USER REQUIREMENT SPECIFICATIONS
LYOPHILIZER
EQUIPMENT ID: FG-LYO 01

Revision index

Revision	Date	Reason for revision
00	29.03.2012	First Draft for Client's Review
01	05.04.2012	After comments from Internal Experts
02	13.07.2012	After comments from Client
03	2012-10-16	Format changed as per HLL requirement
04	2103-03-25 & 2013.03.28	As per the technical discussions with the HLL/BCGVL
05	2013.04.08	As per HLL's inputs dated 2013.04.08 by email.

URS Annexure List

URS Annex No.	Detail
1.	Layout showing location of the Lyophilizer Technical area
2.	List of components and make
3.	Mobile LAF loading-unloading Cart
4.	Process Flow Diagram for transfer of lyophilizer loading and unloading cart

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1.0 Approval Signature

This document is prepared by the Validation and GMP compliance team of "NNE Pharmaplan India for the project "Revival of BCG Vaccine Laboratory" (**project number:-110729**) of BCG Vaccine Laboratory, Guindy, Chennai under the authority of their Project Manager. Hence, this document before being effective shall be approved by the QA team and authorized by the appropriate Project Authority.

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2.0 Equipment description

The Lyophilizer shall be used to freeze-dry the BCG vaccine filled in half-stoppered 2R (0.1-1 ml) glass vials. Lyophilizer shall stopper the vial before unloading.

S. No.	Identification no.	Chamber Size
1.	FG-LYO 01	10 m^2

The lyophilizer shall be of single door type for loading and unloading from the same Class A/B room. The Pizza Type door shall opening in the Aseptic Area for loading / unloading of vials. Whereas at the back side of the Chamber – Opening in the Technical Area shall be the Full Body Swing Door for maintenance access. Accordingly, the condenser shall be placed on one side of the chamber.

As per the equipment location layout the lyophilizer shall be horizontally configured i.e. condenser and refrigeration unit shall be installed at the back of the lyophilizer with all accessories.

The vial loading and unloading shall be done with semi-automatic loading-unloading machine using transfer carts/frames. Stoppering conditions should be in inert atmosphere with nitrogen / air at slight vacuum of ~30mbar absolute. (required).

This equipment is a part of an integrated line.

The machine should consist of following parts in order to run operation smoothly

S. No.	Description	Purpose
1	Chamber with the shelves	For keeping the vials for lyophilization
2	Condenser with the cooling coil	For trapping the vapour on the coil from the chamber
3	Refrigeration system	For cooling the product as per the product specification
4	Heating system	For heating the product as per the product specification
5	Vacuum System	For creating the desired vacuum as per the product requirement
6	Hydraulic system	For movement of the shelf for auto stoppering of the lyophilized vials inside the chamber
7	Silicon oil circulating system	For transferring the heat by convection and conduction by circulation of silicon oil
8	CIP system	For cleaning the lyophilizer after use
9	SIP system	For sterilizing the lyophilizer before use
10	Loading and Unloading system	For loading the vials in to the chamber shelf and unloading the vials from the shelf for sealing. For Specs please refer **URS Annex 3**
11	Aeration system with provision for filter integrity test	To validate the filter integrity

Note:

I.	This Technical Specification is the basis for an inquiry to a vendor and therefore the basis for the vendor's proposal.
II.	The vendor is asked to state in "REMARKS" column with "yes" if the described requirement will be completely fulfilled and with "no" in case the requirement will not or cannot be fulfilled with the proposed equipment. I n case of an deviation a comment must be inserted or enclosed as a separate annexure by referring to the respective URS specification number.
III.	The vendor must clearly comment each item of the Technical Specification. The comments must be in English language. If extra cost for necessary options becomes necessary the item must be clearly stated.
IV.	In case that the requirement includes a question or request or information from the vendor, the answer / information should be stated in the "REMARKS" column.
V.	The final version of this document including the vendor's comments will become basis of a potential purchase order or contract.
VI.	The Technical Specification serves to define a summary of all vendor’s requirements concerning scope of delivery and services.
VII.	The vendor is responsible for technically unobjectionable function of the equipment. This TS is not intended to dictate a technical design to the vendor. If agreed upon with the vendor, the vendor can apply his practically proven design.
VIII.	Special Instruction a. If no comments against any specification shall be considered as "NO" and b. If there is no reply / comments against the complete URS by the vendor then it shall be treated as unresponsive / technically non compliant and rejected.
IX.	All the instruments and controls mentioned in the URS(s) are expected to be standard supply and part of your standard equipment model. In case of any deviation or redundancy or additional scope of supply is noticed, vendor is required to obtain clarification from HLL before submitting the quotes.
X.	The makes requested are standard international makes. In case of any deviation, vendor to seek clarification from HLL before submitting the offers.
XI.	Refer document Installation Requirement Specification and Specific Instructions with URS; NPI_110729_IRS_BCG_01
XII.	Refer Tender document with URS; NPI/110729/EQP/TD/09

Specifications	Remarks
3.0 Process Description	
3.1 Input & Charging method	
3.1.1. **Pre filled half stoppered vials**: The half stoppered filled vials will be transferred to cassetting station which will be collected on frames and transferred from the vial filling machine to the loading unit of lyophilizer with the help of a trolley. The loading unit shall be semiautomatic • Input: Liquid solution of product filled in half stoppered glass vials.	
3.1.2. **Filtered compressed Air/Filtered Nitrogen:** Filtered (0.22 micron) compressed air or shall be used for purging for the products not sensitive to the Oxygen during the total lyophilization cycle and during vacuum break in the chamber and condenser. Filtered compressed air is also used for drying the chamber and condenser after the SIP or CIP cycle. Further in case if the product is senstive for oxygen, filtered (0.22 micron) nitrogen shall be used during the total lyophilization cycle and during vacuum break in the chamber and condensor.	
3.1.3. Fixed lyophilization process time is 18 hrs excluding CIP/SIP	
3.2 Brief Process Steps	
The Lyophilizer shall perform the following process step:	
3.2.1 Automatic leak test of the chamber along with shelves	
3.2.2 CIP of the chamber and condenser.	
3.2.3 SIP of the chamber and condenser.	
3.2.4 Lyophilisation process	
3.2.5 Purging of air/nitrogen during the lyophilization process	
3.2.6 Vacuum break	
3.2.7 Partial aeration of the chamber	
3.2.8 Vial stoppering	
3.2.9 Aeration of the chamber to atmospheric pressure	
3.2.10 De-icing	
3.3 Output & Discharging method	
3.3.1 Full-stoppered lyophilised vials: The full-stoppered lyophilised vials with the product shall be unloaded from the shelf of the lyophilizer. Further the vials shall be transferred to the vial sealing machine by means of a transfer cart (LAF trolley).	
4.0 Productivity Requirement	
4.1 Desired/ suggested capacity	
• The lyophilizer shall be capable of lyophilising 40,000 vials of DIN **ISO 8362-1:**	

Specifications	Remarks
1989(E) 2R (Tubular) • Minimum Ice capacity to be 50 kg with all other accessories complying with the above requirement.	
4.2 Standard batch size	
4.2.1 Single load should contain 40,000 vials / batch (approximately). • Format size to be processed: 2R vial , **Ø16mm, Height: 35mm** • For lyophilization fill volume : **0.2ml (for Product 1), 1 ml (for Product 2)** 4.2.2 Vendor shall provided the following requirement on the basis of batch size (40,000 vials / batch), a) Frame size and numbers of vials/frame b) Frame/ FD Load c) Frame per shelf 4.2.3 Frames: The frame size need to be designed based on the quality of the glass, homogeneity, tolerance for robust loading and unloading of vials. The arrangement of the vials in the frame should be row shape, so as to place maximum vials in the frame using optimal space (pce/m^2). ***Note:*** *The quantity of the frames should be equivalent to 1 batches.*	
4.3 Change Over Time (if applicable)	
Not applicable	
4.4 Other Productivity Requirement	
4.4.1 The following sequence to be accomplished within eight hours: • De-icing • CIP • SIP • Drying in place • Leak test • Re-cooling • Filter test	
5.0 Containment	
Not applicable	
6.0 GMP requirements	
6.1 Process Control	
6.1.1 Shelf temperature from ambient should reach - 55°C should be reached in a 60 minutes.	
6.1.2 Refrigerant circuit must work in overpressure also when condenser is at -70°C	

Specifications	Remarks
6.1.3 Shelf temperature from - 55°C up to + 40°C (standard deviation among all shelves +/- 2°C)]	
6.2 Failure mode detection	
6.2.1 Equipment shall be capable to detect the following failure, notify the operator with alarm and shutdown during the process.	
6.2.1.1 Emergency stop activated	
The steam temperature during the SIP hold time below the set limit (only alarm required)	
6.2.1.3 The vacuum pump stop during the process (only alarm required)	
6.2.1.4 The compressor stop when during the process (only alarm required)	
6.2.1.5 The silicone oil circulating pump stop during the process (only alarm required)	
6.2.1.6 The Hydraulic pump stop during the process (only alarm required)	
6.2.1.7 Purging stop during the process (only alarm required)	
6.2.1.8 Electrical Heater (Silicone oil Heating system) failure during the process (only alarm required)	
6.2.1.9 Water ring vacuum pump stop during the process (only alarm required)	
6.2.1.10 Failure in data communication during the process (only alarm required)	
6.2.1.11 The hydraulic movement of the shelf shall be stopped when the generated pressure in the system goes beyond the set limit. (alarm & shutdown required)	
6.2.2 Equipment shall be capable to detect the following failure, notify the operator for procedural control	
6.2.2.1 The compressed air / Nitrogen pressure below the set value.	
6.2.2.2 The purified water and WFI pressure below the set value during the CIP cycle	
6.2.2.3 The condenser cooling failures during the lyophilization cycle	
6.2.2.4 The set vacuum level not achieved	
6.2.2.5 GMP critical test failure i.e.chamber leak test failure, pressure rise test, water load test	
6.3 In –Process control	
Not Applicable	
6.4 Level of instrumentation	
Sufficient and suitable instrumentation for the process, safety and productivity control as indicated in the following table:	

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User Requirement Specifications

Equipment/System	Lyophiliser		
Identification	FG-LYO 01	**Document**	URS/FG-LYO 01
Effective Date	2013-04-08	**Revision**	05

Specifications								Remarks
Type of control	**Purpose**	**Operation range**	**Desired Least Count**	**Extent of Instrumentation**				
				Indication	**Alarm**	**Control**	**Recording**	
Temperature	For controlling/ monitoring the shelf temperature	(- 60)°C to (+ 60°C)	0.1°C	Y	Y	Y	Y	
Temperature	For controlling/ monitoring the condenser temperature	(- 90)°C	0.1°C	Y	Y	Y	Y	
Temperature	For controlling/ monitoring the Chamber drain temperature during SIP	0-150 °C	0.1°C	Y	Y	Y	Y	
Temperature	For controlling/ monitoring the condenser drain temperature during SIP	0-150 °C	0.1°C	Y	Y	Y	Y	
Temperature	For controlling/ monitoring the vent filter temperature during SIP	0-150 °C	0.1°C	Y	Y	Y	Y	
Pressure	For controlling/ monitoring the lyophilizer chamber pressure	1 bar (a) to 2.5 bar (a)	1 mbar	Y	Y	Y	Y	

Specifications								Remarks
Pressure	For monitoring/ controlling the pressure across the sterilizing grade vacuum break filter	1 bar (a) to 8.0 bar (a)	0.01 x 10^6 µbar	Y	Y	Y	Y	
Pressure	For monitoring the main compressed air line pressure for pneumatic control	1 bar (a) to 8.0 bar (a)	0.1 x 10^6 µbar	Y	Y	Y	N	
Pressure	Hydraulic Pressure	1 bar (a) to 160 bar (a)	0.1 x 10^6 µbar	Y	Y	Y	N	
Vacuum	Chamber Vacuum	1 µ bar (a)	--	Y	Y	Y	Y	
Y *Required,* **N** *Not required*								

6.5 Batch Data and Display

Refer Installation Requirement Specification

6.6 GMP requirements (others)

6.6.1	The stoppering system of the lyophilizer should not create any particle or affect the sterility of the system	
6.6.2	The installation of piping and components in the technical area must be as such that all the pipes and components are easily reachable for maintenance.	
6.6.3	Separate control cabinets that are not integrated into the equipment shall be located outside the clean room environment in the technical area, refer attached layout. The necessary length of connecting cables must be considered	

6.7 Specific requirements

6.7.1	**Electric Motors**	
6.7.1.1	Possible leakage currents from the frequency transmitters or upstream filters must not influence the automation networks or analogous measuring signals resp.	
6.7.1.2	All electrical components like motors must be controlled by control cabinets.	

Specifications	Remarks
6.7.1.3 Motors must be protected by safety switches.	
6.7.1.4 In order to avoid high start-up currents of large actuators (as from 7.5 kW) without frequency transmitter, suitable measures (soft starter) must be projected.	
6.7.2 **Chamber:**	
6.7.2.1 The chamber must be pressure rated to withstand conditions up to 130°C and 2.5 bar (a) found during sterilization.	
6.7.2.2 All safety features relevant for pressure vessels must be provided as stipulated in the pressure vessel and safety standards	
6.7.2.3 Special attention must be given to the safety valves being tight also in vacuum.	
6.7.2.4 Chamber bottom, all ports and flanges welded to the chamber and all interface lines and dead legs must be sloped with minimum 2% for proper drainage.	
6.7.2.5 All internal corners must be rounded for easy cleaning (r > 20 mm where possible).	
6.7.2.6 All area on top of the chamber that must be accessed for maintenance or calibration purpose must be reinforced.	
6.7.2.7 A bellow must be provided to cover the hydraulic cylinder shaft of the shelf movement in order to maintain sterility of the unit. A continuous leak control must be provided to assure no leakage of the chamber during SIP. The system design must facilitate CIP and SIP cycles. Sterility must be maintained during the full cycle.	
6.7.2.8 The sampling valve shall be provided at the inlet and in the drain line to chamber for sampling the wash water during CIP cycle.	
6.7.2.9 The chamber shall have at least following ports and connection: • Vacuum measuring probes • Pressure transmitter for overpressure • Air/ inert gas inlet • Connection to condenser • 2 validation ports (integral to the entire machine). • Rods of stoppering system • CIP/ SIP inlets • Overpressure safety valves • Sight glass (1 no.) with illumination to the chamber. • Drain • Refrigerant inlets/ outlets • Cooling jacket inlet /outlet • Cooling jacket safety valve	
6.7.2.10 The chamber must be equipped with a system (e.g. sieve) to prevent glass of broken vials entering the chamber drain or other piped outlets. The sieve must be easily assessable for removal of trapped particles.	
6.7.2.11 The chamber have to be designed for automated CIP/SIP cycles	

Specifications	Remarks
6.7.2.12 Suitable liquid-ring pump shall be in place to evacuate the CIP solution from the chambers after CIP	
6.7.3 **Ice condenser:**	
6.7.3.1 The distance between the ice condenser and the drying chamber should be kept to a minimum. Preferably the condenser is integrated into the main chamber of the freeze dryer.	
6.7.3.2 Depending on the configuration of chamber and condenser the vendor is asked to describe the design of the isolation valve between chamber and condenser.	
6.7.3.3 Direct visual contact between condenser and product should be avoided (radiation influences) for example by the use of a large poppet valve plate.	
6.7.3.4 The condenser must be pressure rated to withstand conditions up to 130°C and 2,7bar (a) found during sterilization.	
6.7.3.5 The condenser have to be designed for automated CIP/SIP cycles	
6.7.3.6 All safety features relevant for pressure vessels must be provided as stipulated in the pressure vessel and safety standards	
6.7.3.7 Special attention must be given to the safety valves being tight also in vacuum.	
6.7.3.8 Condenser bottom, all ports and flanges welded to the chamber and all interface lines and dead legs must be sloped with minimum 2% for proper drainage.	
6.7.3.9 All internal corners must be rounded for easy cleaning (r > 20 mm where possible).	
6.7.3.10 Design should be based on maximum ice thickness on condenser tubes.	
6.7.3.11 The condenser chamber, refrigerant cooling coil and jacket must be provided with safety devices stipulated in the pressure vessel and safety standards.	
6.7.3.12 The insulation should be complete to avoid icing in the technical area. Catchment tray to be provided to collect the condensed ice and further this catchment should lead to the main drain point in the room.	
6.7.3.13 The ice condenser shall have at least following ports and connection: • Pressure transmitter for overpressure • Air/ inert gas inlet • Vacuum systems • Main vacuum valve to the chamber • Spare flange • Validation flange • CIP/ SIP inlets • Overpressure safety valves • Drain • Refrigerant inlets/ outlets	
6.7.3.14 The ice condenser must be equipped with an automatic aeration independent from the chamber	

Specifications	Remarks
6.7.3.15 A bellow must be provided to cover the hydraulic cylinder shaft of the valve in order to maintain sterility of the unit. A continuous leak control must be provided to assure no leakage of the chamber during SIP. The system design must facilitate CIP and SIP cycles. Sterility must be maintained during the full cycle.	
6.7.3.16 Cycle life of bellow must be not less than 10^5 cycles.	
6.7.3.17 The condenser must be equipped with a system (e.g. sieve) to prevent glass of broken vials entering the chamber drain or other piped outlets. The sieve must be easily accessible for removal of trapped particles.	
6.7.3.18 The vendor shall provide the detail nozzle schedule of the chamber and condenser in the documentation.	
6.7.3.19 It has to be assured that fallen vials cannot reach the condensers under all conditions. The used precaution should be described	
6.7.4 **Chamber Door:**	
6.7.4.1 The door shall open only after the chamber temperature is well below the 60 ^{0}C	
6.7.4.2 Manual hinged full size door for maintenance access to chamber, shelves and condenser. Opening at least 100° angle. The closing bolts shall be operated automatically.	
6.7.4.3 The chamber door must be foreseen with a door contact to detect the position of door.	
6.7.4.4 Door locking switch: Only individually coded safety switches must be used.	
6.7.4.5 Door contacts must have an interlock with the venting valve to make sure no N_2 can enter the chamber with the door open.	
6.7.4.6 Door gaskets must be able to withstand CIP/ SIP. The sealing of the door must be designed in a way that no condensate or CIP water remains between the door and the chamber.	
6.7.4.7 The door operation (opening and closing) should be manual and sealing will be automatic with door locking indication in the PLC.	
6.7.4.8 The door must be auto locked if the pressure in the chamber goes above atmospheric pressure.	
6.7.4.9 The door sealing must operate without any additional lubricant.	
6.7.4.10 The replacement of any door sealing must be possible without disassembling of any other parts or components.	
6.7.4.11 Full swing door shall be provided in service area.	
6.7.4.12 The panelling of the equipment should reach the suspended ceiling. The cladding panel should be constructed to allow easy removal for inspection and maintenance.	
6.7.5 **Loading/Unloading**	
6.7.5.1 Mobile LAF cart will be used for loading and unloading of vials from the lyophilizer loading & unloading of vials will be semi-automatic mode.	

Specifications	Remarks
6.7.5.2 Loading and unloading height will be between ~900 ± 30 mm	
6.7.5.3 Vials have to be pulled or pushed manually frame by frame from/to the shelf for unloading/loading	
6.7.5.4 Mechanical changes or adjustments for format change must be avoided.	
6.7.5.5 For transportation of vials from filling line cassetting station to lyophilizer loading and from lyophilizer unloading side to loading side of sealing machine will be done by LAF trolley having battery/ inverter provision (This trolley shall be under the scope of lyophilizer vendor) - 1 number of the trolley to be provided.	
6.7.6 **Shelves**	
6.7.6.1 Shelf distance has to be optimized for 2R vials (half stoppered). The vendor to mention the clearance.	
6.7.6.2 Roughness of top side of all shelves should have an Ra value < 0.8 µm	
6.7.6.3 Bottom side of all shelves should be designed suitably to prevent sticking of stoppers	
6.7.6.4 The planarity of the shelves must not to exceed 1.0 mm over the whole shelf.	
6.7.6.5 A radiation shelf must be foreseen between load frame first shelf to ensure that drying conditions on all shelves are the same.	
6.7.6.6 One product probe per shelf for product temperature to be provided	
6.7.6.7 Special arrangements to be provided to secure the temperature probe during stoppering/moving the shelves.	
6.7.6.8 Shelf guiding and positioning in all directions must be reproducibly accurate to ensure docking of the LUS accurate loading and un-loading process So as to avoid flipping vials or damaged vials	
6.7.6.9 Fixed guide stoppers shall be provided within the shelves to prevent high friction force during loading and unloading (semi-automatic mode) of the vials.	
6.7.6.10 The flexible tubes must be free of tension during upwards and downwards movement	
6.7.6.11 The connections of the cooling / heating media flexible pipes to the shelves must be welded (preferred solution) or with leak-proof coupling.	
6.7.6.12 All quality tests to ensure robust design should be carried out post fabrication and documented	
6.7.6.13 It has to be sure, that no vials will fall from the sides of the shelves. Therefore the shelves shall be executed with a border system on the sides to ensure coherent lyo conditions even on the shelf edges.	
6.7.6.14 The collapsing (and levelling after CIP/SIP) of shelves should be performed automatically. The construction should be described in the documentation.	
6.7.6.15 The connection of heating/cooling media to the shelves should be leak proof.	

Specifications	Remarks
6.7.6.16 In addition the position of each shelf must be mechanically adjustable (to ensure minimum tolerances concerning constant loading level for each shelf).	
6.7.7 **Hydraulic System for Shelves**	
6.7.7.1 The positioning must be accurate enough to harmonize with the transfer cart / frames	
6.7.7.2 Hydraulic drive for the shelves to allow loading at constant level and closing of vials	
6.7.7.3 The shelf lifting mechanism should not pull any contaminants into the chamber	
6.7.7.4 The bellow shall be removable from the chamber without removing the complete piston.	
6.7.7.5 The effective stoppering function required	
6.7.7.6 Shelves and the hydraulic cylinder must be designed in a way to prevent the need for spacers even if only one shelf is loaded.	
6.7.7.7 Shelves must be kept compressed after stoppering of the product until the pressure in the chamber has reached a value (adjustable).	
6.7.7.8 All the shelves shall be pressure tested at 20% higher than the design pressure.	
6.7.7.9 A leak tight bellow must be provided to cover the hydraulic cylinder shaft in order to maintain the sterility of the unit.	
6.7.7.10 The hydraulic pump should be provided with high pressure interlocking	
6.7.7.11 Hydraulic system shall be operated by both the side (sterile, Unsterile) .	
6.7.8 **Heating and Cooling for Shelves**	
6.7.8.1 The heating and cooling system must operate automatically.	
6.7.8.2 The preferred heat transfer medium in the secondary loop is silicon oil.	
6.7.8.3 A backup pump system must be provided, which is automatically activated when the primary system fails.	
6.7.8.4 An expansion vessel (with filter cartridge) with pressure indication should be provided.	
6.7.8.5 Each shelf must be separately fed with cooling / heating medium.	
6.7.8.6 Pt 100 (min. 3 wired) temperature probes placed in stainless steel tubes both at the inlet and the outlet of the shelf manifold should be provided. (1 Pt 100 used for cycle control, 1 for measurement).	Auditor objection
6.7.8.7 Distribution of heating and cooling media should be uniform throughout the shelves (without any dead spaces) so that proper and uniform freeze drying of the product can be achieved.	
6.7.9 **Primary Cooling System**	
6.7.9.1 The cooling system shall consist of two independent refrigeration circuits. - The first circuit works with a heat exchanger in the silicon oil circulation system for shelf	

Specifications	Remarks
cooling. The second circuit works by direct expansion on the tubes of the ice condenser.	
6.7.9.2 The cooling circuit must be built in that way that all compressors can be used for the cooling of the shelves (initial freezing) and that during drying one compressor can be used for the shelves and the others for the cooling of the condenser.	
6.7.9.3 Compressors shall be two stages.	
6.7.9.4 Redundancy for compressor, vacuum pump, to be in place so that if one of the above equipment fails, cycle must complete safely and automatic switching off should be considered.	Cant do without this
6.7.9.5 The following safety devices have to be provided: • A pressure valve to avoid overload during starting: start pressure regulation • Hand valves in the upstream and downstream of the compressors. • Thermal circuit breaker • Thermistors in the motor coils with control unit. • High pressure lubrication system with a gear pump. • Auxiliary cooling system by expansion of refrigerant through the motor including: temperature switch with bulb on the discharge line, solenoid valve, expansion system, bypass line and electrical control. • Differential oil pressure switch • High pressure switch. • Pump down must be done during stand by of the compressor When the pressure is low enough the compressor must stop running • Crankcase heater to avoid any refrigerant condensation when the compressor is switched off. • Check-valve on the discharge line. • Double safety valves for each compressor unit.	
6.7.9.6 Only HFCs according to Montreal protocol are permitted as refrigerants. Vendor to specify the type of refrigerants used.	
6.7.9.7 Temperature measurements at the inlet and outlet of the cooling water. Measurements must be visible on SCADA.	
6.7.9.8 Pressure switch at low, intermediate and high pressure side of the compressors.	
6.7.9.9 Intermediate pressure side must always be > 1 bar (a).	
6.7.9.10 Pressure transducers in refrigerant circuit at outlet of the ice condenser and silicon oil heat exchanger of the cooling system. Measurements must be visible on SCADA.	
6.7.9.11 Oil separator (after compressor) and liquid separator (before compressor) must be provided.	
6.7.9.12 Possibility to open oil separator for cleaning.	
6.7.9.13 A separate connection for filling the compressors with cooling liquid must be provided.	
6.7.9.14 Drainable trays to collect the condensate below the compressors have to be provided.	

Specifications	Remarks
6.7.9.15 All components reachable to perform maintenance	
6.7.9.16 During a WIT, the condenser needs to be cooled to gain time during the leak test if this follows the WIT.	
6.7.9.17 If leak test fails, option to be provided in the lyophiliser to abort the cycle or restart.	
6.7.10 **Vacuum System**	
6.7.10.1 Vibration dampers need to be foreseen to minimize effect of vibration of pumps to the surrounding operations.	
6.7.10.2 The rotary vane vacuum pumps should operate with gas ballast in order to avoid water vapour condensation and to force oil diffusion to the exhaust.	
6.7.10.3 Oil sealed primary pumps are used. A system should be provided to avoid oil diffusion into the condenser.	
6.7.10.4 As an alternative the vendor shall propose a suitable oil free system (dry pumps) .	
6.7.10.5 A safety valve between the condenser and the vacuum system must be provided. In case of power failure this valve has to close immediately and automatically.	
6.7.10.6 A vacuum system capable of generating a vacuum of up to: • 0.01 mbar(a) in the chamber • 0.003 mbar(a) at pump head	
6.7.10.7 The evacuation time of the system from atmospheric pressure to: • 0.1 mbar(a) should take less than 40 min	
6.7.10.8 The control system incorporates the following • 1 pressure transmitters (MKS) installed on the drying chamber.	
6.7.10.9 High pressure alarms Pmax-x (stop of heating) and Pmax (refreezing of shelves) have to be split up in primary and secondary drying.	
6.7.11 Provision for intergrity testing shall be provided.	
6.7.11.1 Chamber vacuum should be maintained after the completion of cycle (with Alarm). Vacuum should be released only on human intervention.	
6.7.11.2 Choice of aeration with either N2 or process air: selectable by software and recipe driven	
6.7.12 **Ergonomic requirements**	
6.7.12.1 Equipment which must be calibrated will be installed that it is easy accessible from the ground floor and without difficult dismantling	
6.7.12.2 To improve the accessibility pedestals and stairs (steep ladders are not acceptable) have to be designed and provided	
6.7.12.3 Good accessibility of all buttons, switches and components for operator handling is required	
6.7.12.4 All buttons, switches, and components which must be used by the operator are clearly indicated to make human errors impossible	

Specifications	Remarks
6.7.12.5 The specified equipment must be designed and executed without sharp hooks and borders to avoid injuries	
6.7.13 **Performance requirement**	
6.7.13.1 Chamber: Maximum leak rate of < 0,01 mbar * l *s-1 in the range of 0.01mbar till 0.1 mbar at condenser temperature of - 40 Deg C	
6.7.13.2 Condenser: Maximum leak rate of < 0.01 mbar l/s starting with initial vacuum at < 0.01 mbar.	
6.7.13.3 A leakage rate between drying chamber and the ice condenser of less then 1*10-7mbar*l*s-1 should be guaranteed. The valve between the product chamber and the condenser chamber must have stable positioning and be absolutely tight in both directions against atmospheric pressure. A pressure rise test with an open and with a closed valve (atmospheric pressure in the condenser chamber) must be performed.	
6.7.13.4 Water Load Test: - A purified water load test will be performed. This test will evaluate the systems sublimation rate capacity and ice loading pattern on the condenser. - Purified water will be put upon the full loaded surface area of each shelf utilizing thin aluminium trays. Each tray will be equally filled such that the total load will equal to the specified ice capacity.	
6.7.13.5 Minimum ramping velocity with full chamber at least 1°C /min	
6.7.13.6 Temperature difference between manifold inlet and outlet should be ± 1°C in a steady state with load.	
6.7.14 **General Design Requirements**	
6.7.14.1 During the loading, process and unloading any damage of vials and friction between vials is not allowed	
6.7.14.2 The max. Length of the flanges and ports must be designed so that these flanges and ports are cleanable and sterilizable. Dead ends <1.5d where possible.	
6.7.14.3 All blind flanges must be able to withstand the full vacuum as well as the sterilization pressure.	
6.7.14.4 Moving parts which are going outside of the sterile area should be foreseen with a leak-tight bellow (with possibility to verify.) Air from bellow is blown in technical area.	
6.7.14.5 Critical process valves (min. requirement: process water valves, media lines, bottom valves, pressure release valves, etc.) must be equipped with end position switches.	
6.7.14.6 Activation of the emergency stop button or opening of the protective door (if available) leads to immediate stop of all outputs via the safety circuit.	
6.7.14.7 Activation of the emergency stop button or opening of the protective door (if available) leads to immediate stop of the valve clusters.	
6.7.14.8 Installation of equipment with refrigerants has to be done by a certified cooling technician. Before starting the works, a copy of the certificate has to be delivered.	
6.7.14.9 The specified equipment must be completely free of asbestos	
6.7.14.10 An over-temperature switch has to be installed in the control circuit of the heating	

Specifications	Remarks
relay	
6.7.14.11 All lines and equipment surfaces which represent a danger to operators and maintenance personnel with regard to freezing or burns shall be adequately insulated.	
6.7.14.12 A central vacuum valve between the condenser and the vacuum system must be provided. In case of power failure this valve has to close immediately and automatically.	
6.7.14.13 In case of power failure the valve between the drying chamber and ice condenser should remain in previous position before power failure.	
6.7.14.14 During the SIP cycle after power failure recovery, another new SIP cycle shall restart from the beginning (if temperature drops below the set value).	
6.7.14.15 During the CIP Cycle, De-Icing Cycle, and lyophilization cycle after power failure recovery the remaining sequence of the cycle shall restart from the stop point.	
6.7.14.16 Provision to provided to connect the control system to Centralised UPS system. The UPS power will be used for sensors, PLC controls, LAF and differential pressure cascade. After power failure the system should start automatically with last recipe loaded. Primary cooling, vacuum pumps, condensers, silicone oil circulation pump etc should run on generators. All the major components and processes must start automatically within 3 minutes. When on emergency power, all components should restart automatically except the heating elements. In this case it must be possible to switch on heating manually.	
6.7.14.17 All hygienic lines, WFI, CIP water and pure steam must be orbital welded. All welded lines in contact with WFI, CIP water or clean steam must be inspected by endoscope (10% of welds). Inspection certificate with photographs with P&ID tags to be provided.	
6.7.15 **Cleaning and Sterilisation requirement**	
6.7.15.1 Automatic CIP and SIP	
6.7.15.2 The Clean in Place system shall include manifolds, nozzles/ spray ball and sanitary valves to allow the CIP media to be sprayed onto product chamber, condenser and shelf surfaces	
6.7.15.3 No. of spray ball, position, location and height of the spray ball shall be provided by the vendor	
6.7.15.4 CIP consists typically following repeatable steps: • first rinse with Purified water (re-circulated-3 cycles) • last rinse with WFI (once through passage) The respective media, quantities and durations shall be defined as parameters in the recipe.	
6.7.15.5 Recirculation pump shall be included for CIP. Pump shall be self drainable during and after the sterilization.	
6.7.15.6 SIP consists typically following steps:	

Specifications	Remarks
• Vacuum to evacuate all the air • Heat up • Sterilization • Cooling and drying The respective pressures, temperature and durations shall be defined as parameters in the recipe. 6 log reduction shall be achieved during SIP on all surfaces within the chamber, condenser, and CIP system.	
6.7.15.7 The integrated CIP system shall be designed to minimize water consumption.	
6.7.15.8 Only 1 connection point is foreseen for each media. A signal needs to be given from the lyophiliser PLC to specify which media is requested	
6.7.15.9 The CIP cycles will be recipe driven and fully automated with temperature, flow rate and volume control.	
6.7.15.10 The CIP system must ensure 100% of the critical surfaces, such as shelves, are cleaned. Suitable and sufficient spray nozzles and balls for complete impact cleaning must be provided.	
6.7.15.11 The drying chamber, the shelves, the ice condenser and all connecting lines and all the ports on the chamber have to be cleaned in place.	
6.7.15.12 All valves in CIP lines and lines to be CIP'ed must be aseptic valves.	
6.7.15.13 Vendor to specify spray pressure, spray time, selection sequence of the spraying nozzle along with their spray time	
6.7.15.14 The temperature difference across and between shelves during the sterilization hold period must be less than 1 deg C.	
6.7.15.15 The sterilization cycle must be controlled by the temperature at the coldest spot and the pressure in the chamber.	
6.7.15.16 The pure steam piping for the SIP cycle must be equipped with automatic actuated control valves and steam traps.	
6.7.15.17 The supplier of the lyophilizer shall ensure to cool down the condensate < 60ºC.	
6.7.15.18 Adequate space will be provided for manual cleaning and inspection of shelves and chamber area from the access door on the mechanical side of operations.	
6.7.15.19 The configuration of any flanges and ports must ensure that all internal surfaces are covered by the CIP system and will reach and maintain sterilization conditions during the sterilization cycle.	
6.7.15.20 The SIP cycle sterilization hold time shall reset as the drain probe temperature comes below 121 ^{0}C and recounting of the time shall start after achieving the set sterilization temperature.	
6.7.15.21 The exhaust valve shall be closed during the SIP cycle.	
6.7.15.22 The pressure gauge needs to be installed immediately after the CIP pump and another pressure gauge at the inlet of the WFI for the chamber.	
6.7.15.23 Vendor to provide details of different cleaning media that is compatible for cleaning of the equipment	

Specifications	Remarks
6.7.16 **Maintenance requirement**	
6.7.16.1 Lubricating points: All lubricating points must be registered, shown and clearly labeled in an overall plan. Inaccessible lubricating points must be made accessible by installing corresponding lines without opening the protective door. It must be guaranteed by suitable measures that oils or lubricants do not reach the product. The lubricant type applied must be registered. Oils and lubricants applied must be approved by USFDA.	
6.7.16.2 Testing means lists The suppliers must provide the testing means lists electronically as tables. Testing means include all process and quality relevant measuring points, e. g. temperature, pressure, LF, flow etc. Testing means must be classified in terms of Biotechnology or technical relevance. For measuring points the following must be indicated: measuring range, calibration range, working range, set-point, accuracy class, recommended calibration frequency.	
6.7.16.3 Access to testing means: The testing means must be easily accessible and assembled under due consideration of an easy and quick recalibration. Necessary auxiliary energies (220 V, compressed air) must be available in the proximity of the measuring points.	
6.7.17 **Interface to other systems**	
6.7.17.1 Interface: The required interconnection to other systems takes place by means of potential free contacts. Besides those mentioned in this URS, 5 additional potential free contacts must be provided for further occupation (e. g. control of a vapor extractor.	
6.7.17.2 Collective Alarm: In order to centrally visualize the general system condition, a collective alarm signal shall be provided on a potential free contact.	
6.7.17.3 Interfaces to on site utility supply systems: The onsite utilities are specified in attached utility spec.	
6.7.17.4 If the specified equipment is connected or integrated into on site partition walls or ceiling panels dimensions and locations for necessary cutouts must be stated in the equipment layout drawings.	
6.7.17.5 Parts of the specified equipment must not be attached to clean room ceiling panels	
6.7.17.6 Interface with building and building services such as process utilities	
6.7.18 **Level of Automation**	
6.7.18.1 The freeze drying process operates without operator's assistance. Operator selects or downloads recipes and starts the freeze dry cycle. All operations shall be controlled by PLC-controller and the SCADA-system with a variety of different recipes for different products. Industrial Computer system and Printer shall be provided.	
6.7.18.2 Data loss is not admissible.	
6.7.18.3 Fail safe position: In case of auxiliary energy failure (electric or pneumatic) the armatures and actors must run into defined fail safe position so that no hazard is caused to persons and products.	

Specifications	Remarks
6.7.18.4 Energy efficiency class: All electric motors must at least comply with the current requirements of the EC energy efficiency class (EFF2).	
6.7.18.5 Actors: In case of error or failure of the field bus communication the actors must be switched to fail safe position.	
6.7.18.6 Actors: Identification labels must be fixed undetectably (e. g. on the base plate of a valve but not on interchangeable valve) and must be resistant against materials used in the system and its environment.	
6.7.18.7 Actors must be protected in useful groups to enable easy and quick localization of possible error/failure (short circuit).	
6.7.18.8 **Wiring and installation**	
a) Final wiring between the single components, machines and devices must be installed. It must be stable and equipped with step protection. Signal and data lines must be separated from power lines.	
b) In the technical area wires shall be run in grating channels.	
c) Metric packed screwing with segments shall be used as cable ducts.	
d) Corresponding to the ambient conditions as well as mechanical and chemical load caused by the system and its materials, suitable cable types must be installed. The cable types installed must be described in the machine documentation.	
6.7.18.9 **Switching and control systems**	
a) The switching and control cabinets shall not prejudice access to the PU so that maintenance and repair works can be carried out without problems.	
b) Multiple terminals are not admissible, except double terminals.	
c) Modem (with activation switch) to be installed for online problem redressals. Supplier to install an Ethernet socket in the control cabinet to connect remote maintenance system. Remote maintenance is established by means of laptops which are connected to the Ethernet socket by the maintenance technician	
6.7.18.10 **Supply**	
a) Adjustments must be corresponding to the requirements for selective switch- off	
b) Feed-in to be supervised on low voltage and phase failure. Supervision to be registered in the pertaining automation system.	
c) Feed-in must be assigned on input terminals in the control cabinet and conducted over a switch.	
d) Control voltage supply must be provided: • Industrial PC • PLC • Decentralized I/O system • As well as all other control and instrumenting components (actors/sensors) • All network components concur	
e) Additional auxiliary voltage required (e. g. 24 V) must be generated in the system itself and distributed selectively.	
f) Signals and control commands from the control system must be switched to decentralized I/O modules or I/O modules of the automation system respectively	
g) Power control units, power outputs, electronic devices and circuits of the control system must be arranged and designated according to EMC (EMC guideline 204(108/EU for	

Specifications	Remarks
electromagnetic compatibility).	
6.7.18.11 **Field Bus**	
a) Profibus DP to be installed as field bus system for connection of periphery.	
b) Connection of Profibus DP components generally to be equipped with screened connecting plugs, termination resistors which can be switched off and additional programming socket.	
c) Supplier to issue measuring protocols for all data lines (Profibus, network, LWL etc.) showing function and capacity.	
6.7.18.12 **Automation system (AS) control**	
a) For safety relevant functions, the correspondingly fail safe hardware (e. g. Safety Integrated, F controls) must be applied. Field bus system users installed at site shall be connected to the AS.	
b) I/O cards can be used for the AS. This must be specified.	
c) Continuation must not be possible without acknowledgement and new start by the operator.	
d) Connection to all systems involved to be established automatically, i. e. in case of failure of one component, connection must be established automatically after repair.	
6.7.18.13 **PC as Operating System**	
a) Industrial PC to be provided for freeze dryer data management with a monitors of at least 19 inch size.	
b) An Ethernet network card and cable for connection to network must be provided.	
c) For data recovery (e. g. after hard disc failure), corresponding programs, back-ups and descriptions must be supplied. By means of these systems it must be possible to restore 5 GB data per hour. Data manipulation must be excluded.	
d) Easy machine operation by clear structures of the operating panel to enable the operator to view all relevant information.	
e) The main operating panel must be installed on the loading/unloading side.	
f) Layout of Templates: Industry standard templates to be provided to represent the utilities, process parameters etc	
g) Provision for manual operation of all the sequences connected to the PLC to be made for controlling lyo cycle manually.	
6.7.18.14 **Software Development**	
a) Development of the software applied according to current version of the GAMP standard. Critical parameters, modification of user level and limit values are protected by password or equivalent authorizations	
b) Supplier of the automation system to deliver all application software to realize required functions, displays, protocols etc. as source code.	
c) Storage Capacity: A storage capacity must be specified at which data are deleted in order to avoid an overflow.	
d) Cycle Time: The cycle times can be freely selected and can be allocated to the single measuring points according to the process and system requirements.	
e) CPU capacity utilization:	

Specifications	Remarks
Capacity utilization of the PLC storage must not exceed 50% of the available capacity.	
6.7.18.15 **Display and operating components**	
a) OS's to be connected to the automation system via available interfaces.	
b) OS to be installed in the system to the PC through SCADA.	
c) An audit trail must be integrated in the OS. The audit trail must include at least: • user ID • date (day, time) • parameters • old value • new value • It must be possible to read out the audit trail from the OS and store	
6.7.18.16 **Measurement and Sensors**	
a) Measurement and sensorics of the system to be connected to the pertaining decentralized I/O and control systems resp. with clear identification label.	
b) For internal device errors the measuring device must be adjusted to generate a defined malfunction being detected by the control system. eg., at a temperature range of 80 - 120 °C, 40 °C may be a malfunction.	
c) GMP relevant measurement must be suitably calibrated, mainly by means of 3 point calibration over the complete measuring chain. The corresponding calibration points shall be within the required measuring range.	
d) Measuring devices must be easily detachable from the process, if required, shut-off units or relief facilities (e. g. for pressure) resp. must be provided.	
e) For all devices installed in the measuring chains, adjustment facilities must be specified or adjustment must be described, and complete operating instructions must be supplied.	
f) Measurement and sensors must be particularly easily accessible and interchangeable.	
6.7.18.17 Vendor should ensure vendor shall include all necessary parts / components for the smooth operation of the machine as per technical specs:	

7.0 Constraints

7.1 Equipment location and available space

This equipment will be installed in the Fill-Formulation Area of Revival of BCG Vaccine Facility at BCGVL, Guindy, Chennai.

Equipment Location:

Floor: Ground floor-Formulation

Plant: Revival of BCG Vaccine Manufacturing Facility

Room dimension : 101.04 sq.m

The equipment location is indicated in the relevant block of the layout enclosed as **URS Annex-1.**

Physical condition of the rooms:

Filling and stoppering + lyo loading:

Specifications	Remarks
1. Room will be non-hazardous 2. Class: EU Class “B” 3. Differential Pressure: 55Pa Absolute 4. Temperature maintained: 22°C ±2°C 5. Relative Humidity: <55% RH	

7.2 Utility Requirement

a) Electricity: Single (220 V) & 3 phase (420 - 440 V) (Report Requirement) b) Compressed air 6-8 bar (Report Requirement) c) WFI @ 3-5 bar at 80 deg C (Report Requirement) d) Purified water @ 3-5 bar (Report Requirement) e) Chilled Water @2.0 bar at 12 deg C (Report Requirement) f) Pure steam @ 3 bar (Report Requirement)	

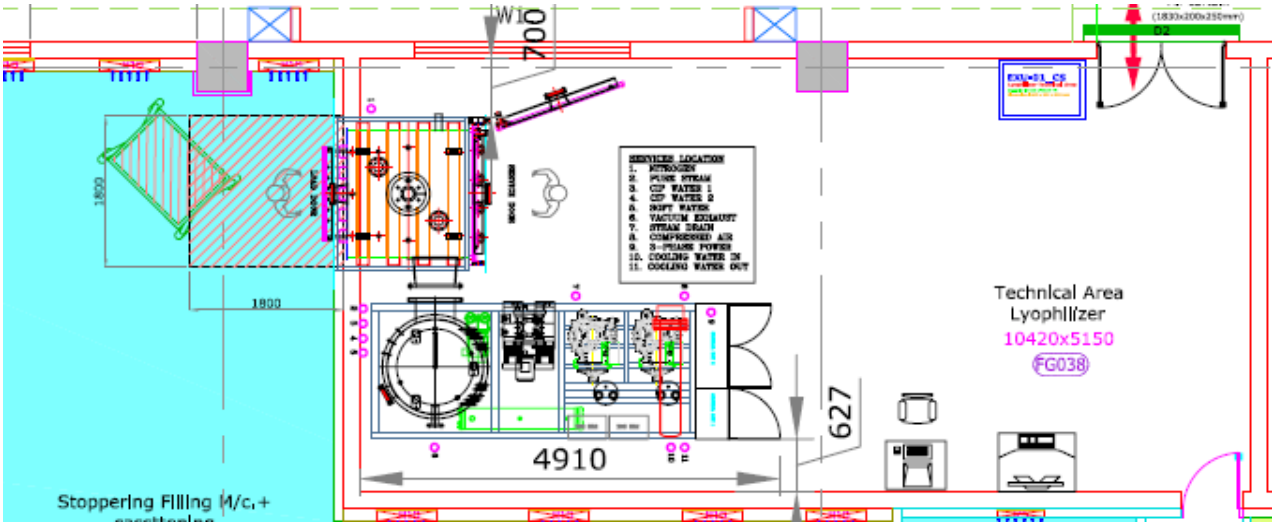
8.0 Abbreviation

Abbreviation	Definition
FAT	Factory Acceptance Test
GAMP	Good Automated Manufacturing Practice
GMP	Good Manufacturing Practice
ISO	International Standards Organization
NPI	NNE Pharmaplan India
PLC	Programmable Logic Controller
QA	Quality Assurance
LUS	Loading-Unloading System

URS ANNEXURE 1: LAYOUT SHOWING THE LAYOUT AREA

Room No: FG034 - Loading Side

Room No: FG038 - Technical area of the Lyophilizer



URS Annexure - 2
List of components and make for Lyophilizer

S.No	Description	Preferred List
1.	Refrigeration Compressor Two Stage	Carlyle/ Bitzer/ Copeland
2.	Oil Separator	Henry/ Temprite/ Danfoss
3.	Suction Accumulator	AC and R / Henry/GVN
4.	Refrigeration Valves	Danfoss / Sporlan / Henry
5.	Expansion Valves	Danfoss / Sporlan / Henry
6.	Plate Heat Exchanger	Alfalaval / Danfoss /WTT
7.	Refrigeration Ball valves	Danfoss / Sporlan / Henry
8.	Vacuum Pump	Pfeiffer Vacuum / Edwards / Leybold
9.	Vacuum Valves	Elomatic / Danfoss / Pentair
10.	Vacuum Sensors	MKS
11.	Isolation Valves	Elomatic / Danfoss / Tyco/Swagelok / Pentair
12.	Fluid Pump	Grundfos / 3M Pumps
13.	Steam PRV Sanitary	Spirax / Steriflow
14.	Steam Valves only Diaphragm	Burkert / Gemu / ITT
15.	Safety Valves Sanitary	Spirax / Steriflow
16.	Steam Traps Sanitary	Spirax / Steriflow
17.	Check valves Sanitary	Spirax / Steriflow
18.	Pneumatic Controls	Burkert / Festo / Janatics
19.	Water Ring Pump	Atalntic Fludics / Nash Elmo
20.	Fluid Fittings	Swagelok / Parker / Gemu
21.	Hydraulic Pump	Bosch / Parker / Rexroth
22.	Industrial PC	DELL / SONY /LENOVO
23.	PLC and Controls	Allen Bradley / Siemens / Mitsubushi
24.	Pressure Sensors	Wika / Endress Hauser / Honeywell
25.	Temperature Sensors	Omega / Wika / Endress Hauser
26.	Servo Motors	SEW Germany / Allen Bradley /Siemens
27.	Electrical Controls	Schneider Electric / Allen Bradley / Siemens

nne pharmaplan	URS Annexure 3			
	Equipment/System	Mobile Cart Loading and Unloading System		
	Identification #	FG-LUS 01	**Document#**	DS/FG-LUS 01
	Effective Date	2013-04-01	**Revision#**	01

1. INTRODUCTION

A Mobile LAF trolley will be provided for the transfer of filled vials from the cassetting station of the filling and stoppering line to the loading side of the lyophilizer and from lyophilizer to the capping machine.

2. TECHNICAL SPECIFICATIONS OF CART

	Technical Specification	
1.	Model	cGMP Mobile Cart Loading and Unloading System with inbuilt LAF
2.	Overall Area/ Foot Print (mm) (L x W)	***vendor to specify exact dimension***
3.	Inner Area (mm)	***vendor to specify exact dimension***
4.	Type & Capacity	a)Uni-directional Laminar Air Flow type b)Double Stage filtration c)Horizontal Downward direction/ vertical direction ***(vendor to conform)*** d)two side open with supporting structure and door interlocking
	Machine Compliance	EU GMP / USFDA
5.	Pre- Filter	To filter the inflow air, protecting against damage and prolonging HEPA filter life. Size and efficiency: **vendor to specify**
6.	HEPA Filter (H-14)	Efficiency >99.999% for 0.1 to 0.3 micron ***Size: vendor to specify***
7.	Air flow velocities	0.45 m/s
8.	Quantity	1 Nos
	Material of Construction	
9.	Body Construction	SS 316L
10.	Support Stand	SS 304 or better
11.	Coving	SS in built
12.	Working Shelves	SS 304 - matt finish
13.	MOC Fan	Aluminum or better
14.	Door	Safety glass
15.	All welds shall be ground finish	
	Other Requirement	
16.	Blower System shall be balanced for vibration free operation and noise level.	
17.	The dead working table shall be SS type with zero vibration and perforated sheet. One piece formed stainless steel work surface with a curved front edge is designed for maximum operator comfort.	

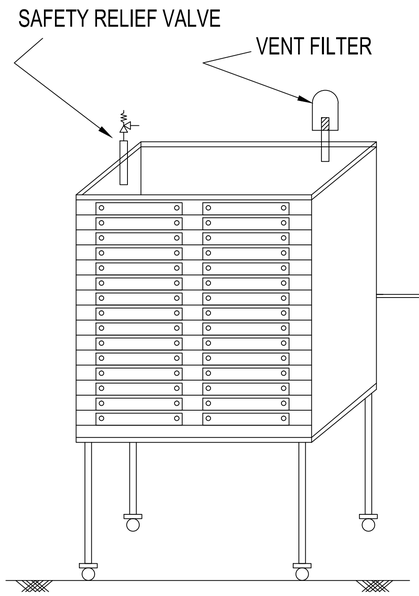
18.	1 no.- magnahelic / photohelic pressure gauge to be provided
19.	Soft touch controls for blower, light.
20.	Lockable Castor wheels shall be provided
21.	LAF shall be provided with lamp suitable to provide >400 lux level
22.	Battery backup with inverter for atleast 30 minutes along with chargeable point. So that LAF can work on battery as well as direct electrical supply
23.	**Audio visual alarm system:** a) Blower tripping Alarm
24.	Height of the cart shall be adjustable with the help of hydraulic system to match the working of cassetting station and lyophiliser loading / unloading shelves. ***Note: Design of the mechanism shall be as per the clean room requirement***
25.	Mechanized bridge plate shall be provided to provide the platform between cart shelf and lyophiliser shelf for easy jerk free movement ***Note: Design of the mechanism shall be as per the clean room requirement***
26.	Cleaning shall be done manually.
27.	Vendor to submit detailed fabrication drawing for approval before fabrication.
28.	DOP/PAO test port to be provided
	Safety Requirement
29.	Emergency stop function on accessible area.
30.	Noise level below 75 decibel.
31.	No sharp edges/Corners, crevices, pin holes in the process wetted parts of the equipment.
32.	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 product remain in a safe condition.
33.	Antimicrobial coating shall be there on all painted surfaces.
	Documents
34.	Operation Manual
35.	DQ Document
36.	IOQ Protocol
37.	MOC certificates
38.	Test Certificate
39.	List of MAKE with certificate (to be used during fabrication of this unit)
	NOTE: Accurate size and technical specification need to be mentioned by the vendor.

3. OPERATION

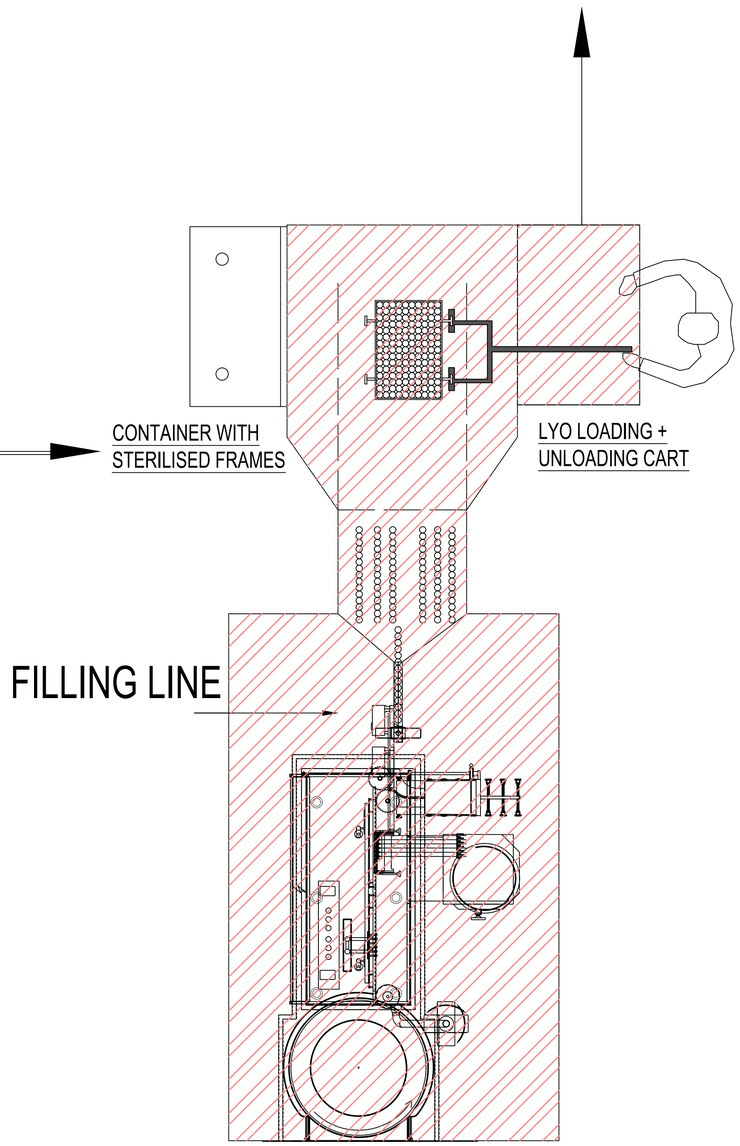
1) The vials from the filling station will be collected on cassettes (by means of frames) using mechanized arms provided along with the cassetting station by the filling line vendor. This vial arrangement will be row in shape.
2) The sterilized frames will be placed manually around the vials and the operator will transfer these frames onto the surface of mobile LAF with the help of SS tong. This process will continue until the sufficient frames along with vials are transferred.
3) The operator will move this mobile LAF and dock it in-front of the lyophilizer loading door (pizza door).
4) The height of the lyophilizer shelves will be adjusted with the height of the mobile LAF so that the transfer of frames will be smooth. This adjustment of the shelves will be done hydraulically. Transfer of the frames will be manual by means of mechanized pushing device on to the shelf under LAF provided above the loading door.
5) The next set of frames will be transferred from filling line to lyophilizer following the above mentioned process. These frames will be loaded onto the shelves. These frames will link to the previous set of frames with the help of hooks / clips and these will move inside the chamber as one assembly.
6) The process will begin with the loading of the uppermost shelf and proceeds until the lowermost shelf will be loaded, while when unloading the sequence will be reversed. This interaction between loading/unloading system and lyophiliser is termed ‘Constant Level Loading’.
7) The pizza door of the lyophilizer will be closed and lyophilization process will start.
8) After the completion of lyophilization process, the unloading operation will start, the pizza door will open and the shelf will be positioned at the unloading height and the frames will be pulled manually using sterile mode i.e.; SS Tong
9) This process will continue until one shelf completely unloaded, at which time the next shelf will be brought to the unloading height until the entire lyophiliser has been emptied
10) After the unloading of the frames with lyophilized vials, the operator will move the mobile LAF trolley and dock the trolley in-front of the loading side of the capping machine.

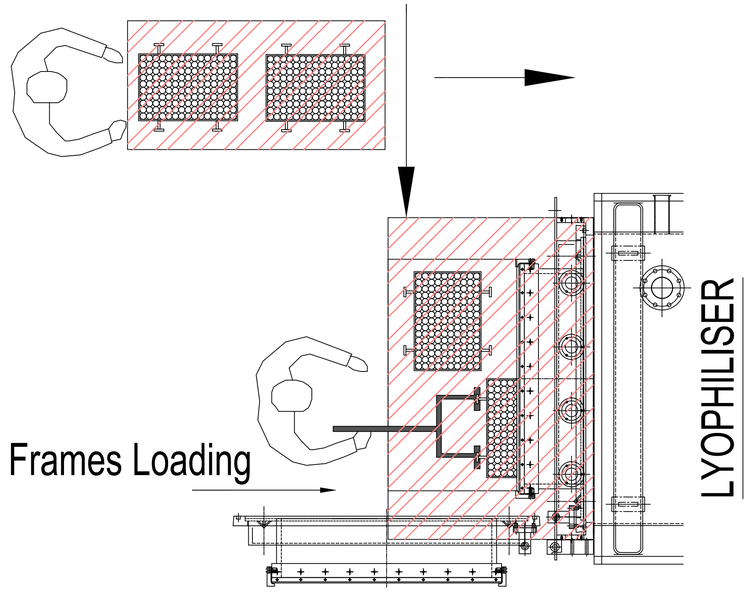
4. FRAMES:

1	Stainless steel frames with a specially designed linkage system on the front and rear to enable them to be connected to and disconnected from neighbouring frames in front and behind by the lift/lower motion of the loading platform.
2	Dimensions (W x L x H): ***(Vendor to specify)***
3	The link design maintains the frames on each shelf together as one assembly so they can be unloaded by pulling the first row.



CONTAINER WITH
STERILISED FRAMES





FOR INFORMATION ONLY

Rev.	Date	Changed	Checked	Kind of revision	No. Of Prints	Date	Issued To
01	13.07.2012	NHSG	NVNG	Transfer trolley will have inbuilt LAF instead of Ceiling suspended LAF which will eliminate the ceiling suspended LAF from the path.	--	--	--

File name :

Originated From Drg. No :

Project:
REVIVAL OF BCG VACCINES LABORATORY
GUINDY, CHENNAI
HLL LIFECARE LIMITED

Project No.: 110729

Location: CHENNAI

nne pharmaplan®
NNE Pharmaplan India Limited
#14, Achiah Shetty Layout,
Bangalore - 560 080., INDIA.

Description:

URS ANNEXURE 4

PROCESS FLOW DIAGRAM FOR TRANSFER OF LYO LOADING+UNLOADING CART

	Date	Name
Drawn	13.07.2012	SRTR
Checked	13.07.2012	NHSG
Approved	16.07.2012	NVNG
Scale-NTS	Units : mm	Size : A4

Drawing no: NPI/110729/PFD(SCH)/03

Rev. 01