter (H-14)	Integrity test is not possible	Yes	Hygiene level in the room will not be confirmed.	No	NA	High	• PAO port is provided to check the upstream concentration during Filter integrity test after installation and at regular interval. • Integrity test to be conducted by vendor on site after installation.	Acceptable	IQ & OQ	
15.	HEPA filter (H-14)	Filter choking or damage	Yes	• Desired quantity or quality of air will not be supplied. • Hygiene class could not be maintained.	No	NA	High	• Differential Pressure provision will be provided for verification of DP across H-14 filters at regular defined frequency as per the maintenance Procedure. • Periodic Validation of HEPA filters is in place to verify the Condition of HEPA Filters.	Acceptable	IQ & OQ	
16.	HEPA filter (H-14)	Filter doesn't fit tight in housing frame	Yes	• Filtration could not be achieved. • Hygiene class could not be maintained.	No	NA	High	• Suitable space shall be provided to fit HEPA filter. • GEL Seal type Mini pleat HEPA filter should be provided to avoid side leakages. • SOP: preventive maintenance is to be developed.	Acceptable	IQ & SOP	

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17.	Pre filter in Return	Pre filter is not provided in return	Yes	Return air is not filtered before transferring to mixing chamber.	No	NA	Medium	• Approved EU- 4 grade pre- filter should be installed. • Certificate of EU-4 shall be available.	Acceptable	IQ	
18.	HEPA filter in exhaust	The exhaust air from manufacturing area may contain product molecules.	No	Does not affect the quality of the product.	EHS	Exhaust air may contaminate the environment	Low	• Exhaust air shall be passed through HEPA filters. • The risers shall be sealed to the top of the duct level. • There shall not be any opening in return duct up to AHU.	Acceptable	IQ & OQ	
Piping											
19.	**Piping**	Leakage	No	No direct relation with the supply air	Operational	Loss of energy	Low	Pressure test of the pipes is to be done.	Acceptable	IQ	
Duct											
20.	Duct	Duct eroded / Leakage	Yes	• Contamination or leakage of air can take place • Leakage may lead to disturbances in temp./ RH conditions and room pressures	Operational	Leakages will lead to loss of energy.	High	• Duct's MOC should be of Galvanized iron. • Duct work should be free from internal obstruction. • Installation leak test is to be carried out and correction if any leak found. • USFDA approved material	Acceptable	IQ	

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21.	Duct	Improper insulation	Yes	Air temperature cannot be maintained	Operational	Energy losses	Medium	• Proper insulation should be provided • Insulation is to be verified during installation of ductwork • Insulation material shall be Nitrile rubber.	Acceptable	IQ	
22.	Duct	Transmission of sound & vibrations	No	It will not affect the final air quality.	EHS	Direct contact of duct work with building and other utility systems / installations and heavy sound due to vibration.	Medium	• System shall have anti-vibration mounting • Duct shall be isolated from fans through canvas connections	Acceptable	IQ	
Damper											
23.	Manual Damper	Non- Availability, Improper size and malfunctioning	Yes	Specified room conditions (air change rates, pressure cascade, temperatures, humidity) may not be maintained.	EHS	Uncomfortable conditions for personnel	Medium	• Dampers of suitable sizes and quantity are to be provided in supply and return duct. • Damper operation is to be verified during OQ and during routine process and preventive maintenance. • Room conditions is to be monitored	Acceptable	IQ, OQ & SOP	
Motorized Dampers											

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24.	Motorized Damper	Non- Availability, Improper size and malfunctioning	Yes	Specified room conditions (air exchange rates, pressure cascade, temperatures, humidity) may not be maintained	EHS	Uncomfortable conditions for personnel	Medium	• Availability, Sizes is to be checked with the drawings. • Motorized dampers shall be provided in rooms to regulate room pressure. • Air mixing damper shall be motorized to regulate air flow. • Motorized damper operation is to be verified during OQ and routine preventive. maintenance • Shall be provided in supply and return duct in AHU plenum for regulating pressure	Acceptable	IQ & OQ	
Air flow rate											

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25.	Air flow rate	Velocity sensor/ Differential pressure sensor across fan not available	Yes	CFM of supply air cannot be measured.	No	NA	High	• Velocity sensor/ Differential Pressure sensor across fan shall be installed in the supply duct/ AHU. • Low velocity should automatically increase & decrease the blower RPM through VFD, so as to maintain total CFM. • DP Gauge shall be provided across the fine filter which gives the progressive data regarding the Pressure drop in order to identify the discrepancies. • Air changes for each area shall be verified during OQ	Acceptable	IQ & OQ	
Nuts & Bolts											
26.	**Nuts and Bolts**	Not as per clean room design	Yes	All items shall be suitable for clean room, must not shed /deposit particles/dust.	Operational	Difficult for the operator for cleaning	Low	Counter sunk / clip/ push type fixing arrangement shall be considered in design.	Acceptable	IQ	
Insect Mesh & Interlocking											

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27.	**Insect mesh**	Not provided	No	Downstream coarse filter takes care	Operational	Downstream filter will be choked due to unfiltered air.	Low	HDPE insect mesh is provided to control insects coming through fresh air in TFA units & exhaust ducts.	Acceptable	IQ	
28.	**Interlocking**	The casing door may open during the blower running.	No	It will not affect the final air quality.	Operational/ Financial	Downstream filter will be choked due to unfiltered air.	High	Interlock will be made with the motor and the door to stop the motor when the door opens.	Acceptable	OQ	
Variable Frequency Drive											
29.	VFD	Improper function / defect	Yes	Air change rates and pressure cascade may not be maintained	No	NA	Medium	• Performance of VFD is to be monitored in control system by verifying the downstream flow by providing Differential pressure sensor output/through Multi point velocity sensor. • Check for correct functioning during qualification and routine maintenance is to be done • SOP: preventive maintenance is to be developed.	Acceptable	OQ & SOP	
Process Room Conditions for Classified Areas											

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30.	Temperature	Temperature is out of limit	Yes	Environmental conditions will not be suitable for operation	Operational	Not suitable for human working	High	• AHU design is made to achieve desired temperature. • Temperature sensor installed in return duct shall sense the room temperature and accordingly regulate the operation of cooling coil or heating coil to maintain required temperatures within range. • Out of limit condition is alarmed • SOP: Regular monitoring of room temperature, Pressure and RH is to be done.	Acceptable	IQ, OQ & SOP	
31.	**Relative Humid**	RH is out of limit	Yes	Environmental conditions will not be suitable for operation	Operational	Not suitable for human working	High	• AHU design is made to achieve desired RH in product processing areas. • Room RH shall be monitored and controlled heating coil & cooling coil. • Heater MOC: SS304 • Out of limit condition is alarmed • SOP: Regular monitoring of room temperature, Pressure and RH is to be done.	Acceptable	IQ, OQ & SOP	

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32.	**Hygiene zone**	Room condition parameter does not meet specified hygiene class	Yes	Environmental conditions will not be suitable for operation	No	NA	High	• AHU system design is based on the requirement of hygiene zone. • Qualification of the room hygiene class is to be done. • Sequence of AHU operation to be established and study during qualification. • The supply air shall be through diffuser & HEPA filter in classified areas. • Return air shall be picked up through return air risers with low level pick-up to provide vertical airflow pattern in classified areas • Maintenance and monitoring of pressure cascade is to be done.	Acceptable	IQ, OQ, PQ & SOP	
33.	**Differential pressure**	Differential pressure between two different hygiene zone is not maintained	Yes	Air may enter in higher hygiene zone from lower hygiene area	No	NA	Medium	• A higher pressure cascade is designed from higher to lower hygiene zone. • Regular monitoring of the differential pressure is to done • Differential pressure of different room shall be monitored through EMS. • Local display for differential pressure shall be provided.	Acceptable	IQ & OQ	

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34.	**Fumigation**	No provision for fumigation inside clean rooms	Yes	Viable particle count may increased; It may lead to the product contamination during filling & manufacturing activities.	No	NA	High	• Double Decker AHUs should be provided for classified areas. • SOP shall be developed for Fumigation as per time required during qualification stage. • Supply & exhaust damper should be 100% open during fumigation.	Acceptable	IQ & SOP	
Controlling System/ BMS/EMS for Classified Areas											
35.	Control System/ BMS	Process / process status not visible for operating personnel.	Yes	Operating personnel must have knowledge on the process status.	No	NA	High	BMS system shall be provided with adequate display and key board for operation and entering process parameters with authorization level.	Acceptable	IQ	
36.	Control System/ BMS/EMS	Display language not identified.	Yes	Pre-requisite for the GMP compliant operation	No	NA	High	The language on the display of BMS & EMS should be English language.	Acceptable	OQ	
37.	Control System/ EMS	Recorder failure	Yes	Basis GMP requirement (incomplete / no documentation)	No	NA	High	• Data backup for process data must be possible through EMS (electronic recording, 21 CFR parts 11 compliant). • Diagnostic function test to be a part of qualification activity.	Acceptable	IQ & OQ	

RISK ASSESSMENT FOR HVAC SYSTEM

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								Mitigation Method (9a)	Residual risk level (9b)	Verification (9c)	
38.	Environment Monitoring System (EMS)	Monitoring/recording and documentation of GMP relevant data not possible	Yes	Basic GMP requirement	No	NA	High	• It should be possible to monitor/record GMP relevant data (e.g. recorder with compliance to GAMP 5 / 21 CFR, Part 11 etc.) • Batch records / print outs to be defined. • Printout facility should be available with fade proof prints. • EMS shall be provided for monitoring & recording of critical parameters like DP, temperature & RH of Classified areas.	Acceptable	OQ	
39.	Control System/ BMS/EMS	Control system does not detect failures and generate alarms	Yes	Process optimization and validation is not possible	No	NA	High	• Alarm messages on operator panel and recorder or alarm printer shall be designed. • Popup alarm display shall be provided on computer.	Acceptable	OQ	
40.	Control System/ BMS	Power Failure	Yes	Temperature, RH and differential pressure cannot be maintained	No	NA	High	• Maximum acceptable power failure period is determined. • SOP: Action in case major power breakdown is to be developed.	Acceptable	OQ & SOP	

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								Mitigation Method (9a)	Residual risk level (9b)	Verification (9c)	
41.	Control System/ BMS/EMS	Power failure / emergency stop	Yes	Process out of specification	Safety	Unsafe if start automatically on restoration of power	High	• Operator settings unchanged and restored after emergency stop / power failure; • Alarm message; • On power failure equipment should come to rest to protect operator, equipment itself & the product (vials). • Provision for UPS. • Machine must not start automatically without operator intervention after incident • SOP for 'Maintenance and operation of BMS & EMS'.	Acceptable	OQ/ SOP	
42.	Control System/ BMS/EMS	Status parameters not clear	Yes	Process for the particular product at particular stage can't be regulated easily.	No	NA	High	• Status parameters should remain displayed at each process stage. • The flow of the process shall be provided with the help of arrows. • Alarm should also be visualized along with the fault displayed.	Acceptable	OQ	

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43.	Control System/ BMS/EMS	Malfunction	Yes	Correct function basic requirement for GMP-compliant operation	No	NA	High	• Supplier assessment (quality management system for software and control system hardware development) • Input/ Output test implementation in qualification activities • The system must contain all necessary protection devices to ensure that the equipment and article remain in safe condition. • A UPS supply should be provided to the control system for uninterrupted power.	Acceptable	OQ	
44.	Control System/ BMS/EMS	Parameter settings not identified universally	Yes	Basic GMP requirement	No	NA	High	Parameters settings should be in numeric only.	Acceptable	OQ	
45.	Control System/ BMS/EMS	Time measurement works incorrect	Yes	Process insufficient	No	NA	High	• PLC Clock verification • SOP “calibration and maintenance” • Time synchronisation of system	Acceptable	OQ & SOP	

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								Mitigation Method (9a)	Residual risk level (9b)	Verification (9c)	
46.	Control System/ BMS/EMS	No protection of PLC against manipulation & changes.	Yes	Basic GMP requirement.	No	NA	High	• Minimum 3 level password protections should be provided. ➢ Level 1: for operator settable parameters. ➢ Level 2: for editing cycle parameters. ➢ Level 3: for admin/ engineering level setting.	Acceptable	OQ	
Measuring Instruments											
47.	Measuring Instruments	Measuring instruments are not within defined range	Yes	Instrument is not suitable for use.	No	NA	High	• Measuring instruments must have a suitable measuring range. • Operational range of measuring instruments > equipment's working range. • Measuring instruments must have appropriate accuracy	Acceptable	IQ & OQ	
48.	GMP relevant measuring instruments	Measuring instruments cannot be dismounted	Yes	Defective instruments must be dismounted for exchange and calibration	No	NA	High	• Mounting of instruments must give the possibility for dismounting and replacement • Constructional solution: easy access for calibration activities shall be given	Acceptable	IQ	

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49.	Measuring Instruments	• Instruments not calibrated. • Re-calibration is not possible	Yes	Non calibrated instruments may lead to false machine functions	No	NA	High	• Measuring instruments should be calibrated, traceable to national or international standards. • Re-calibration of instruments should be possible.	Acceptable	IQ & OQ	
Safety											
50.	Safety	• No Safety against fire smoke • Improper handling of system.	Yes	May lead to product contamination	EHS	• May pass the flame to all production area. • System malfunction.	High	• Fire proof double canvas connections shall be provided. • Fire damper shall be provided in the AHU plenum. • Proper training to all operating and Maintenance staff.	Acceptable	IQ & OQ	
51.	Emergency stop	Emergency stop of the system is not possible.	No	Final air quality will not be affected.	EHS	The system cannot be switched off immediately if necessary exists.	Medium	Local operating Emergency stop switch /power off will be provided in each block system wise.	Acceptable	IQ & OQ	
52.	Noise level	Noise level liberated by the system is high.	No	It will not affect the final quality of air.	EHS	Heavy noise will cause problems to the service persons	Medium	System shall be designed for noise level below 75 db at a distance of 1 m from the equipment.	Acceptable	OQ	

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53.	Visibility inside AHU plenum	Low or No visibility inside AHU plenum.	No	NA	Operational	Minimum visibility is required for doing maintenance activity.	Low	A fluorescent light /LED shall be provided inside the AHU plenum at blower section.	Acceptable	IQ	
Documentation											
54.	User	Faulty operation & maintenance	Yes	SOPs are basic GMP requirement.	No	NA	High	• All end-users have to be trained on SOPs • Training of SOPs has to be documented • Training on the job of end users by vendor. • Training on operation, setting parameters, trouble shooting & maintenance related activities.	Acceptable	OQ & SOP	
55.	User	Operation SOP does not contain proper information and user may operate system.	Yes	User may make a wrong decision.	No	NA	High	System operation SOP must be reviewed with all aspects and approved.	Acceptable	OQ	
56.	User	Unauthorized person tries to start/stop the system	Yes	Untrained persons may damage the system or product quality may be affected	No	NA	High	• System should not start without password. • Key-switch should be provided for system power up. OR • Physical entry to equipment room is restricted.	Acceptable	IQ & OQ	

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57.	Vendor Documents	Technical documentation from vendor not adequate	Yes	Adequate technical documentation is basic GMP requirement for qualification and operation of the System	No	NA	High	▪ Vendor documentation (English) shall comprise: -Data sheets -DQ,IQ and OQ protocols -FDS -Material certificates -Operating & maintenance instructions - Certificates of initial calibration of sensors - Filter certificates -Parts lists(sufficient detailed: part number, supplier, type) ▪ Drawings - P&I-diagrams - Electrical diagrams - GA drawings ▪ Certificate of bought out ▪ Relevant SOP's	Acceptable	IQ	

8 Summary & Conclusion

- The Risk Assessment was performed to establish the design parameters of the equipment so as to meet the desired performance of the equipment i.e. HVAC System.
- The critical risks pertained 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 during the performance of the OQ.
- The risks where conceptual procedures shall be employed, standard operating procedures (SOPs), Preventive maintenance schedules, Certificates and related documents indicated as mitigation procedures shall be ensured at respective test points

*"It is concluded that the **Risk Assessment** performed for the equipment will prevent the risk of failures of critical parameters during, design commissioning, installation, operation and performance of the equipment".*

9 Abbreviations

EU-GMP	:	European – Good Manufacturing Practice
EHS	:	Environment Health Safety
GMP	:	Good Manufacturing Practice
RH	:	Relative Humidity
AHU	:	Air Handling Unit
ACPH	:	Air Changes per Hour
VFD	:	Variable Frequency Drive
CFM	:	Cubic Feet per Minute
HEPA	:	High Efficiency Particulate Air
HVAC	:	Heating, Ventilating & Air-conditioning
RA	:	Risk Assessment
NMT	:	Not More Than
SOP	:	Standard Operating Procedure
SS	:	Stainless Steel
CFR	:	Code of Federal Regulations
UPS	:	Uninterrupted Power Supply
CE	:	Conformité Européene
db	:	Decibel
FS	:	Functional Specification
IQ	:	Installation Qualification
OQ	:	Operational Qualification
PQ	:	Performance Qualification
O&M	:	Operation and Maintenance
GA	:	General Arrangement
IPSI	:	Integrated Project Services International, New Delhi

10 Revision History

Date	Revision	Reason for Revision
	00	New Document