User Requirement Specifications Aseptic Liquid and Powder Filling LineEquipment ID: ……

Revision index

Revision	Date	Reason for revision
00		First Issue

USER REQUIREMENT SPECIFICATION

NAME OF ITEM: ASEPTIC LIQUID AND POWDER FILLING LINE	**PROTOCOL No.:** .....
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2.0 Overview

2.1 Equipment description

The filling line consists of machines for the required basic process steps stated as follows:

- **Vial washing**
- **Vial sterilization & dehydrogenization**
- **Aseptic filling of sterile product (Liquid & Powder)**
- **Stoppering of the vials (Liquid/Powder/Lyophilized)**
- **Capping of vials by aluminium seals**

Following equipments will be connected together in sequence as one line

- **Vial washing machine**
- **Sterilization & depyrogenating tunnel**
- **Turn table**
- **Aseptic filling and stoppering machine (Liquid & Powder)**
- **A turn table**
- **Crimping machine**

The **filling line shall be configured in linear shape, with vial movement from left to right**, so vial washing machine, depyrogenating tunnel will be in the same room. Refer equipment layout attached as Annex 1.

The aseptic filling, stoppering and crimping machine will be under LAF. The charging of vials to lyophilizer will also be carried out within LAF.

This URS shall cover the requirement of above all six equipments (highlighted) with an intension that complete line shall be provided by a single vendor

In this equipment chain following is the process sequence:

- The manual loading of vials in washing machine indeed.
- Washing and subsequent removal of residual water from vials internally and externally achieved byfiltered circulated water, purified water, water for injection and filtered compressed air
- Automatic and continuous transfer of vials to sterilizing and depyrogenating tunnel
- Drying of vials and subsequent heating of vials by HEPA filtered hot air (more than 300 deg C) for depyrogenation followed by cooling
- Automatic and continuous transfer of vials under grade A environment to the filling station of fillingand stoppering machine
- Filling of sterile liquid/powder in the vials at predefined volume/weight with optional pre and postgassing by sterile nitrogen. Filling takes place under grade A environment
- Stoppering or half stoppering of vials under grade a environment.
- Automatic transfer of stoppered vials to crimping machine or transfer of half stoppered vials tocasetting station for lyophilizer loading under grade an environment.
- Crimping of vials by aluminium cap under grade A environment

2.3 Reference standard/guideline for equipment

The equipment should comply with the following guidelines / standard:

GMP-Regulations

- EU-GMP-Guideline Part 1, Annexes 1, 11 & 15
- Regulation for implementation of the drug administration law of the People's Republic of China
- Code of Federal Regulations (CFR) 21, Part 210: cGMP in Manufacturing, Processing, Packing andHolding of Drugs; General
- 21 CFR Part 211: Current Good Manufacturing Practice for finished Pharmaceuticals
- 21 CFR Part 11: Electronic Records; Electronic Signatures

FDA Guidance for Industry

- Sterile Drug Products Produced by Aseptic Processing
- Documentation for Sterilization Process Validation

GAMP

- The Good Automated Manufacturing Practice (GAMP) Guide for Validation of Automated Systems in Pharmaceutical Manufacture, Vol. 5

Vendor shall provide response as Yes or No against each specification for the compliance of theiroffered equipment in the remarks column and send the copy along with the quotation.

Specifications	Compliance
3.0 Process Description	
3.1 Input & Charging method *Note: This section also include the charging method of process media along withcharging method for material input.*	
3.1.1 Vial Washing machine	
3.1.1.1 **Unwashed vials:** The vial washing machine require a tray loading station wherevials will be manually loaded from a tray.	❑ Yes ❑ no
3.1.1.1.1 Trays shall be provided by the user	Informationonly
3.1.1.1.2 Vial sizes are 5ml,10 ml	❑ Yes ❑ no
3.1.1.1.3 Vendor shall inform the required dimension of tray so that it can effectively fit to theloading station and optimum number of vial can be charged at one time.	❑ Yes ❑ no
3.1.1.2 **Purified water or PW:** PW shall be used as washing media in the vial washing machine. The vial washing machine should be suitable to collect PW directly from theroom supply valve of PW distribution loop. The interface location of connecting PW collection pipe to the room supply valve is to be decided during detail engineering stage. The purified water should pass through a 10 micron cartridge filter.	❑ Yes ❑ no
3.1.1.3 **Water for injection or WFI:** WFI shall be used as washing media in the vial washing machine. The vial washing machine should be suitable to collect WFIdirectly from the room supply valve of WFI distribution loop. The interface location of connecting WFI collection pipe to the room supply valve is to be decided during detail engineering stage. The purified water should pass through a 5 micron cartridgefilter.	❑ Yes ❑ no
3.1.1.4 **Re-circulated water:** PW & WFI used in the rinsing of vial, shall be recirculated for initial washing of vials. The vial washing machine should have all arrangement for recirculation of water. The recirculated water should pass through a 20 micron cartridge filter. The vendor shall inform the exact arrangement of recirculation systemin its technical offer. *Vendor shall quote for filter housing (suitable for connection with integrity test apparatus)* ***as optional****.*	❑ Yes ❑ no
3.1.1.5 **Filtered compressed air** : Filtered (0.2 micron) compressed air shall be used for flushing of internal surface of vial to remove larger particulate and in final blowing step to remove water from the washed vials to make it visually dry. *Vendor shall*	❑ Yes ❑ no

Specifications	Compliance
quote for filter housing (suitable for connection with integrity test apparatus) ***as optional***.	
3.1.2 Sterilization & depyrogenating Tunnel	
3.1.2.1 **Washed Vials from Vial washing machine**: The washed vials shall be transported atthe end washing step automatically to in feed zone of the tunnel by a conveyor.	❑ Yes ❑ no
3.1.2.1.1 The transportation of washed vials should be covered or protected by HEPA filteredair from a laminar airflow unit.	❑ Yes ❑ no
3.1.2.2 **Air**: The room air shall be sucked, supplied and recirculated by the air handling system of the tunnel. Final filtration is done by EU 14 HEPA filter and delivered as unidirectional airflow from the laminar flow unit of the equipment. Vendor shall inform the quantity of air intake from room	❑ Yes ❑ no
3.1.3 Filling & Stoppering machine	
3.1.3.1 **Sterilized and Depyrogenated vials from depyrogenating tunnel**: The sterilized & depyrogenated vials after cooling cycle in the tunnel shall enter into LAF. The vial shall be collected in a turntable. From the turn table vials should be singled on a conveyor and reach filling station.	❑ Yes ❑ no
3.1.3.2 **Steam sterilized siliconized/ unsiliconised rubber stopper (20mm or 13mm size according DIN-ISO 8362-2 for liquid vials /DIN-ISO 8362-5 for freeze dried vials/powder vials):** The rubber stopper will be sterilized in SS perforated baskets. Sterilised rubber bungs from SS perforated baskets shall be collected automatically insterilised S bins. The SS bins containing sterilised rubber bungs shall be charged to the charging hopper of the stoppering station under LAF (Class ISO 5).	❑ Yes ❑ no
3.1.3.3 **Product Liquid:** The product is aqueous based. The product liquid shall be hold in sterile vessel under nitrogen overpressure before filling (optional). During filling the product liquid shall be transferred by filtered (0.2 micron) nitrogen pressure from the holding tank to the buffer tank of the filling machine through a sterilizing grade Capsule/cartridge/membrane filter (0.2 micron). *Vendor shall consider the connection of cartridge/capsule/membrane filter (0.2 micron) with online integrity testing ports and recommend the size of housing. The User shall provide the filter. However vendor shall quote filter as* ***optional***.	❑ Yes ❑ no
3.1.3.4 **Product Powder:** The product is powder. The product shall be kept in sealed aluminium container of 4 Kg or 10 Kg capacity. The product bulk density shall bearound 0.4 to 0.6 g/cc. The equipment should have suitable facility to dock the container aseptically on the product hopper for charging of powder in closed condition. Or product shall be manually charged within the product hopper.	❑ Yes ❑ no

	Specifications	Compliance
3.1.3.5	**Filtered compressed Nitrogen**: Filtered (0.2 micron) compressed nitrogen shall be used for pre and post gassing of Vial. Nitrogen pressure and flow rate should be regulated to have consistent removal of oxygen from the vial. *Vendor shall quote forfilter housing (suitable for connection with integrity test apparatus)* ***as optional***.	❑ Yes ❑ no
3.1.4	**Crimping machine**	
3.1.4.1	**Stoppered filled Vials**: The filled vials after stoppering in filling machine or in lyophilizer shall be transported manually/automatically to the crimping machine. There are two different crimping machine; one for liquid vial and other for lyophilised vials. The transfer shall be under Grade A condition. As per draft Annex 1 of EUGMP, the crimping is proposed in microbiologically Class A condition in new facility.	❑ Yes ❑ no
3.1.4.2	**Aluminium seals (20 mm or 13 mm, tear off or flip off according DIN-ISO 8362-6) :** As crimping operation will be carried out in Grade A/B condition, the seals shall be transferred sterile. The seals shall be sterilized in SS containers. Sterilised aluminium seals shall be charged to the charging hopper of the crimping unit.	❑ Yes ❑ no
3.2	**Brief Process Steps**	
3.2.1	**Vial Washing machine**	
3.2.1.1	Washing of glass vial is to be completed using four selectable washing media i.e. recirculated water (Ambient temp), Purified water (Ambient temp), WFI (>70 deg C) and filtered (0.2 micron) compressed air.	❑ Yes ❑ no
3.2.1.2	Exact cleaning sequence is to be proposed by the vendor. However following rules areto be complied:	❑ Yes ❑ no
3.2.1.2.1	Initial cleaning by recirculated water (refer section 3.1.1.4.) for internal and externalsurface cleaning	❑ Yes ❑ no
3.2.1.2.2	Filtered (0.2 micron) compressed air blowing after every water cleaning	❑ Yes ❑ no
3.2.1.2.3	Second wash by purified water (refer section3.1.1.2) for internal surface cleaning	❑ Yes ❑ no
3.2.1.2.4	Final wash by WFI ((refer section 3.1.1.3.) for internal and external cleaning.	
3.2.1.2.5	Final steps is to dry the vials (no visual droplets or wetting) by filtered (0.2 micron) compressed air blowing	❑ Yes ❑ no
3.2.1.2.6	Total washing station shall be minimum 6 even if proposed sequence comprised of	❑ Yes ❑ no

	Specifications	Compliance
	lesser number of stations.	
3.2.1.3	The final step siliconization of vial is to be considered as future option.	❑ Yes ❑ no
3.2.2	**Sterilizing & depyrogenating tunnel**	
3.2.2.1	Depyrogenating tunnel is to perform following process steps: ♦ Transportation of washed vials in rows to drying zone ♦ Drying of vials by hot (~100°C)HEPA filtered air (unidirectional air flow) ♦ Transportation of dried vials to depyrogenation zone ♦ Depyrogenation of vials by hot (>300°C) HEPA filtered air (unidirectional airflow) ♦ Transportation of sterilized & depyrogenated vials to cooling zone ♦ Progressive cooling of hot vials to 25 –30°C by cold HEPA filtered air (unidirectional air flow) ♦ Transportation of cooled (sterilized & depyrogenated) vials to the turn table infilling room	❑ Yes ❑ no
3.2.3	**Filling and stoppering machine**	
3.2.3.1	Filling and stoppering machine is to perform following process steps: ♦ transportation of depyrogenated vials singlized on a conveyor belt upto fillingstation ♦ Selection of vial for in process check weighing of empty vials (i.e. tare weight) bya load cell (optional) ♦ Pre gassing by nitrogen purging within vials (product selective process) (optional) ♦ Dosing of product liquid/powder within vial 10 ml based on the vial size ♦ Identification of vial weighed for tare and post weighing to obtain fill weight by aload cell. (inprocess control- optional ♦ Post gassing of vials by nitrogen purging (optional). ♦ Transportation of vial to stoppering station. ♦ Inspection for the presence of vial and stopper placement followed by pressing thestopper for full stoppering or half stoppering ♦ Transportation of vial out of filling & stoppering machine to turn table and subsequently to crimping machine or to casetting station for half stoppered	❑ Yes ❑ no

	Specifications	Compliance
	lyophilized vials	
3.2.4	**Crimping machine**	
3.2.4.1	Crimping machine is to perform following process steps: ♦ Transportation of stoppered vials to crimping stations ♦ Placement of seal over the stopper ♦ Crimping through number of stations ♦ Ink jet / UV marking of batch code on the over seal (Optional)	❑ Yes ❑ no
3.3	**Output & Discharging method**	
3.3.1	The sealed vials shall then be automatically transferred to the turntable, from wheresealed vials are transported to visual inspection area with the help of conveyor.	❑ Yes ❑ no
4.0	**Productivity Requirement**	
4.1	**Desired/ suggested capacity**	
4.1.1	The filling line should be suitable to produce filled and stoppered vials at the rate of170 vials per minute, 120 vials per minute, based on the vial size of 5ml,10 ml. The vendor shall also supply the information of line capacity for all other sizes of vial mentioned in the section 3.1.1.1.2.	❑ Yes ❑ no
4.2	**Standard batch size**	
	Minimum batch size: 5000 vial and maximum batch size: 60000 vials	Information only
4.3	**Change Over Time (if applicable)**	
4.3.1	Vendor shall ensure minimum time for change over of format parts for assembling and disassembling (i.e. within 30 minutes) with minimum usage of tools and also inform the exact time for change over.	❑ Yes ❑ no
4.3.2	To fix the right position of the format parts, they should be marked that is not erasable	❑ Yes ❑ no
4.4	**Cleaning/sanitization Time (if applicable)**	
4.4.1	Not required to specify	-

	Specifications	Compliance
4.5	**Other Productivity Requirement**	
4.5.1	Vendor shall inform the water requirement (L per hour) for washing of vials at saidcapacity for each size of vials in their technical offer.	❑ Yes ❑ no
4.5.2	The filling line shall have one working hours counter and object counter at the vialwashing machine	❑ Yes ❑ no
4.5.3	To minimize the amount of product to be rejected after a machine stop and at the endof filling, the system from the product vessel to the filling needles will be optimized.	❑ Yes ❑ no
4.5.4	Normal production modus has to work until the product volume within the wholefilling system is almost zero.	❑ Yes ❑ no
5.0	**Safety requirement**	
5.1	**General**	
	Following facilities must be provided to protect personnel, article and equipment:	
5.1.1	In the event of equipment malfunction or loss of utilities, the unit must contain all necessary protection devices to ensure that the equipment and the article remain in a safe condition.	❑ Yes ❑ no
5.1.2	Noise level below 80 db at a distance of 1 m from the equipment	❑ Yes ❑ no
5.1.3	Emergency stop function on accessible areas and independent for each machine.	❑ Yes ❑ no
5.1.4	For the safety of the operator the external surfaces should not have temperature morethan 45°C.	❑ Yes ❑ no
5.1.5	Warning stickers on all hot surfaces	❑ Yes ❑ no
5.1.6	Appropriate failure detection and alarm notification	❑ Yes ❑ no
5.1.7	All machine doors, which are closed during production, according to operator safety, have to be supervised by security switches. In case of opening the machine must stop immediately	❑ Yes ❑ no
5.2	**Power failure and recovery**	
5.2.2	On power failure, equipment must come to rest and power restart must not be automatic and human intervention must be required. On power recovery the operationalparameters has to be retrieved by memory back mechanism	❑ Yes ❑ no

	Specifications	Compliance
5.3	**Containment**	
5.3.1	NA	❑ Yes ❑ no
6.0	**GMP requirements**	
6.1	**Process control**	
6.1.1	**Vial Washing machine**	
6.1.1.1	The equipment should have facility for monitoring of pressure and temperature of WFIwith alarm in case of low or very high temperature or pressure.	❑ Yes ❑ no
6.1.1.2	The equipment should have facility for monitoring of pressure of PW with alarm incase of low or very high pressure.	❑ Yes ❑ no
6.1.1.3	The water recirculation system should have all arrangement for controlling andmonitoring the pressure of delivery with alarms in case low or very high values.	❑ Yes ❑ no
6.1.1.4	The compressed air supply pipeline should be provided with the facility to monitor the pressure of delivery with alarm in case of low or very high values of pressure.	❑ Yes ❑ no
6.1.1.5	The equipment control system should be suitable to adjust the equipment speed.	❑ Yes ❑ no
6.1.2	**Depyrogenating Tunnel**	
6.1.2.1	The equipment should be able to control and monitor the temperature of each zone (i.e. Drying, depyrogenation and cooling zone)	❑ Yes ❑ no
6.1.2.2	The equipment control system should be suitable to adjust the speed of tunnelconveyor.	❑ Yes ❑ no
6.1.2.3	The tunnel should control the differential pressure between each zone and connected rooms i.e. filling room and washing/sterilization room with a cascading effect from filling room towards washing and sterilization room.	❑ Yes ❑ no
6.1.3	**Filling and stoppering machine**	
6.1.3.1	Filling machine should consistently and reproducibly meet the following fillingaccuracy at operating ranges of filling speed: Filling accuracy for fill volume less than 1.0 ml should be ± 1.0%.Filling accuracy for fill volume more than 1.0 ml should be ± 0.5 %.	❑ Yes ❑ no
6.1.3.2	The equipment control system should be suitable to adjust and maintain the rate of	❑ Yes ❑ no

	Specifications	Compliance
	filling (number of vials/ minute)	
6.1.3.3	The equipment should control and monitor the flow rate and pressure of sterile nitrogensupply to be used for pre gassing and post gassing of nitrogen.	❑ Yes ❑ no
6.1.4	**Crimping machine**	
6.1.4.1	The crimping machine should be suitable for adjustment of crimping height based onthe vial sizes and should crimp all sizes of the vial	❑ Yes ❑ no
6.1.4.2	The equipment control system should be suitable for adjustment of machine speed	❑ Yes ❑ no
6.2	**Failure mode detection**	
6.2.1	**Vial Washing machine**	
6.2.1.1	Equipment shall be capable to detect the following failure, notify the operator withalarm and shutdown the process:	❑ Yes ❑ no
6.2.1.2	Very low pressure of WFI/PW or pressure less than low/high limit for longer period	❑ Yes ❑ no
6.2.1.3	Very low pressure of recirculated water or pressure less than low/high limit for longerperiod	❑ Yes ❑ no
6.2.1.4	Very low temperature of WFI less than low/high limit for longer period	❑ Yes ❑ no
6.2.1.5	Very low pressure of compressed air or pressure less than low/high limit for longerperiod	❑ Yes ❑ no
6.2.1.6	Level of recirculation water tank is very low	❑ Yes ❑ no
6.2.1.7	Continuous malfunction of washing process e.g. malfunction of vial clamps	❑ Yes ❑ no
6.2.1.8	Overload	❑ Yes ❑ no
6.2.1.9	In feed empty	❑ Yes ❑ no
6.2.1.10	Maximum out feed condition reached at the inlet of tunnel	❑ Yes ❑ no
6.2.1.11	Sterilizing tunnel belt stops	❑ Yes ❑ no
6.2.1.11.1	Emergency stop activated	❑ Yes ❑ no
6.2.1.12	Following condition need only notification to operator for procedural control	❑ Yes ❑ no
6.2.1.12.1	Malfunctioning of vapour exhaust system	❑ Yes ❑ no

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6.2.2	**Depyrogenating Tunnel**	
6.2.2.1	Equipment shall be capable to detect the following failure, notify the operator withalarm and shutdown the process:	❑ Yes ❑ no
6.2.2.1.1	Emergency stop activated	❑ Yes ❑ no
6.2.2.1.2	In feed empty	❑ Yes ❑ no
6.2.2.1.3	Overload	❑ Yes ❑ no
6.2.2.1.4	Maximum out feed reached in the indeed turntable of filling machine	❑ Yes ❑ no
6.2.2.1.5	Negative differential pressure at depyrogenation zone with respect to washing andsterilization zone	❑ Yes ❑ no
6.2.2.1.6	The temperature uniformity / distribution measured by the equipment temperature probes in hot zone should be within + 5 deg C.	❑ Yes ❑ no
6.2.2.1.7	High temperature at the beginning of the depyrogenation zone	
6.2.2.2	Following condition need only notification to operator for procedural control	❑ Yes ❑ no
6.2.2.2.1	Low temperature at the beginning of the depyrogenation zone	❑ Yes ❑ no
6.2.2.2.2	Low temperature at the end of the depyrogenation zone with conveyor stop.	❑ Yes ❑ no
6.2.2.2.3	High temperature at the end of the depyrogenation zone	❑ Yes ❑ no
6.2.2.2.4	Low temperature at cooling zone	❑ Yes ❑ no
6.2.2.2.5	Low air velocity at cooling zone	❑ Yes ❑ no
6.2.2.2.6	Out of limit differential pressure across HEPA filter	❑ Yes ❑ no
6.2.3	**Filling**	
6.2.3.1	Equipment shall be capable to detect the following failure, notify the operator withalarm and shutdown the process:	❑ Yes ❑ no
6.2.3.2	Emergency stop activated	❑ Yes ❑ no
6.2.3.3	Indeed empty	❑ Yes ❑ no
6.2.3.4	Overload for all pumps, drives and belts	❑ Yes ❑ no

	Specifications	Compliance
6.2.3.5	Maximum out feed condition reached	❑ Yes ❑ no
6.2.3.6	Continuous detection of missing vial on filling station	❑ Yes ❑ no
6.2.3.7	Continuous detection of missing stopper on stoppering station	❑ Yes ❑ no
6.2.3.8	Reaching very low level in buffer container	❑ Yes ❑ no
6.2.3.9	Following condition need only notification to operator for procedural control	❑ Yes ❑ no
6.2.3.9.1	Reject station is full	❑ Yes ❑ no
6.2.3.9.2	Following condition need only notification to operator for procedural control	❑ Yes ❑ no
6.2.3.9.3	Empty vial	❑ Yes ❑ no
6.2.3.9.4	Rejection of vial wit missing stopper	❑ Yes ❑ no
6.2.4	**Crimping Machine**	
6.2.4.1	Equipment shall be capable to detect the following failure, notify the operator withalarm and shutdown the process:	❑ Yes ❑ no
6.2.4.1.1	Emergency stop activated	❑ Yes ❑ no
6.2.4.1.2	In feed vials empty	❑ Yes ❑ no
6.2.4.1.3	Overload for all drives and belts	❑ Yes ❑ no
6.2.4.1.4	Maximum out feed condition reached	❑ Yes ❑ no
6.2.4.1.5	Continuous detection of skewed cap	❑ Yes ❑ no
6.2.4.1.6	Continuous detection of missing cap	❑ Yes ❑ no
6.2.4.1.7	Reaching very low level in seal hopper	❑ Yes ❑ no
6.3	**In –Process control**	
6.3.1	NA	❑ Yes ❑ no

Specifications **Compliance**

6.4 Level of instrumentation

Sufficient and suitable instrumentation for the process, safety and productivity controlas indicated in the following table:

Type of control	Purpose	Range of measurement	Desired Least Count	Extent of Instrumentation				Compliance
				Indication	Alarm	Control	Recording	
Vial Washing Machine								
Temperature	To monitor the temperature of WFI supply	0° - 150°C	1°C	Yes	Yes	No	No	❑ Yes ❑ no
Pressure	Pressure of WFI supply	1 – 5 Kg/cm^2	0.1 Kg/cm^2	Yes	Yes	No	Yes (Optional)	❑ Yes ❑ no
Pressure	Pressure of re-circulated water supply	1 – 5 Kg/cm^2	0.1 Kg/cm^2	Yes	Yes	No	Yes (Optional)	❑ Yes ❑ no
Pressure	Pressure of compressed air supply	1 – 10 Kg/cm^2	0.2 Kg/cm^2	Yes	Yes	No	Yes (Optional)	❑ Yes ❑ no
Pressure	Pressure of PW supply	1 – 5 Kg/cm^2	0.1 Kg/cm^2	Yes	Yes	No	Yes (Optional)	❑ Yes ❑ no
Depyrogenating tunnel								
Temperature	To monitor and control the temperature of drying zone	0° - 250°C	0.1°C	Yes	Yes	Yes	Yes	❑ Yes ❑ no

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Temperature	To monitor and control the temperature of depyrogenation zone (beginning)	0° - 400°C	0.1°C	Yes	Yes	Yes	Yes	❑ Yes ❑ no
Temperature	To monitor and control the temperature of depyrogenation zone (end)	0° - 400°C	0.1°C	Yes	Yes	Yes	Yes	❑ Yes ❑ no
Temperature	To monitor and control the temperature of cooling zone	0° - 100°C	0.1°C	Yes	Yes	Yes	Yes	❑ Yes ❑ no
Differentialpressure	To monitor the differential pressure across HEPA filter	0 – 50 P	1P	Yes	Yes	No	No	❑ Yes ❑ no
Differential pressure with respect to adjoining room (Optional)	To monitor and control the pressure cascade from filling room to washing & sterilization room between each zone	0 – 50 P	1P	Yes	Yes	Yes	Yes	❑ Yes ❑ no

		Specifications						Compliance
Air velocity	To measure air velocity of the tunnel laminar flow	*	*	Yes	Yes	Yes	No	❑ Yes ❑ no
RPM/ Speed(mm/min)	To determine the conveyor speed	*	*	Yes	Yes	Yes	Yes	❑ Yes ❑ no
Filling Machine								
Speed	To determine the filling capacity	*	*	Yes	No	Yes	Yes (optional)	❑ Yes ❑ no
Pressure	To monitor nitrogen gassing pressure	1-10 Kg/cm^2	0.1 Kg/cm^2	Yes	Yes	No	Yes (Optional)	❑ Yes ❑ no
Vacuum	To monitor the vacuum for stopper placement	0 – (-) 1 Kg/cm^2	0.1 Kg/cm^2	Yes	Yes	No	Yes (optional)	❑ Yes ❑ no
Flow rate	To monitor nitrogen gas flow rate	*	*	Yes	Yes	Yes	Yes (Optional)	❑ Yes ❑ no

Y *Required,* **N** *Not required* * Vendor to suggest

6.5	**Cleaning requirement**	
6.5.1	Manual cleaning all equipments of the filling line is proposed. Vendor to suggest and quote for different possible options for the same.	❑ Yes ❑ no
6.5.2	Recommended cleaning agents are mild alkaline solution of sodium hydroxide or ammonium hydroxide, 70% IPA and WFI	❑ Yes ❑ no
6.5.3	Design of equipment should enhance cleaning feasibility by providing minimumsharp corners, minimum crevices & smooth finished welds joints.	❑ Yes ❑ no
6.5.4	Parts, which are required for cleaning, should be provided with quick fixing	❑ Yes ❑ no

	Specifications	Compliance
	arrangement.	
6.5.5	All gaskets provided to avoid leakage should be amenable for easy removed & re-fixing.	❑ Yes ❑ no
6.5.6	All bolts, nuts on the exterior part of equipment will be with cap head or cap nut.	❑ Yes ❑ no
6.6	**Qualification requirement**	
6.6.1	**General**	
6.6.1.1	All equipments shall be qualified with life cycle approach, i.e. DQ, IQ, OQ & PQ. Vendor shall provide all documentation support including protocol subject to approval by the user.	❑ Yes ❑ no
6.6.1.2	Vendor shall provide execution support to the user to complete all stages of the qualification report.	❑ Yes ❑ no
6.6.2	**Vial Washing Machine**	
6.6.2.1	Vial washing machine should consistently remove the soluble and in-soluble contaminant from the glass vials when the washing process is conducted within operating ranges of the process parameter. Washed vials should be essentially free from the visual particulate	❑ Yes ❑ no
6.6.2.2	At the end of washing cycle, vials should be free from any water droplet or wettingwhen checked visually.	❑ Yes ❑ no
6.6.3	**Depyrogenating Tunnel**	
6.6.3.1	Tunnel should be capable to reduce the endotoxin load in the vials by more than 3 log when articles are challenged with at least 1000 EU endotoxin reference standard.The endotoxin challenge should meet the requirement even in vials of leading and trailing edge.	❑ Yes ❑ no
6.6.3.2	After passing through complete depyrogenation process in sterilizing tunnel, vial should be sterile	❑ Yes ❑ no
6.6.3.3	The complete sterilizing tunnel should meet ISO 5 particulate cleanliness class.	❑ Yes ❑ no
6.6.4	**Filling & Stoppering Machine**	
6.6.4.1	Filing & stoppering machine should demonstrate the stated filling accuracy (refer 6.1.3.1) consistently in all stated sizes of vial (refer 3.1.1.1.2) when the equipment is operated at desired range of filling speed.	❑ Yes ❑ no

	Specifications	Compliance
6.6.5	**Crimping Machine**	❑ Yes ❑ no
6.6.5.1	Crimping machine should demonstrate vial crimping without any visual defects of sealing in all stated sizes of vial (refer 3.1.1.1.2) when the equipment is operated at desired range of filling speed.	❑ Yes ❑ no
6.6.5.2	The sealed vials should pass the standard test of seal integrity using Helium or dye penetration/leak and microbial challenge test.	❑ Yes ❑ no
6.7	**Material of construction**	
6.7.1	All following metallic critical contact surfaces should be constructed of 316L grade stainless steel or better with internal mirror surface finish < 0.5µm Ra and external surface finish < 1.2µm Ra, matt finish. a) Surfaces coming in direct contact of product b) Surface coming in contact of vial washing media i.e. WFI, recirculated water andfiltered compressed air c) Surface coming in contact of sterile gas i.e. nitrogen used for gassing of vials	❑ Yes ❑ no
6.7.2	All non product contact metallic surfaces should be constructed of 304 gradestainless steel or better (316 steel for sterile area equipment), external surface finish < 1.2 µm Ra, matte finish.	❑ Yes ❑ no
6.7.3	Gaskets, seals and O-rings coming in direct / indirect contact surfaces should be constructed of USFDA approved polymeric materials only.O-rings internal dia shallbe equal to internal dia of the pipe.	❑ Yes ❑ no
6.7.4	All welds should be ground finished to < 1.2 µm Ra and properly passivated.	❑ Yes ❑ no
6.7.5	Clean media pipes should be orbital welded	❑ Yes ❑ no
6.7.6	Insulation material should be non-fibrous and covered with completely welded SS304 or better cladding.	❑ Yes ❑ no
6.8	**Use of lubricants**	
	Any lubricant, if used in the equipment must be food grade and non-toxic. Used lubricants must not come in contact of the potential product contact surfaces.	❑ Yes ❑ no
6.9	**21 CFR Part 11 compliance**	
	A criticality assessment is to be made to assess the applicability of the system to Part11 regulation. Software, if used to generate, process, store the quality critical data	❑ Yes ❑ no

	Specifications	Compliance
	must be validated and must comply 21 CFR Part 11 requirements	
6.10	**Data integrity**	
6.10.1	System security access shall consist of the following profiles-:	❑ Yes ❑ no
6.10.1.1	Operator: Shall provide operator access to allow routine operation of all equipment features	❑ Yes ❑ no
6.10.1.2	Supervisor: Shall provide access to operator level features in addition to critical operating parameter configuration	❑ Yes ❑ no
6.10.1.3	System administrator: Shall provide the access to the Operator and Supervisor level features in addition to system security parameters.	❑ Yes ❑ no
6.11	**Batch record printing**	
6.11.1	Each process step equipment, i.e. washing machine, depyrogenating tunnel, filling and stoppering machine and crimping machine should generate on line printing of independent batch record, which should contain the following	❑ Yes ❑ no
6.11.1.1	Equipment identification number	❑ Yes ❑ no
6.11.1.2	Set and process values of process parameter	❑ Yes ❑ no
6.11.1.3	Start date and time	❑ Yes ❑ no
6.11.1.4	End date and time	❑ Yes ❑ no
6.11.1.5	All alarms generated (refer 6.2)	❑ Yes ❑ no
6.11.1.6	Identified space to sign for operator & supervisor.	❑ Yes ❑ no
6.11.1.7	There should be a possibility to store and archive the data for future retrieval and analysis. (To be quoted as optional)	❑ Yes ❑ no
6.11.1.8	The tunnel should be provided with a strip chart recorder for continuous graph of temperature of all zone and differential pressures between different zones andadjoining rooms.	❑ Yes ❑ no
6.12	**Desired documents**	
6.12.1	Following documents, but not limited to these, are expected from the vendor as partof the supply package as hard copy and electronic editable version in English language	❑ Yes ❑ no

USER REQUIREMENT SPECIFICATION

NAME OF ITEM: ASEPTIC LIQUID AND POWDER FILLING LINE	**PROTOCOL No.:** .....
FUNCTIONAL AREA: PRODUCTION	**Page No.:** 23 of 31

	Specifications	Compliance
6.12.1.1	Functional design specification containing:	❑ Yes ❑ no
6.12.1.1.1	Equipment descriptions	❑ Yes ❑ no
6.12.1.1.2	Equipment operation steps	❑ Yes ❑ no
6.12.1.1.3	HMI functions with screen shot	❑ Yes ❑ no
6.12.1.1.4	List of failure indications	❑ Yes ❑ no
6.12.1.1.5	List of interlocks and block diagram with their functions and Alarms.	❑ Yes ❑ no
6.12.1.1.6	Critical list of major component, devices and instruments with their specificfunctions, specification data sheet.	❑ Yes ❑ no
6.12.1.1.7	Schematic diagram of the equipment	❑ Yes ❑ no
6.12.1.2	Operation and maintenance manuals, preventive maintenance schedule for equipmentmajor component as well as the operating system	❑ Yes ❑ no
6.12.1.3	Operation and maintenance manuals for the bought out items.	❑ Yes ❑ no
6.12.1.4	Installation instructions/ guideline for equipment	❑ Yes ❑ no
6.12.1.5	Final As-built drawing for equipment	❑ Yes ❑ no
6.12.1.6	Detailed drawing (Plan and minimum one elevation) marking clearly all the necessary dimensions and locations of utilities along with requirement of utilities on the drawing along with the offer.	❑ Yes ❑ no
6.12.1.7	Other drawings (such as PID, electrical, instrumentation etc.)	❑ Yes ❑ no
6.12.1.8	Software ladder logic/ operation and controls flow charts	❑ Yes ❑ no
6.12.1.9	Spare and/ or change parts list with ordering information	❑ Yes ❑ no
6.12.1.10	MOC certificates for all direct/ indirect product contact surfaces.	❑ Yes ❑ no
6.12.1.11	Instrument calibration certificates with respect to the traceable national reference standard instrument and their calibration procedure.	❑ Yes ❑ no
6.12.1.12	Factory acceptance test specifications and reports with actual test results/ data for equipment	❑ Yes ❑ no
6.12.1.13	Recommended SOP's for operation, cleaning and maintenance of each equipment	❑ Yes ❑ no

	Specifications	Compliance
6.12.1.14	Guaranty/ warranty certificates for each equipment and major bought-out items, suchas PLC, printer, recorders, instrumentation etc.	❑ Yes ❑ no
6.12.1.15	21 CFR part 11 compliance report/ certificates for the software(s). (if applicable)	❑ Yes ❑ no
6.12.1.16	Software installation CD/ floppy with 2 back-ups, wherever applicable.	❑ Yes ❑ no
6.12.1.17	Software recovery procedures in case of computer system breakdown, for equipmentcontrol system	❑ Yes ❑ no
6.12.1.18	Shipping checklist.	❑ Yes ❑ no
6.12.1.19	DQ, IQ and OQ protocols	❑ Yes ❑ no
6.12.1.20	Control System input / output verification data & report	❑ Yes ❑ no
6.12.1.21	Types of Lubricant and Lubrication instructions. Food grade certificate.	❑ Yes ❑ no
6.13	**Training**	
6.13.1	A special training for operators has to be included in the offer. A special training for technical staff has to be included in the offer	❑ Yes ❑ no
6.14	**GMP requirement (others)**	
6.14.1	**General**	
6.14.1.1	A clear separation between clean and technical area must be realized in allequipment.	❑ Yes ❑ no
6.14.1.2	Moving parts between the technical and the clean areas are not permitted.Necessary shafts and moving parts have to be tightly sealed.	❑ Yes ❑ no
6.14.1.3	Vendor to give code numbers for each component	❑ Yes ❑ no
6.14.2	**Vial Washing Machine**	
6.14.2.1	The connection of WFI collection pipe of vial washing machine with WFI supplyvalve in the room shall be detachable and sanitary	❑ Yes ❑ no
6.14.2.2	The collection pipe should be provided with a sampling point before the point of delivery at washing machine	❑ Yes ❑ no
6.14.2.3	The supply line should be compatible with hot WFI (> 70 deg C)	❑ Yes ❑ no

	Specifications	Compliance
6.14.2.4	The WFI collection pipe should have sufficient slope (minimum 1%) for complete Drainage of the pipeline.	❑ Yes ❑ no
6.14.2.5	The WFI collection line should not have any dead leg more than 1.5 times the pipe diameter.	❑ Yes ❑ no
6.14.2.6	When vial washing machine stops the machine should have suitable arrangement to prevent the dead leg in the collection pipe line, e.g. automatically close the room supply valve of the distribution pipeline or give alarm for operator intervention.	❑ Yes ❑ no
6.14.2.7	The complete transport of the vials from the last rinsing station of the washing machine up to the indeed part of the LAF tunnel should be either covered or suppliedby unidirectional air flow from a laminar air flow unit.	❑ Yes ❑ no
6.14.2.8	The vial washing machine shall have the arrangement to remove the vapour from thewashing machine / room. A vapour exhaust system should be considered with backflow arrester. Vendor shall inform the detail arrangement of the vapour exhaust system in their technical offer.	❑ Yes ❑ no
6.14.2.9	The washing machine should be designed to prevent the risk of contamination from condensate.	❑ Yes ❑ no
6.14.3	**Depyrogenating tunnel**	
6.14.3.1	In case of power failure at least the ventilators of the LAF tunnel should run by a uninterrupted power supply (UPS) to maintain differential pressure [UPS shall not be in the scope of the vendor]	❑ Yes ❑ no
6.14.3.2	Sterilizing tunnel should be able to adjust the airflow in case of variation in room pressure and maintain the differential pressure within defined range.	❑ Yes ❑ no
6.14.3.3	The floor underneath the tunnel has to be easy cleanable, therefore enough space is necessary	❑ Yes ❑ no
6.14.3.4	All filters must be integrity testable in situ by DEHS testing.	❑ Yes ❑ no
6.14.3.5	The connections of DEHS test in the side cladding of the tunnel have to be Tri-clover connections (inside U-shape of line)	❑ Yes ❑ no
6.14.3.6	All filters in the depyrogenating tunnel must be temperature resistant (in case ofmech. Failure of fans)	❑ Yes ❑ no
6.14.3.7	Automatic bulkhead must be provided for the entire tunnel.	❑ Yes ❑ no
6.14.3.8	In case of any malfunction the vials have to reach a maximum temperature of not	❑ Yes ❑ no

	Specifications	Compliance
	more than 400° C.	
6.14.3.9	The air filtration should be on for all the time if not switched off for long term shutdown.	❑ Yes ❑ no
6.14.3.10	Optionally automatic timer should be provided to run the system at low temperatureat night and during weekends.	❑ Yes ❑ no
6.14.3.11	Provision has to be made for fixing isokinetic nozzle under laminar flow	
6.14.4	**Filling and stoppering machine**	
6.14.4.1	All vials with failures e.g. filling volume, no stopper, etc. have to be rejected at thefilling machine in a reject magazine.	❑ Yes ❑ no
6.14.4.2	All parts of the filling machine exposed A/B area must be resistant to standard disinfectants or vendor should provide the name of specific disinfectants.	❑ Yes ❑ no
6.14.4.3	Every single needle can be selected for IPC check weighing/volume check by the operator.	❑ Yes ❑ no
6.14.4.4	Sampling provision required for in process checks.	
6.14.4.5	Reject verification for rejected vials has to be provided.	❑ Yes ❑ no
6.14.4.6	Vacuum line for stoppering should be provided with appropriate sterilizing gradefilter.	❑ Yes ❑ no
7.0	**Technical requirement**	
7.1	**Basic technical requirement**	
7.1.1	The layout must be taken into account when determining the layouts of the units.Refer Annex 1	❑ Yes ❑ no
7.1.2	A proposal of a possible installation layout should be added to the documentation.	❑ Yes ❑ no
7.1.3	The manufacture has to give the clear details on the dimension, total weight andthe capacity of all equipments of the filling line.	❑ Yes ❑ no
7.1.4	The heat given off by the unit must be stated.	❑ Yes ❑ no
7.1.5	The construction of the complete system should be described in the documentationin detail.	❑ Yes ❑ no

	Specifications	Compliance
7.1.6	Vendor shall provide special tools for assembling, disassembling and maintenance	❑ Yes ❑ no
7.2	**Level of automation**	
7.2.1	The equipment should operate with minimum operator involvement. The equipmentcontrol panel must be provided with a Human machine interface based on English language with appropriate number (a minimum of 10 program) of recipe of all process parameters.	❑ Yes ❑ no
7.2.2	The equipment should control automatically all critical parameter and detect failuremode automatically.	❑ Yes ❑ no
7.2.3	Critical process parameters and failure modes are listed in the preceding sections.	Information only
7.2.4	Human – machine interface must be used to enter the process details, which should appear in the print out. Print out must provide results of all critical process parameterand failure alarms.	❑ Yes ❑ no
7.3	**Specific requirements**	
7.3.1	In general the equipment has to be designed in a way to get easy and quick accessto all necessary maintenance points e. g. pumps, motors, filters, etc.	❑ Yes ❑ no
7.3.2	As a special requirement the machine must allow set up by tip switches with cable	❑ Yes ❑ no
8.0	**Good Engineering Practices Requirements**	
8.1	**General**	
8.1.1	Equipment must be fabricated following all Good Engineering Practices. Thevendor's Quality System must follow applicable national or international standards.	❑ Yes ❑ no
8.1.2	Vendor must generate all applicable documents during all phases of equipment fabrication i.e. design, fabrication, testing and shipment as per applicable standards e.g. GAMP.	❑ Yes ❑ no
8.1.3	All sensors, controllers, PLC, transmitters, indicators and any other controller or indicators to read, print or control any of the parameter, will have to be calibrated, traceable to National or international standards. Original calibration certificate alongwith traceability to be submitted by vendor in their IQ file.	❑ Yes ❑ no
8.1.4	All material of construction should have test certificate	❑ Yes ❑ no

	Specifications	Compliance
8.1.5	Vendor must generate and provide all specifications and test certificates of softwareused in the equipment control and/or monitoring system.	❑ Yes ❑ no
8.2	**Inspection and testing**	
8.2.1	System shall be inspected and tested (FAT) at the supplier's site in the presence ofuser's representative before delivery.	❑ Yes ❑ no
8.2.2	Performance test during FAT: Checking of the 95% reliability of the whole filling line during a running time of minimum 10 minutes after a previous running time of30 minutes (minimum) for every format.	❑ Yes ❑ no
8.2.3	Performance test during SAT: Checking of the 95% reliability of the whole fillingline during a running time of 30 minutes for every format.	❑ Yes ❑ no
9.0	**Constraints**	
9.1	**Equipment location and available space**	
	This equipment will be installed in the Sterile Formulations Facility. The equipment location is indicated in the relevant block of the layout enclosed as **Annex-1**	Information only
9.2	**Available utility**	
	➢ Electricity:_____(Report Requirement) ➢ Water for injection_____(Report Requirement) ➢ Cooling water_____(Report Requirement) ➢ Compressed air / nitrogen pressure_____(Report Requirement)Note: Vacuum system to be supplied by the Vendor	❑ Yes ❑ no
10.0	**Timelines**	
10.1	Response to URS: Within 2 weeks of receipt of URS	❑ Yes ❑ no
10.2	Quotation Submission: Within four weeks of receipt of URS	❑ Yes ❑ no
10.3	Submission of detail functional design specification, Design Qualification (DQ) and schematic drawings: Four weeks after order finalization	❑ Yes ❑ no
10.4	Submission of FAT/SAT Specification-: Four weeks after order finalization	❑ Yes ❑ no

	Specifications	Compliance
10.5	Submission of Installation Qualification (IQ) and Operational Qualification (OQ) protocols -: Two months after order finalization	❑ Yes ❑ no
10.6	Mechanical and electrical drawings-: Two weeks before FAT.	❑ Yes ❑ no
10.7	Submission of control system details and control system verification protocol: 2weeks before FAT	❑ Yes ❑ no

11.0 Abbreviation

Terms	Abbreviation
ANVISA	Agency National Vigilance Sanitaria (Brazil)
CD	Compact Disc
CFR	Code of Federal Regulation
DQ	Design Qualification
EU	Endotoxin Unit
EU-GMP	European –Good Manufacturing Practice
FAT	Factory Acceptance Test
GAMP	Good Automated Manufacturing Practices
GMP	Good Manufacturing Practices
HEPA	High efficiency particulate air
HMI	Human Machine Interface
Hz	Hertz
IPA	Isopropyl Alcohol
IQ	Installation Qualification
ISO	International Standards Organization
MOC	Material Of Construction
OQ	Operational Qualification
Ph	Phase
PID	Proportional Integral Derivative.
PLC	Programmable Logic Controller
PQ	Performance Qualification
RTP	Rapid Transfer Port
SAT	Site Acceptance Test

SOP	Standard Operating Procedures
SS	Stainless steel
TGA	Therapeutic Goods Administration
UPS	Uninterrupted Power Supply
US FDA	United State Food and Drugs Administration
WFI	Water For Injection
WHO	World Health Organization