Risk Assessment Document
For
Sterile Formulation Facility

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RISK ASSESSMENT FOR STERILE FORMULATION FACILITY

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 facility.

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

The facility subjected to risk analysis is the “Sterile Formulation Facility” at ……...

The facility design is carried out after a detailed conceptual design complying with Schedule M (Indian FDA), WHO (World Health Organization), USFDA, EU-GMP and other international regulatory agencies.

The building is designed in such a way that the warehouse, production, utilities, quality control, office area are properly segregated to prevent cross-contamination between these areas.

The facility shall have separate entry for manufacturing and packaging area.

Material flow shall be linear in the facility according to manufacturing process, which is sequentially as follows.

- Material receipt and storage
- Material dispensing
- Bulk manufacturing
- Product filtration
- Product filling & Sealing
- Lyophilization
- Automatic loading unloading
- Manual visual Inspection with space provision for Automatic Optical inspection.

- Secondary packaging
- Finished goods storage and dispatch
- Personnel entry is designed based on the cGMP requirement

Salient features of this facility

Following are the highlighted major features of the facility:

a) Conformance to cGMP and modern manufacturing concepts like:
   - Material and Personnel flow
   - Change procedures
   - Flexible batch sizing
   - HVAC system to support manufacturing activities.
   - Purified water system complying USP
   - Water for Injection complying USP
   - Pure Steam complying USP
   - Compressed air complying ISO specification
   - Monolithic crevices free room finishes with epoxy.
   - Efficient logistics and warehouse design.

b) The most modern manufacturing equipments with latest technology.

c) Latest automation for accurate and energy efficient operations.

d) Rich landscapes to minimize the dust pollution and enhance aesthetics.

e) In-house effluent treatment and strict compliance to pollution board norms.

f) Major emphasis on Environment, Health and Safety, (EHS) requirements.

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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.

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  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

7 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 Automation
- Risks related to protection of the environment and health & safety of personnel.
- Risks related to cleaning, sanitization & 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.

1.0 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.

8 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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Building and Regulations											
1.	Building strength	Weak building strength	No	No impact on product quality	EHS	Weak building construction: Prone to damage and personnel safety	High	▪ Based on the engineering calculations, Structural designing shall be done and the construction shall be carried out based on structural designing. ▪ M30 concrete shall be used for providing the strength to the pillars.	Low	Building stability certificate shall be provided by Engineer based on structural design.	
2.	Statutory Standards	Building/ Facility not meeting the required standards	No	No impact on product quality	EHS	Safety requirements are mandatory. Complete safety of the environment and health of the personnel is statutory requirement.	High	▪ Building construction should follow all local safety regulation applicable. ▪ Height of the buildings and area coverage shall be kept according to local statutory rules. ▪ All building material and Utilities shall be designed as per Indian Codes and Standards. ▪ The building drawings shall be approved by the statutory bodies.	Low	Certificates and NOC's issued by the authority	
Site Master Plan											
3.	Master Plan	Necessary infrastructure to support the production facility has not been provided.	No	NA	EHS / Operational	▪ Does not comply with safety norms like provision of roads for movement of	High	The master planning shall be done considering: ▪ Different buildings/ areas for different activities.	Low	Site Master plan	

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						vehicles and provision of pavements for personnel movement. ▪ Reasonable distance between various buildings to maintain safety norms will not achieve. ▪ Future expansion flexibility will hamper. ▪ Proper co-ordination of all services in the site for easy maintenance will hamper.		▪ Separate Quality Control lab consisting of both Chemical and Microbiology lab for testing of RM, PPM, SPM, FG and in-process samples. ▪ Safe distance between these buildings / areas. ▪ Roads to access all areas. ▪ Future expansion possibility provided so that on-going operations will not be disturbed. ▪ Proper drainage system to avoid water clogging. ▪ Roads, yards, parking lots etc. shall be paved with a hard non dusting material (like concrete etc.) where necessary			
Warehouse											
4.	Warehouse	No area provided in the facility design for warehouse.	Yes	A separate warehouse area with multiple rooms for storage, is a basic GMP requirement.	No	NA	High	A separate warehouse area shall be provided in the facility for storage of RM, PPM, SPM and Finished goods.	Acceptable	Facility qualification	
5.	Loading/ Unloading	Platform is not provided for loading/ unloading of material.	No	No impact on product quality.	Operational	Difficulty in docking vehicle and loading/ unloading material.	Low	Sufficient loading platform & ramp shall be provided for docking vehicle and loading/ unloading material to/ from warehouse.	Acceptable	Facility qualification	

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6.	Receipt & De-dusting	▪ Sufficient area not provided for staging & de-dusting. ▪ No system provided for de-dusting. ▪ Environment contamination may enter the warehouse area.	Yes	The external contamination on RM/ PPM/ SPM containers may enter the clean areas of warehouse and subsequently production.	No	NA	Medium	▪ Sufficient space shall be provided at unloading area, wherein de-dusting shall be performed using de dusting tunnel. ▪ De-dusting tunnel shall be provided at receipt entry of raw material and PPM and SPM entry and receipt area vacuum cleaner shall be utilized for de-dusting. ▪ Air tight door with air curtains shall be installed at the receipt of the warehouse, where the material shall be unloaded. ▪ Insecticutor System shall be provided for killing insects and flies.	Acceptable	Facility qualification	
7.	Quarantine	No designated space allotted for storing quarantine/ under test raw material.	Yes	Chances of mixing of quarantine material with approved material.	No	NA	High	A designated & clearly marked space & racks shall be provided for quarantine/ under test RM/ PPM/ SPM.	Acceptable	Facility qualification	
8.	Reject material storage	No designated area is provided for reject RM, PPM or SPM storage.	Yes	Basic GMP requirement so as to prevent chances of mixing of reject material with approved material.	Safety	Reject RM/ PPM may get mixed with approved material and may be processed.	High	A reject material store shall be provided with lock and key arrangement.	Acceptable	Facility qualification	

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9.	Primary Packaging Material Store	No designated storage area is provided for primary packaging material storage.	Yes	Separate storage area for PPM is a GMP requirement.	No	NA	High	Separate room with sufficient space shall be provided to store the primary packaging material in the warehouse area.	Acceptable	Facility qualification	
10.	Primary Packaging material store	Area is not a clean room.	Yes	The primary packaging material comes in direct contact with product, hence should be stored in a clean room.	No	NA	High	▪ The Primary Packaging material shall be stored in CNC (controlled not classified) area with temperature control (<25˚C) and proper air filtration. ▪ The rooms shall be provided with proper AHU supply and return air, with temperature control.	Acceptable	Facility qualification	
11.	Secondary Packing material store	No designated area provided for secondary packaging material storage.	Yes	Separate storage area for SPM is a GMP requirement	No	NA	Medium	Dedicated room with sufficient space shall be provided for storage of the secondary packing material.	Acceptable	Facility qualification	
12.	Raw material Store	No designated area provided for raw material storage.	Yes	Separate storage area for RM is a GMP requirement	No	NA	High	Dedicated room with sufficient space shall be provided for storage of raw material.	Acceptable	Facility qualification	
13.	Material Storage in storage areas	RM/ PPM/ SPM containers kept on floors in the storage areas	Yes	Chances of damage/ contamination of the containers in case of any water/ solvent spillage.	No	NA	Medium	Pallets/ racks shall be provided for storage of material containers/ drums/ shippers in respective dedicated storage areas.	Acceptable	Facility qualification	

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14.	Raw Material Store	▪ Raw material not stored under temperature controlled environment. ▪ Area is not a clean room.	Yes	Some raw material needs to be stored under recommended controlled temperature conditions or else may degrade.	No	NA	High	▪ The Raw material shall be stored in controlled area (CNC area) with temperature control (<25˚C) ▪ The storage rooms shall be provided with proper AHU supply and return air, with temperature control ▪ Separate RM cold store/deep freezer shall be provided for storage of temperature sensitive raw material at 2 – 8°C. ▪ Temperature mapping shall be carried out for the RM cold store/deep freezer to ensure temperature uniformity. ▪ Routine temperature monitoring shall be carried out for RM cold store/deep freezer, as per SOP	Acceptable	Facility qualification & SOP	
15.	Material segregation	No segregation between quarantine, under test & approved RM, PPM and SPM in their designated storage areas	Yes	Basic GMP requirement to avoid chances of mixing of quarantine/ under test material with approved material.	No	NA	High	Physical demarcation shall be required in respective storage areas, so as to segregate the quarantine, under test and approved material from each other.	Acceptable	Facility qualification	

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16.	Dispensing of RM	No area provided for dispensing of Raw material.	Yes	Separate dispensing room of Raw material is a basic GMP requirement.	No	NA	High	▪ A dispensing room with pass box shall be provided in the warehouse area for dispensing of RM. ▪ Dispensing booth shall be provided inside the dispensing room, wherein dispensing shall be carried out.	Acceptable	Facility qualification	
17.	Sampling of RM	No area provided for sampling of Raw Material.	Yes	Sampling of raw material is a basic GMP requirement, for testing of incoming material before usage.	Financial	Failed RM may lead to failure in FP which may not meet specified quality and thus may lead to financial losses.	High	▪ A separate sampling room with pass box shall be provided for Raw Material Sampling. ▪ Sampling booth (RLAF) shall be provided inside the Sampling room, wherein sampling shall be carried out.	Acceptable	Facility qualification	
18.	Sampling & Dispensing area (RM)	Flow of material and man to the sampling & dispensing area is through same path.	Yes	Different path for man and material entry to the sampling area is a GMP requirement.	No	NA	Medium	▪ Separate Pass box shall be provided for entry of Raw Material in sampling room. ▪ Separate path shall be provided for entry of material to be sampled/ dispensed and exit of dispensed/ sampled material to avoid mix-up.	Acceptable	Facility qualification	

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19.	Sampling of PPM	No area provided for sampling of PPM	Yes	PPM needs to check for quality prior to use.	No	NA	High	Separate sampling area shall be provided in the Primary packaging storage area for sampling of PPM.	Acceptable	Facility qualification	
20.	Finished goods Storage	No area provided in the warehouse for finished goods storage prior to dispatch.	Yes	Basic GMP requirement to store all finished goods in the plant itself unless tested and approved.	No	NA	High	Finished goods storage area with sufficient space and pallets shall be provided in the warehouse area for storage of finished goods before approval and dispatch.	Acceptable	Facility qualification	
21.	Finished goods Storage	No segregation between under test & approved and rejected FG in FG storage area.	Yes	Basic GMP requirement to avoid chances of mixing of under test, approved and rejected FG.	No	NA	High	Physical demarcation shall be done in FG storage areas, so as to segregate the under test, approved and rejected material from each other.	Acceptable	Facility qualification	
22.	Finished goods storage	Finished goods not stored under temperature controlled environment.	Yes	Some finished goods needs to be stored under recommended controlled temperature conditions or else may degrade.	No	NA	High	▪ Finished goods storage area shall be provided with temperature control (<25˚C). ▪ Routine temperature monitoring shall be carried out for FG Area, as per SOP.	Acceptable	Facility qualification & SOP	
23.	RM & FG transfer	The transfer of RM and FG is carried out through same path.	Yes	Unidirectional flow is required to prevent cross contamination of FG with RM.	No	NA	Medium	Separate path shall be provided for transfer of RM from RM store to production area and for transfer of FG from secondary packing area to the finished goods store and then dispatch,	Acceptable	Facility qualification	

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								so as to maintain unidirectional flow of material in the plant.			
24.	Recalled goods storage	No area provided for storage of recalled finished goods.	Yes	Dedicated room for storage of recalled goods with lock & key arrangements is a GMP requirement.	No	NA	High	A separate Recalled goods store is provided in the warehouse for storage of any recalled goods.	Acceptable	Facility qualification	
25.	Floors	▪ The floor of the warehouse is not cleanable. ▪ Accumulation of dust at corners ▪ Floor is not load bearing.	Yes	Cleaning is a basic requirement to prevent contamination.	Operational	Frequent breaking of floor will hamper warehouse & production operation	Medium	▪ The flooring of the warehouse shall be made of Industrial tiles/Kota stone/ epoxy without any cracks or gaps. ▪ Floor shall be made up of load bearing material to avoid cracks ▪ Coving shall be done at the wall to floor joints, to prevent accumulation of dusts.	Acceptable	Facility qualification	
26.	Light	Low visibility in the warehouse area	Yes	Suitable lux level is required for comfortable operation.	No	NA	Medium	Operational areas in warehouse shall be designed for minimum 400 lux level, whereas non-operational areas shall be designed for minimum of 300 lux.	Acceptable	Facility qualification	
27.	Walls	The walls of warehouse are particle shedding.	Yes	Cleanroom conditions in the area may be compromised. Dust may be transferred to the adjoining production areas.	No	NA	High	▪ The walls in the warehouse area shall be painted with PU paint/ epoxy paint to prevent particle shedding. ▪ Alternatively, GI powder coated panels may be used in the warehouse instead of	Acceptable	Facility qualification	

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								walls.			
28.	Personnel Entry to warehouse area	Persons enter into warehouse area without changing their street clothes.	Yes	Contamination of storage area and material.	No	NA	High	▪ Change rooms shall be provided at the main production area, RM/PPM Warehouse entry for both gents & ladies, where persons remove their street garments and wear protective plant garments before entering warehouse area. ▪ A separate change room shall be provided for entry into RM/PPM/SPM. ▪ Warehouse SPM, packaging & FG store should have provision of both complete change or for over gowning.	Acceptable	Facility qualification	
Production –Areas											
29.	Media Fill Room	No Rooms are available to incubate the media fill vials	Yes	Media fill vials should be incubated at specified temperature (30-35º & 20-25ºC) for checking the growth of micro organism.	NA	NA	NA	▪ Media fill Rooms/Walk-In Incubator with sufficient space and racks should be provided. ▪ Temperature monitoring & indication facility should be provided in media fill incubator room.	Acceptable	Facility qualification	

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30.	Staging	No day store room provided in the production area for staging of dispensed PPM, RM & SPM required for the batch manufacturing.	No	No impact on product quality.	Operational	Transfer of material from warehouse to production during batch processing may take long time. Process may be intermittently stopped.	Medium	▪ Staging room (day store) shall be provided in the manufacturing area for staging of RM. ▪ Staging area shall also be provided with the ampoule filling line & vial filling line.	Acceptable	Facility qualification	
31.	Manufacturing	Manufacturing of vials and ampoules is not possible in the same facility.	No	No impact on product quality	Financial	Business loss, as different products cannot be manufactured.	Medium	Separate lines with separate set of equipments shall be provided in the same production facility for manufacturing of Liquid/ lyophilized vials and ampoules.	Acceptable	Facility qualification	
32.	Washing & Depyrogenation of vials/ampoules	Non-sterile & particle laden vials are used for sterile product filling.	Yes	The vials/ampoules in which sterile product is to be filled should be properly washed and depyrogenated, so as to prevent product contamination.	No	NA	High	▪ Vial/Ampoule washing machine shall be provided for proper washing and subsequent drying of vials/ampoules. ▪ Depyrogenation tunnel shall be provided for depyrogenation & sterilization of vials/ampoules prior to filling.	Acceptable	Facility qualification	

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33.	Sterilization	Non-sterile accessories, garments, machine parts, rubber stoppers, seals, etc, are used inside the filling area.	Yes	Using non-sterile accessories will contaminate the sterile product and clean room environment.	No	NA	High	▪ Double door steam sterilizer shall be provided for sterilization of all accessories, garments, machine parts etc. which are going to be used for vial/ampoule filling operations. ▪ A preparation room shall be provided wherein, the steam sterilizer shall be installed and the components shall be prepared and packed for sterilization.	Acceptable	Facility qualification	
34.	Washing	No area provided for cleaning of machine parts prior to sterilization.	Yes	Proper cleaning of machine parts is a pre-requisite for sterilization.	No	NA	High	▪ Separate washing room with sufficient space shall be provided for cleaning of used machine parts. ▪ Separate room shall be provided for holding/ storing of cleaned machine parts.	Acceptable	Facility qualification	
35.	Post washing	Contamination of machine parts during washing, holding or during transfer to steam sterilizer for sterilization or during loading inside sterilizer.	Yes	Particulate contamination of machine parts may occur, which may indirectly have an impact on product quality.	No	NA	High	▪ Clean air shall be provided over the machine parts washing station. ▪ Ceiling mounted LAF shall also be installed at the unloading side of steam sterilizer so as to prevent re-contamination of articles after sterilization.	Acceptable	Facility qualification	

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36.	Washing & drying	▪ The quality of water used for vial/ampoule washing &, machine parts washing is not appropriate. ▪ Compressed air used for drying is contaminated	Yes	▪ Quality of water to be used for washing should meet GMP requirements. ▪ Re-contamination of articles is possible.	No	NA	High	▪ Vial/Ampoule washing machine shall be provided with supply of PW and WFI for washing. ▪ Initial washing shall be designed using recirculated water, then with PW and final washing with WFI. ▪ Filtered (0.2 µm) compressed air supply shall be provided to washing machine for drying of vials/ampoules after each washing step. ▪ Equipment Wash room shall also be provided with PW and WFI supply for initial & final washing of machine parts. ▪ PW and WFI qualification shall be carried out prior to usage to verify its quality. ▪ Routine in-process testing of PW and WFI shall also be carried out as per SOP, to ensure quality.	Acceptable	Facility qualification & SOP	

RISK ASSESSMENT FOR STERILE FORMULATION FACILITY

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								Mitigation Method (9a)	Residual risk level (9b)	Test Document (9c)	
37.	Mixing of product	Preparation of product solution not possible.	Yes	Facility is designed for manufacturing of liquid injectable for which liquid solution needs to be prepared.	No	NA	High	▪ A solution preparation room shall be provided inside manufacturing area for preparation of product solution. ▪ Compounding vessel (s) of sufficient capacity and fixed with mixer of suitable range shall be provided for manufacturing of product solution. ▪ Compounding vessel (s) shall be provided with sufficient nozzles, required components and instrumentation, which are required for product manufacturing. ▪ Separate solution preparation rooms shall be provided for both Vial line & ampoule line with vessels, as per production requirement.	Acceptable	Facility qualification	
38.	Compounding vessel (s)	▪ No provision in the vessel for adding product. ▪ Product addition carried out under open condition.	Yes	Environmental contamination of product solution may lead to increase in initial bio-burden.	No	NA	High	LAF shall be provided over the top torispherical dish of the vessel to provide clean environment for product addition as well as for other connections.	Acceptable	Facility qualification	

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								Mitigation Method (9a)	Residual risk level (9b)	Test Document (9c)	
39.	Compounding vessel (s)	Compounding vessels used for product manufacturing are not cleaned properly.	Yes	Residues of previous product may be left over in the vessel. Product crosses contamination possible.	No	NA	High	▪ An automated CIP system with required instrumentation shall be provided for cleaning of compounding vessel (s) of both Vial and Ampoule line. ▪ PW and WFI line shall be provided in both the compounding rooms (Vial & ampoule line) for cleaning of vessels through CIP system. ▪ The CIP system should have provision for addition of Acid and alkali system, which might be required for efficient cleaning of the vessels. ▪ The cleaning process shall be validated for all vessels.	Acceptable	Facility qualification	
40.	Compounding vessel (s)	Compounding vessels used for product manufacturing are not sterilized.	Yes	The initial bio-burden of the product solution may increase. Process out of validated procedure.	No	NA	High	▪ An automated SIP system with required instrumentation shall be provided for sterilization of all compounding vessels. ▪ Pure Steam supply shall be provided in both the Compounding vessel rooms (Vial & Ampoule line) for sterilization of vessels through SIP system. ▪ SIP process shall be validated for all the mixing vessels.	Acceptable	Facility qualification	

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								Mitigation Method (9a)	Residual risk level (9b)	Test Document (9c)	
41.	Personnel entry	No change rooms at the entry to Grade C areas	Yes	Personnel are required to wear protective gown in the entry change room, as per clean room requirement.	No	NA	High	▪ Sufficient number of change rooms shall be provided for entering into the Grade C areas. ▪ Gowning provision shall be provided in the change rooms for personnel entering change room. ▪ Area qualification shall be carried out to demonstrate compliance to Grade C. ▪ Gowning philosophy shall be followed as per Entry & Exit SOP.	Acceptable	Facility qualification & SOP	
42.	IPQA room	No room provided for in-process checks of product at different stages.	Yes	In-process checks needs to be done at every stage of the production.	No	NA	Medium	IPQA room with sufficient space shall be provided inside manufacturing area, with necessary instruments for in-process testing of samples.	Acceptable	Facility qualification & SOP	
43.	Change/ Spare parts & Tool room	No room provided to keep the change parts, tools etc required of all equipments.	No	No impact on product quality.	Operational	The change parts, tool kit should be kept in the production area for immediate installation, rectification.	Low	A Change parts & Tool room with sufficient space shall be provided in the production manufacturing area for storage of change parts & other tools, required for production equipments.	Acceptable	Facility qualification	

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								Mitigation Method (9a)	Residual risk level (9b)	Test Document (9c)	
44.	Sterile Garments	Re-contamination of sterile garments while transfer from steam sterilizer to filling area entry change rooms.	Yes	Re-contamination of garments may take place. Product contamination possible.	No	NA	High	▪ Filling area garments shall be packed in breathable bag for sterilization. ▪ After unloading the garments shall be transferred to Sterile Garment cubicle in entry Change room using mobile LAF or in a closed container to prevent re-contamination.	Acceptable	Facility qualification	
45.	Personnel entry	No change rooms provided for entering into filling area or the change room provided are not as per GMP criteria.	Yes	The change room for filling area should be designed as per GMP requirement to prevent contamination.	No	NA	High	▪ Different set of change rooms shall be provided for entering into filling area. ▪ The hygiene level of change room shall be planned as per GMP requirements i.e. from CNC → Grade D → Grade C→ Grade B.	Acceptable	Facility qualification	
46.	Product filtration	No provision provided for sterilization of product solution prepared in compounding vessel.	Yes	Product solution shall be contaminated.	No	NA	High	▪ Sterile filtration assembly shall be provided for filtration of product solution. ▪ Sterilizable grade filter shall be provided for filtration of product solution.	Acceptable	Facility qualification	
47.	Sterile product holding	No provision provided for holding of sterile filtered product from compounding vessel, prior to filling.	Yes	Sterile product needs to be holded prior to filling, so as to maintain a buffer.	No	NA	High	▪ Holding vessel (s) of sufficient capacity shall be provided for collection and holding of sterile filtered product solution from the compounding vessel (s). ▪ Separate Holding room with separate holding vessel (s) shall be provided for Vial and	Acceptable	Facility qualification	

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								Mitigation Method (9a)	Residual risk level (9b)	Test Document (9c)	
								Ampoule lines.			
48.	Holding vessel (s)	▪ No provision in the vessel for adding product. ▪ Product addition or sampling carried out under open condition.	Yes	Environmental contamination of product solution may lead to increase product contamination and false results during sampling.	No	NA	High	▪ A LAF shall be provided over the entire top torispherical dish of the vessel to provide Grade A environment for product addition as well as for other connections. ▪ A separate Vertical LAF may be provided for providing Grade A environment for sampling or else vendor should demonstrate Grade A level till the sampling valve level.	Acceptable	Facility qualification	
49.	Holding vessel (s)	Holding vessels used for product manufacturing are not cleaned properly.	Yes	Residues of previous product may be left over in the vessel. Product cross contamination possible.	No	NA	High	▪ An automated CIP system with required instrumentation shall be provided for cleaning of holding vessel (s) of both Vial and Ampoule line. ▪ PW and WFI supply shall be provided for all holding vessels (Vial and Ampoule line) for cleaning of vessels through CIP system. ▪ The CIP system should have provision for addition of Acid	Acceptable	Facility qualification	

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S.No. (1)	Process steps/ component (2)	Risk (3)	GMP Risk Yes/ No (4)	Justification (5)	Other Risk type (6)	Justification (7)	Risk Level (8)	Risk Control (9)			Status of RA (10)
								Mitigation Method (9a)	Residual risk level (9b)	Test Document (9c)	
								and alkali system, which might be required for efficient cleaning of the vessels. ▪ The cleaning process shall be validated for all holding vessels.			
50.	Holding vessel (s)	Holding vessel used for product manufacturing are not sterilized.	Yes	Sterile filtered product may be re-contaminated.	No	NA	High	▪ An automated SIP system with required instrumentation shall be provided for sterilization of all holding vessels. ▪ Pure Steam supply shall be supplied to all Holding vessels (Vial & Ampoule line) for sterilization of vessels through SIP system. ▪ SIP process shall be validated for all the Holding vessels.	Acceptable	Facility qualification	
51.	Sterile product transfer	No provision provided for transfer of sterile product from holding vessel to filling machine	Yes	Product cannot be filled in vials or ampoules.	No	NA	High	▪ 0.2 µm Filtered Nitrogen gas/air supply shall be provided at the top of the holding vessel for transfer of sterile product from vessel to the buffer vessel on filling machine. ▪ Alternatively, centrifugal pump could also be provided for transferring of sterile product solution.	Acceptable	Facility qualification	

RISK ASSESSMENT FOR STERILE FORMULATION FACILITY

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								Mitigation Method (9a)	Residual risk level (9b)	Test Document (9c)	
52.	Filling	No provision provided for filling of product from holding vessel into vials or ampoules.	Yes	Product needs to be filled in vials or ampoules for further use.	No	NA	High	▪ A separate Vial filling room with Vial filling & stoppering machine shall be provided for filling & subsequent stoppering of product filled vials. ▪ A separate Ampoule filling room with Ampoule filling & sealing machine shall be provided for filling & subsequent sealing of product filled ampoules. ▪ A buffer vessel of sufficient capacity shall be provided on both the filling machines for maintaining required buffer during filling and preventing fill volume errors.	Acceptable	Facility qualification	
53.	Filling	Product filling is carried out under unclean environment.	Yes	Product contamination possible.	No	NA	High	LAF/oRABs (Grade A) shall be provided over entire Vial filling & stoppering, as well as on Ampoule filling machine to prevent environmental contamination during product filling.	Acceptable	Facility qualification	
54.	Transfer of vials from Filling to sealing or Lyo loading area	Transfer of stoppered vials after vial filling & stoppering machine is carried out in unclean environment.	Yes	Product contamination possible as vials are not sealed.	No	NA	High	▪ The complete transfer of vials from filling to sealing machine shall be carried out under LAF/ORAB (Grade A). ▪ The transfer of half stoppered vials from filling to Lyo loading area shall be through online	Acceptable	Facility qualification	

RISK ASSESSMENT FOR STERILE FORMULATION FACILITY

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								Mitigation Method (9a)	Residual risk level (9b)	Test Document (9c)	
								conveyor covered with LAFs to the Automatic Loading-Unloading system of Lyophilizer. ▪ In case ALUS is installed, it shall be covered under LAF to provide Grade A environment.			
55.	Crimping	Vial crimping is carried out under unclean environment.	Yes	Product contamination possible.	No	NA	High	▪ LAF/oRABs (Grade A) shall be provided over entire Vial crimping machine to prevent environmental contamination. ▪ Sterilized vials seals shall be used for sealing of vials.	Acceptable	Facility qualification	
56.	Lyophilization	No provision provided for lyophilization of liquid product filled vials.	Yes	Some product needs to be lyophilized for stability.	No	NA	High	▪ A lyophilizer with sufficient capacity shall be provided adjacent to the Vial filling room, ▪ The half stoppered product filled vials, which are to be lyophilized shall be loaded inside the lyophilizer through ALUS.	Acceptable	Facility qualification	

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								Mitigation Method (9a)	Residual risk level (9b)	Test Document (9c)	
57.	Lyophilizer	Lyophilizer technical part is installed inside the filling area	Yes	The components of lyophilizer can contaminate or disturb the filling area environment during usage.	No	NA	High	▪ The lyophilizer technical area shall be installed outside the filling area. ▪ The lyophilizer operating area shall be isolated from the technical area, so that it doesn't have any impact on filling area conditions.	Acceptable	Facility qualification	
58.	Transfer of sterilized machine parts, bungs, seals, accessories, garments from autoclave to respective room in filling area.	The transfer of machine parts to the filling machine, garments to sterile garment cubicle and other accessories to respective area (after sterilization & unloading) is carried out openly.	Yes	Chances of contamination of sterile articles and subsequently product contamination.	No	NA	High	A mobile LAF shall be provided for transfer of sterilized machine parts, bungs, seals, garments, and other accessories to subsequent area from cooling zone.	Acceptable	Facility qualification	
59.	Ampoule terminal sterilization	No provision provided for terminal sterilization of ampoules & vials.	Yes	Some products filled in ampoules & vials needs terminal sterilization.	No	NA	High	▪ A super heated hot water spray sterilizer shall be with sufficient capacity shall be provided for terminal sterilization of Ampoules & vials. ▪ Ampoules shall be loaded on trays and the trays shall then be loaded in the terminal sterilizer.	Acceptable	Facility qualification	

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								Mitigation Method (9a)	Residual risk level (9b)	Test Document (9c)	
60.	Material of construction	The material of product contact parts of equipments are not suitable, may react with product.	Yes	Product contamination may occur.	No	NA	High	The product contact parts of all machines shall be made up of SS 316 or better grade.	Acceptable	Facility qualification	
61.	Packing	No provision for labeling and secondary packing of product filled vials and Ampoules.	Yes	Labeling is a basic GMP requirement for providing product information to patient.	No	NA	Medium	Packing room with sufficient space and 2 packing lines consisting of necessary instruments such as Labeling machine, cartoning machine, Taping machine etc. shall be provided for labeling & secondary packing of vials and ampoules.	Acceptable	Facility qualification	
62.	Particulate contamination in vials or ampoules	Particulate matter (black, white particles & foreign pieces) may be present in the product filled vials/ Ampoules.	Yes	Foreign material may have impact on patient's safety.	No	NA	High	Visual inspection rooms shall be provided for both Vial and Ampoules inspection. The rooms shall have visual inspection tables with black and white board for detecting any foreign particles in the product filled vials/ Ampoules.	Acceptable	Facility qualification	
63.	Labels	No space provided for storing of labels.	Yes	Approved labels should be placed in lock and key arrangement to prevent mixing.	No	NA	High	▪ A Label store shall be provided in the warehouse area for storage of labels. ▪ A label printing room shall be provided in the packing area for printing of text matter on labels.	Acceptable	Facility qualification	

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								Mitigation Method (9a)	Residual risk level (9b)	Test Document (9c)	
64.	FG Storage in packing area	FG shippers are kept on floors in the packing area.	Yes	Chances of damage/ contamination of the shippers in case of any water/ solvent spillage.	No	NA	Medium	Pallets shall be provided for placing of FG shippers in packing areas.	Acceptable	Facility qualification	
65.	Change/ Spare parts & Tool room	No room provided to keep the change parts, tools etc required of all packing line equipments.	No	No impact on product quality.	Operational	The change parts, tool kit should be kept near the machines for immediate installation, rectification.	Low	A Change parts & Tool room with sufficient space shall be provided in the packing area for storage of change parts & other tools, required for packing line equipments.	Acceptable	Facility qualification	
Packing Area											
66.	FG Storage in packing area	FG shippers are kept on floors in the packing area.	Yes	Chances of damage/ contamination of the shippers in case of any water/ solvent spillage.	No	NA	Medium	Pallets shall be provided for placing of FG shippers in packing areas.	Acceptable	Facility qualification	
67.	Change/ Spare parts & Tool room	No room provided to keep the change parts, tools etc required of all packing line equipments.	No	No impact on product quality.	Operational	The change parts, tool kit should be kept near the machines for immediate installation, rectification.	Low	A Change parts & Tool room with sufficient space shall be provided for storage of change parts & other tools, required for packing line equipments.	Acceptable	Facility qualification	
Production – General Points											

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S.No. (1)	Process steps/ component (2)	Risk (3)	GMP Risk Yes/ No (4)	Justification (5)	Other Risk type (6)	Justification (7)	Risk Level (8)	Risk Control (9)			Status of RA (10)
								Mitigation Method (9a)	Residual risk level (9b)	Test Document (9c)	
68.	Process flow	Area/ Equipments are not arranged to ensure unidirectional or logical flow in the facility	Yes	Chance of cross contamination or mix up	Operational	Difficulty in handling the process operations	High	The plant layout shall be designed with a logical uni-directional flow based on the following: ▪ Process Operation ▪ Material flow starting from the receipt of raw material/ components to the production of finished goods and its dispatch. ▪ Waste disposal	Acceptable	Facility qualification	
69.	Cleanability	▪ Difficult to clean and maintain the manufacturing facility. ▪ The cleaning media is not compatible with building material. ▪ Building material is absorptive in nature. ▪ Equipment surface is not suitable for cleaning	Yes	▪ Improper cleaning causes contamination in the area; desired hygiene room specification may not be achieved. ▪ Reactive cleaning media can lead to deterioration of surface evenness resulting shredding of particles. ▪ Improper surface contour can lead to difficulty in cleaning and particle deposition.	No	NA	High	Following measures shall be taken to ensure Cleanability: ▪ The building material shall be non-fibre shedding, non absorbable type and clean room suitable. ▪ Building finishes with coving, epoxy flooring and plastic emulsion painting for walls ▪ Easy access to the walls, ceiling and corners for ease of cleaning. ▪ The equipment shall have smooth, crevice free surface.	Acceptable	Facility qualification	
70.	Production area floor	▪ The floor is not cleanable ▪ Accumulation of dust at corners ▪ Floor is not load bearing	Yes	▪ Accumulation of dust on the floor & corners– may contaminate product. ▪ Damage to floor during material transfer.	No	NA	Medium	▪ The production area floor shall be smooth without any cracks or gaps. ▪ Floors shall be epoxy screed laid on concrete screed. ▪ Epoxy screed shall be of	Acceptable	Facility qualification	

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								Mitigation Method (9a)	Residual risk level (9b)	Test Document (9c)	
		▪ Floor is reactive						suitable thickness to prevent damage. ▪ Coving shall be applied at all corners, floor-wall joints for better cleaning.			
71.	Ceiling	▪ Ceiling not smooth. ▪ Duct/ Diffusers/ Light cut outs not sealed properly. ▪ Ceiling – wall joints are not cleanable	Yes	▪ Accumulation of dust particles in gaps and ceiling-wall joints. ▪ Leakage of environmental air through cut outs.	No	NA	High	▪ Ceiling in clean room areas shall be smooth without any crevices. ▪ All ceiling cut outs shall be properly sealed using silicon sealant. ▪ Coved skirting shall be provided on ceiling – wall joints.	Acceptable	Facility qualification	
72.	Fogging	No provision for fogging 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 Grade-B area • SOP shall be developed for fogging as per time required during qualification stage. • Supply & exhaust damper should be 100% open during fogging	Acceptable	Facility qualification	
73.	False ceiling	▪ Height above false ceiling is too low. ▪ False ceiling is not load bearing	No	No impact on product quality.	Servicing	Space is required above false ceiling for maintenance purpose.	Low	▪ Adequate space shall be provided above false ceiling for maintenance purpose. ▪ False ceiling of clean rooms shall be crevice free and smooth finish. It shall be possible to access all components above false ceiling which need servicing. ▪ Clean room false ceiling shall be load bearing and walkable.	Acceptable	Facility qualification	

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								Mitigation Method (9a)	Residual risk level (9b)	Test Document (9c)	
74.	Doors	▪ Door opening is not according to pressure zoning. ▪ Doors MOC is not suitable.	Yes	▪ Door might remain open due to pressure. ▪ Reactive Door MOC may cause area contamination	Operational	Door closure will need frequent maintenance	high	▪ The doors opening in clean room areas shall be designed according to pressure zoning i.e. it opens towards room with higher pressure, wherever possible. ▪ In areas where it is not possible, high strength door closure shall be affixed. ▪ Doors shall be made of powder coated steel construction of clean room finish	Acceptable	Facility qualification	
75.	Change rooms/Airlocks	Change rooms/Airlocks are congested	No	No impact on product quality.	Operational	Leads to difficulty in personnel movement and plant efficiency will be hindered.	Medium	Change rooms/Airlocks shall be sufficient size and shall be designed based on the estimated number of personnel supposed to pass through the change rooms.	Acceptable	Facility qualification	
76.	Corridors	Narrow corridors in production area	No	No impact on product quality.	Operational	Leads to difficulty in personnel and material movement	Medium	Corridors shall be of sufficient size for men & material movement	Acceptable	Facility qualification	
77.	Room size	Insufficient area/ size of process rooms.	Yes	The defined number of the activities cannot be accommodated in the proposed area.	Operational / EHS	Leads to difficulty in man/ material movement; Operation. and maintenance activity	High	▪ All the area shall be prepared taking in to consideration the number and size of equipments based on the production capacities target and production cycle time ▪ Adequate free space for operation and equipment maintenance and man / material movement shall be	Acceptable	Facility qualification	

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								Mitigation Method (9a)	Residual risk level (9b)	Test Document (9c)	
								provided.			
78.	Equipment installation and operating space	Improperly installed equipments (technical area is not separated from clean area) & inadequate space for operation and maintenance with respect to room layout	Yes	Contamination of processing area	EHS	Insufficient workspace makes it prone to accidents	High	▪ Separate technical area from clean areas, accessible from outside, shall be provided wherever possible. ▪ Availability of adequate space around the equipments for operation, cleaning, inspection and maintenance.	Acceptable	Facility qualification	
79.	Office	No separate office	No	No GMP Impact	Operational	Not convenient for working	Low	Separate area for offices shall be provided in the facility.	Acceptable	Facility qualification	
80.	Scrap removal	▪ No exit route provided for scrap removal from production area. ▪ No control on disposal of scrap/ waste.	Yes	Basic GMP requirement	No	NA	Medium	▪ An air lock or pass box shall be provided for scrap removal from Production Area. ▪ Disposal of waste from the factory is in accordance with the requirement of Environmental pollution Control Board. ▪ Scrap removal SOP should mention the exact route and process of scrap removal from the production area.	Acceptable	Facility qualification & SOP	

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								Mitigation Method (9a)	Residual risk level (9b)	Test Document (9c)	
81.	Sound level	More noise is produced by the equipments during the operation	No	No impact on product quality	EHS	High noise may cause deafness and anxiety	Medium	▪ Equipments wherever required shall be provided with anti-vibration mountings to reduce vibration and noise. ▪ Noise level for all equipments in production area shall be below 80 db at a distance of 1 m from the equipment.	Acceptable	Facility qualification	
82.	Illumination system	Insufficient and improper lighting	Yes	▪ In critical places lack of minimum illumination may affect the process. ▪ Chances of contamination in clean room area due to improper lighting design. ▪ Higher risk during visual inspection, data reading and recording.	Operational/ EHS	▪ Inconvenient for the operator to work in less light ▪ Chance of accidents in hazard area	High	▪ Working area shall be designed with sufficient illumination i.e NLT 400 lux in operational area and NLT 300 lux in non-operational area. . ▪ Adequate natural or artificial lighting shall be provided throughout the establishment. ▪ Adequate lightning shall be provided in the process area e.g. visual inspection area etc.	Acceptable	Facility qualification	
83.	Lights	Light fittings are not suitable for clean room conditions	Yes	▪ Accumulation of dust particles. ▪ Leakage from improper light fittings.	No	NA	Medium	▪ Lights in clean room areas shall be of flush fitted type and sealed with silicon sealant. ▪ The lights shall be replaceable from above the false ceiling without compromising clean room environment. ▪ The light fitting within the clean room shall be with smooth surface, without any crevices. ▪ Flame proof type lightning shall be designed in hazard area, if applicable. ▪ For Photosensitive product halogen lamp or yellow light	Acceptable	Facility qualification	

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								Mitigation Method (9a)	Residual risk level (9b)	Test Document (9c)	
								shall be provided.			
84.	Emergency door	▪ Emergency door not provided ▪ Emergency door not fire proof.	No	No impact on product quality	Safety	Required during any mishappening	High	▪ Emergency doors shall be provided in the main production area corridor. ▪ Doors shall be of fire proof design. ▪ Emergency crash full length windows shall be provided at suitable places for emergency exit. ▪ A smooth & round finished hammer or other suitable device shall be provided for breaking of crash window inside the clean rooms.	Acceptable	Facility qualification	
85.	Equipment entry panel	No entry panel is provided for entry or removal of large equipment.	No	NA	Operational	New equipments could be installed in future or else non-working equipments may have to be removed	Low	A suitable sized equipment entry panel should be provided for the entry or removal of large equipments.	Acceptable	Facility qualification	
86.	Windows	The activity in the critical area is not visible from outside.	No	NA	Operational	The critical activity should be visible for ease of monitoring	Low	The critical areas shall be designed with windows of the required sizes and number to view the operation without entering the critical area.	Acceptable	Facility qualification	
87.	Windows	Windows are not flushed.	Yes	Accumulation of dust in the crevices.	No	NA	High	▪ Windows in clean room areas shall be flushed from both sides with no ledges or crevices. ▪ Double glazed windows shall	Acceptable	Facility qualification	

RISK ASSESSMENT FOR STERILE FORMULATION FACILITY

S.No. (1)	Process steps/ component (2)	Risk (3)	GMP Risk Yes/ No (4)	Justification (5)	Other Risk type (6)	Justification (7)	Risk Level (8)	Risk Control (9)			Status of RA (10)
								Mitigation Method (9a)	Residual risk level (9b)	Test Document (9c)	
								be installed in the entire production area.			
88.	Service penetration	▪ Service penetrations through wall are not leak proof. ▪ MOC of service penetrations is not suitable to clean room.	Yes	Contamination of clean room.	No	NA	High	▪ Service penetrations shall through manifold/ pendants and the joints shall be properly sealed with silicon sealant. ▪ The service penetrations shall be made of SS 304 or better.	Acceptable	Facility qualification	
89.	Furniture	▪ Furniture may be particle shedding. ▪ MOC may not be resistant to decontaminating agents	Yes	Clean room conditions may be compromised	No	NA	Medium	Any furniture inside clean room should be made of SS 304 or better material and the design should not allow any dust accumulation.	Acceptable	Facility qualification	
90.	Seepage in the building	Water seepage	Yes	Moisture within the room wall can lead to fungal growth	No	NA	Medium	▪ All building materials shall be resistant to water. ▪ Proper water proofing shall be been done in all areas.	Acceptable	Facility qualification	
91.	Production area	Manufacturing areas not pressurized	Yes	Proper differential pressure should be maintained in the production facility to prevent contamination	No	NA	High	▪ Proper differential pressure .i.e. NLT 15 Pascal shall be designed between 2 rooms of different hygiene level and NLT 10 Pascal between rooms of same hygiene level. ▪ Air flow study shall be conducted to demonstrate differential pressure.	Acceptable	Facility qualification	

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								Mitigation Method (9a)	Residual risk level (9b)	Test Document (9c)	
92.	Hygiene level	Breach in the system	Yes	Difficulty to maintain the desired class, temperature and RH conditions	No	NA	High	▪ In this entire blocks, HVAC system shall be designed to achieve respective ISO class as per criticality of operation. ▪ In addition, appropriate supporting measures such as change room, airlocks; GMP complying water-proof, non-absorbent, cleanable Floors, walls and ceiling will be considered during design and execution. ▪ All product processing activity shall be carried out in their respective grade areas as per defined standards. ▪ Temperature and RH conditions shall be designed as per clean room & product requirement.	Acceptable	Facility qualification	
Utilities											

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								Mitigation Method (9a)	Residual risk level (9b)	Test Document (9c)	
93.	Utilities	Lack of utility	Yes	Realization of product to be produced with desired quality is not possible	EHS / Operational	Basic process requirement	High	Following utilities shall be provided: ▪ Chilled water ▪ Cooling water ▪ Plant Steam ▪ Electricity ▪ Purified Water ▪ Water for Injection ▪ Compressed air ▪ Nitrogen ▪ Pure Steam	Acceptable	Facility qualification	
94.	Chilled water system	Not designed of adequate capacity (TR)	No	No direct impact on product quality	Operational	Room condition may get out of specification.	Low	System is properly designed considering its requirement in process & HVAC.	Acceptable	Facility qualification	
95.	Cooling water system	Not designed of adequate capacity	No	No direct impact on product quality	Operational	Room condition may get out of specification.	Low	System is properly designed considering its requirement in process & HVAC	Acceptable	Facility qualification	
96.	Cleaning of product contact parts of machine.	Final cleaning is performed using unclean water.	Yes	For Sterile facility the final cleaning should be performed using purified water & WFI only.	No	NA	High	▪ PW & WFI generation & distribution system shall be designed and installed in the facility for cleaning of manufacturing equipment. ▪ Required number of user points of PW & WFI user shall be provided. ▪ PW & WFI generated shall meet the pharmacopoeial	Acceptable	Facility qualification	

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								Mitigation Method (9a)	Residual risk level (9b)	Test Document (9c)	
								specifications.			
97.	Labelling of pipes and cables	Labelling of utility pipelines & cables inappropriate	Yes	Prerequisite for qualification	Safety	Wrong utility may be opened	High	▪ All piped service pipe and cables shall be clearly labelled and pipes should have proper directional flow arrows. ▪ All labelling shall be in English language and according to project standard.	Acceptable	Facility qualification	
98.	Drains	▪ Unwanted drains provided in the manufacturing area. ▪ Drains are not properly designed.	Yes	May contaminate the area.	No	NA	High	▪ The drains in manufacturing area shall be optimum and drain points facilitate cleaning & sanitization. ▪ Sanitary type drain system of adequate size shall be designed for unit operation and to prevent back flow and/ or prevent insects & rodent entering the premises. ▪ Drain verification shall be carried out during area qualification. ▪ SOP for cleaning and maintenance of drains shall be prepared.	Acceptable	Facility qualification & SOP	
99.	Pest Control	Easy entry of pest into the facility	Yes	Affect product quality	EHS	Health hazard	High	▪ Facility design shall minimize the risk of entry of pests by closing of all openings. ▪ Pest control for the entire facility shall be planned. ▪ Tightly fixed doors with	Acceptable	Facility qualification & SOP	

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								Mitigation Method (9a)	Residual risk level (9b)	Test Document (9c)	
								additional drop seals at the bottom shall be provided. ▪ Air curtains shall be provided for entry from outside environment to plant. ▪ Insecticutor /UV lights, rodent traps shall be provided			
100.	Compressed air	Dry compressed air is not available	Yes	Dry compressed air is required for product processing, drying of equipments and equipment operation	No	NA	High	▪ Compressed air generation and distribution system which would generate required quality of compressed air should be installed in the facility, for the required functions. ▪ 0.2 µm terminal filters shall be installed at the compressed air inlet line to critical equipments, wherein it comes in contact with product or product contact parts. ▪ Compressed air system qualification shall be carried out to confirm quality, before usage.	Acceptable	Facility qualification	
101.	Technical Area	Sufficient space is not provided for technical area for keeping AHU's, Chiller (s), control panels etc.	No	No impact provided on product quality.	Operational	A technical area is required for installation, servicing and maintenance of AHU, and other utilities.	Medium	Sufficient space shall be provided for technical area for installation of AHU, water system, Chiller (s), control panels etc.	Acceptable	Facility qualification	

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								Mitigation Method (9a)	Residual risk level (9b)	Test Document (9c)	
102.	Filter cleaning station	▪ Filter cleaning area not provided in the technical area. ▪ Filter cleaning room not classified.	Yes	Required for routine cleaning of Pre-filters of HVAC system and LAF's, installed in the technical area, manufacturing areas and warehouse.	No	NA	Medium	▪ A separate filter cleaning room with sufficient space and required utilities (water and compressed air) shall be provided for cleaning of Pre-filters. ▪ Dedicated area should be provided for storage of cleaned filters to avoid re-contamination. ▪ Filter cleaning station shall be installed in the Filter cleaning room for cleaning of filters.	Acceptable	Facility qualification	
103.	Plant Garments	▪ No dedicated area provided for cleaning of plant (general area) and lab garments,	No	No impact on product quality, as garments could be sent to any external vendor for washing.	Financial & Operational	Sending garments to external vendor, may require inspection of third party to ensure quality of washing. Washing may also require huge capital cost.	Medium	▪ A separate garments washing room should be provided in the facility for cleaning of general area garments of production and lab. ▪ Washing machines and dryer should be installed in the room. ▪ The room should be clean and should have separate space for storage of cleaned garments.	Acceptable	Facility qualification	
Safety											
104.	Electrical sockets	▪ Electrical sockets are not dust proof. ▪ Short circuit in electrical circuit	Yes	Accumulation of dust inside electrical sockets	EHS	May lead to fire, which can destroy facility including personnel casualty.	High	▪ All electrical sockets shall be provided with dust proof spring cover. ▪ All electrical cables shall be grouted within wall/floor. ▪ Equipment intended for	Acceptable	Facility qualification	

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								Mitigation Method (9a)	Residual risk level (9b)	Test Document (9c)	
								outdoor installation shall have minimum protection of IP66 or NEMA-46			
105.	Earthing & Lightning protection	Improper & inappropriate design	No	No impact on product quality	Operational/ EHS	▪ May affect the product manufacturing operations & product quality. ▪ Affect the entire process operation as it is ▪ Prone to any kind of high electrical energy generation which can lead to casualty.	High	All electrical & lighting fixtures design shall be in Compliance to Indian standards IS 3043 & other statutory regulation	Acceptable	Facility qualification	
106.	Access Control into the site	Easy access for Trespassers	Yes	Possibility of untrained persons enter the technical area	EHS	Theft/ loss of property	High	Access controls shall be provided in the core areas and main production area entry,	Acceptable	Facility qualification	
107.	Fire protection system	Fire in the facility	No	No impact on product quality	EHS	Fire can destroy the facility including personnel casualty	High	▪ NFPA/ NBC/ LPA codes and other relevant standards shall be considered in design of facility. ▪ Fire hydrant system, fire detection & alarm system and fire extinguishers shall be designed & provided in facility.	Acceptable	Facility qualification	

9 Summary & Conclusion

- The Risk Assessment was performed to establish the design of the facility so as to be compliant to expectations of various national and international regulatory agencies.
- 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 facility will prevent the risk of failures of product during manufacturing".*

10 Abbreviations

EU-GMP	:	European – Good Manufacturing Practice
ALUS	:	Automatic Loading Unloading System
EHS	:	Environment Health Safety
GMP	:	Good Manufacturing Practice
RA	:	Risk Assessment
NMT	:	Not More Than
SOP	:	Standard Operating Procedure
USFDA	:	United State Food & Drug Association
AHU	:	Air Handling Unit
PPM	:	Primary Packing Material
SPM	:	Secondary Packing Material
ISO	:	International Organization for Standardization
NEMA	:	National Electrical Manufacturers Association
NFPA	:	National Fire Protection Association
NBC	:	National Broadcasting Company
LPA	:	Local Planning Authority
SS	:	Stainless Steel
db	:	Decibel
DQ	:	Design Qualification
IQ	:	Installation Qualification
OQ	:	Operational Qualification
PQ	:	Performance Qualification
O&M	:	Operation and Maintenance
GA	:	General Arrangement
IPSI	:	Integrated Project Services International, New Delhi

11 Revision History

Date	Revision	Reason for Revision
	00	New Document