User Requirement Specifications

0.45 µm and 0.2/0.22 µm Sterile Filter

Process Code	Area	Equipment code	Qty(Nos)	Capacity
D	**Diphtheria**	**D-SFU 01**	**1**	**Configuration:**10" Code 7 with 0.45 µm + 0.22/0.2µm filters

URS Annexure List

URS Annex No.	Detail
1.	Layout showing the location of the 0.45 µm and 0.22/0.2 µm Sterile filtration unit in the Diphtheria block
2.	List of preferred MAKE of components

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1.0 APPROVAL SIGNATURE

This document is prepared by the Process, Validation and GMP Compliance team of "NNE Pharmaplan India" for the project "Revival of DPT Vaccines manufacturing Facility" (**Project number:-110831**) of Pasteur Institute of India, Coonoor under the authority of their Project Manager. Hence, this document before being effective shall be approved by the QA team of Pasteur Institute of India, and authorized by the appropriate Project Authority.

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2.0 EQUIPMENT DESCRIPTION

The equipment described in this URS is a mobile "**0.45 µm and 0.22/0.2 µm sterile filter**" for carrying out the sterile filtration of the toxin after the Microfiltration step in the fermentation room. The sterile filtration must be performed under sterile conditions.

The unit will be installed in a clean room and therefore has to meet all requirements accordingly. The system shall be operated in manual mode.

Design, function and control of the unit have to be GMP compliant.

2.0.1 Scope of supply

(A) One Skid mounted Sterile Filtration Unit including lockable castor wheels with adjustable pads. The major components are:

- Size 10",Code 7 (0.45 µm and 0.22/0.2 µm) Filter Cartridges for pre-filtration and sterile filtration of the toxin with SS316L housing, all pipelines and connections, which come in contact with the product should be made SS 316 L and electro polished with Ra<0.6 µmfor product contact parts and Ra<1.2 µmfor product non-contact parts.
- Staubli connectors to be provided for the filters for filter integrity testing
- Pressure Gauges/ indicators at inlet and outlet of both the filters
- Air filter for Compressed air should be sterilized along with the whole system
- Manual diaphragm valves (mainly for utilities like pure steam, compressed air)
- Peristaltic Pump (feed pump)
- Interconnecting sanitary process piping.
- Fittings (Such as Triclover clamps, steam traps, reducer (if required) etc)
- Pressure regulator for compressed air
- Product sampling provision
- Instrumentation air assembly control (pre-filter, valve assembly etc)
- Skid mounted with complete assembly with lockable castor wheels with adjustable pads

(B) The filtration unit should contain the followings for a smooth running of the equipment.

S. No.	Description	Purpose
1	Product Inlet with TC end	For attaching to the pipe line from the Pressure vessel
2	Product outlet with TC end	For attaching to flexi hose to transfer to Nalgene bottles sterile to sterile connection to be provided
3	Filter housing	SS316L filter housings for 5 µmfilter, sterile grade filter of 0.45 µm and 0.22/0.2 µm Filter
4	Common drain line	For draining the product remained in the filter housing and the connected piping at the end of filtration. Also to drain the product from the vent of housing during initial purging of the product.
5	Staubli connector	For testing the integrity of the filter

(C) **Clean In Place:** CIP of the system shall be done using Mobile CIP trolley(Once through) with WFI and CIP recipe with the help of pump, manual diaphragm valve, and pressure indicator. The necessary controlling mechanism will be associated with the CIP trolley.

(D) **Sterilization In Place**: Sterilization of the system shall be done by using the Mobile SIP Trolley.

Note: The following points which are there in the IRS(Installation Requirement Specifications) are not applicable for this equipment:

- 4.1.10 , 4.1.11, 4.1.13,4.1.17
- **Sec 5.1 Table 2**
  - **Sl.NO 2 and 3 :**FDA guidance for industry
  - Sl.NO 5 CE Conformity,
  - Sl.NO 7 ANSI/NSF 49-2008, ISO 14664, ISO 8362
  - Sl.NO 8 ISO 14664
  - Sl.NO 9 ISO 8362
- Sec 5.4.1
- Sec 5.6

Note:

1.	This Technical Specification is the basis for an inquiry to a vendor and therefore the basis for the vendor's proposal.
2.	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.
3.	The vendor must clearly comment each item of the Technical Specification. The comments must be in English language. If extra costs for necessary options become necessary the item must be clearly stated.
4.	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.
5.	The final version of this document including the vendor's comments will become basis of a potential purchase order or contract.
6.	The Technical Specification serves to define a summary of all vendors' requirements concerning scope of delivery and services.
7.	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.

8.	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.
9.	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.
10.	The makes requested are standard international makes. In case of any deviation, vendor to seek clarification from HLL before submitting the offers.
11.	Refer document Installation Requirement Specification and Specific Instructions with URS; NPI_110831_IRS_PII_01
12.	Refer Tender document with URS; NPI/110831/EQP/TD/04

Specifications	Remarks
3.0 PROCESS DESCRIPTION	
3.1 Input & Charging method	
Product inlet: Clarified toxin(after Micro-filtration) is transferred to intermediate pressure vessel by using Compressed Air then to the 0.45 micron and 0.22/0.2 micron sterile filter unit.	
3.2 Brief Process Steps	
The equipment will be used for the sterile filtration of the clarified Diphtheria toxin and has to be tested and operated according to biosafety regulations. a) The clarified broth will be sterile filtered in the 0.45 micron filter and then in 0.22/0.2 micron filter b) The aeration of the filtration unit with filtered compressed air and the sterilizable air filter should be sterilized along with SFU.	
3.3 Output & Discharging method	
a) The Filtrate will be collected into 50 L nalgene bottles under Mobile LAF	
4.0 PRODUCTIVITY REQUIREMENT	
4.1 Desired/ suggested capacity	
4.1.1 The filter element should have least protein binding (<4µg/cm^2 for Immunoglobulin G) 4.1.2 Low hold – up volume 4.1.3 The filter element shall be of open channel SIP able PVDF membranes with least extractables (< 20 mg/ml for a 10 inch cartridge)	

Specifications	Remarks
4.2 Standard batch size	
Not Applicable	
4.3 Change Over Time	
Not Applicable	
4.4 Others (if any)	
Not Applicable	
5.0 CONTAINMENT	
The whole transport of the Toxin to be contained to avoid any contamination	
6.0 GMP REQUIREMENTS	
6.1 Process control	
6.1.1 Following parameters shall be controlled manually	
a. Temperature of the sterilization	
b. The drain valve position and control.	
6.2 Failure mode detection	
Emergency stop activated (manual shut down)	
6.3 In –Process control	
Sampling valve shall be provided in the line to collect sample at the end of the filtration.	
6.4 Level of instrumentation	
Vendor shall design and propose the instrumentation according to the process control system for monitoring and control:	

Parameters	Purpose	Instrumentation
Temperature	Monitor and indicate the temperature (during SIP at the drain points.)	Temperature indicator at the lowest point of the system
Pressure	Monitor the pressure at both inlet and out let of SFU	Pressure gauge/ indicator
Valve arrangement	To control pressurized utility(Pure steam and Compressed air)	Manual diaphragm valves
Drain	For product drain and condensate drain	Manual diaphragm valve

Specifications	Remarks
6.5 Batch data display and record printing	
Not Applicable	
6.6 GMP requirements (Others)	
6.6.1 Equipment must be designed for aseptic operation	
6.7 Specific requirements	
In general the equipment has to be designed in a way to get easy and quick access to all necessary maintenance points	
6.7.1 All ports should be attached with Sanitary Tri clamps	
6.7.2 Steam traps should be provided for the drain lines	
6.7.3 All valves shall be sanitary type manually operated valves	
6.7.4 All valves shall be SS316L with diaphragm of PTFE backed EPDM and surface finish of Ra≤0.6 µm with Electro polished.	
6.7.5 Additional requirements: Calibration of measuring instruments according to international standards, full-loop calibration is required for GMP and quality relevant instruments. The Supplier has to provide calibration protocols and guidelines for writing SOPs for recalibration.	
6.7.6 Performance criteria during FAT/SAT: a. Filter integrity test should be performed b. SIP of the whole system along with the compressed air inlet filter. c. Media fill with process simulation during SAT	
7.0 CONSTRAINTS	
7.1 Equipment location and available space	
This equipment will be installed in the **Revival of DPT Vaccine manufacturing Facility**, **PIIC** as follows: **Equipment location:** **Block:** Diphtheria Block **Floor:** Ground Floor **Room Size:** 5.8 m X 6.51 m, 1.6 m x 4.61m , 4.3 m x 4.61 m **False Ceiling height** : 3 m **Physical condition of the rooms: Fermentation room** 1. Room will be BSL 2 2. Class: EU Class "C" 3. Differential Pressure:5 Pa 4. Temperature maintained: 22±2 ºC 5. Relative Humidity: NMT 55%	

Specifications	Remarks
The equipment location is indicated in the layout enclosed in as **URS Annex 1.**	
7.2 Available Utility	
7.2.1 Electricity:1.75 kW(Ceiling suspended LAF)Report Requirement)	
7.2.2 Pure Steam@ 2.4 bar(g)_____ (Report Requirement)	
7.2.3 Compressed air@ 6-8 bar(g)_____(Report Requirement)	

8.0 ABBREVIATION

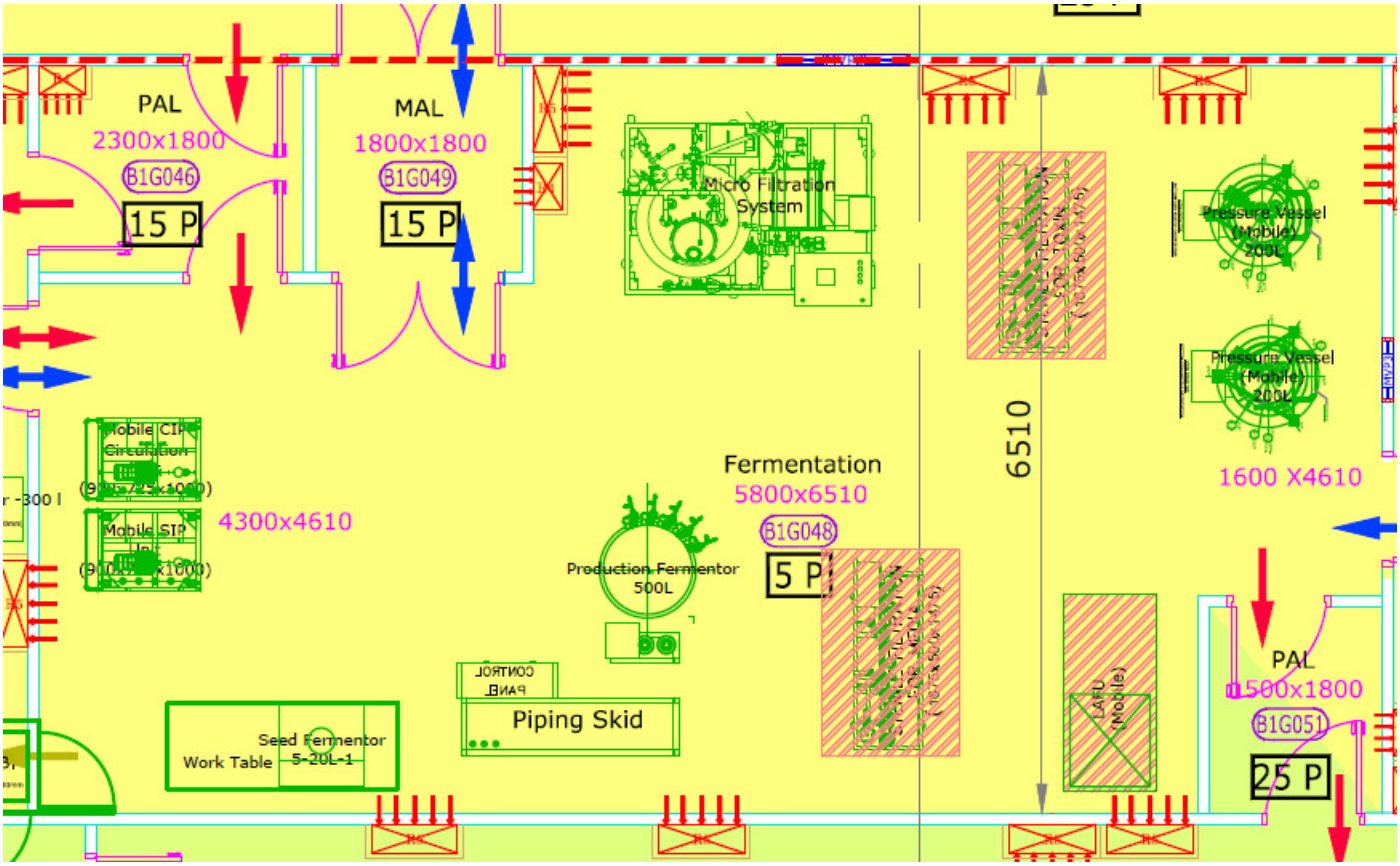
Abbreviation	Definition
^{0}C	Degree Centigrade
NPI	NNE Pharmaplan India Ltd
HLL	HLL Life care Limited
PII	Pasteur Institute of India
SS	Stainless steel
SFU	Sterile Filtration Unit

REVISION INDEX

Revision	Date	Reason for Revision
00	2012.07.04	First draft for Client's review
01	2012-10-22	Format changed as per HLL requirement
02	2013.02.05	Comments from HLL/PIIC incorporated
03	2013.03.18	Comments from HLL/PIIC incorporated_ email dated 2013.03.18
04	2014.01.02	Comments from HLL/PIIC incorporated_ email dated 2013.12.30

URS Annex 1: Layout

Room No: B1G048



URS Annexure 2: List of Preferred Make of components

SL.NO	DESCRIPTION	MAKE
1	Steam trap	STERIFLOW/ITT
A	**MECHANICAL**	
2	Pressure gauges	WIKA/Denver/Negele
3	Pre air filter cartridge	Sartorius/PALL/ Millipore
4	Filter cartridge	Sartorius/PALL/ Millipore
5	Filter housing	Sartorius/ PALL/Millipore
6	Diaphragm valve(Manual)	GEMU/Burkert
7	Ball valve(Manual)	Modentic/Saunders/Alfa laval
8	Sampling valve	Novaseptic/GEMU