USER REQUIREMENT SPECIFICATIONS

ULTRA FILTRATION SYSTEM

PROCESS CODE	AREA	EQUIPMENT CODE	QTY(NOS)
T	Tetanus	T-UFS 01	1

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nne pharmaplan	User Requirement Specifications			
	Equipment/System	Ultra Filtration System		
	Identification #	T-UFS 01	**Document#**	URS/T-UFS 01
	Effective Date#	2013-12-18	**Revision#**	07

URS Annexure List

URS Annex No.	Detail
1.	Layout showing the location of the Ultrafiltration System in the concentration room
2.	Tentative P& ID for Ultrafiltration System

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 by this URS is an "**Ultra Filtration System" (Quantity- 1NO.).** This system will be used for the concentration of Tetanus Toxoid (non-live material) after detoxification of the toxin (live material).

2.1 Operating Conditions:

- Pressure bar: 0 - 4 bar
- Flow range: vendor to specify
- Temperature range: 0 - 40 ℃ during process.
- Surface area of the membrane: 5m^2 with a provision to increase the filter area to 10m^2
- Minimum working Volume: 0.01% of Total Volume

2.2 System Specifications

TABLE 1

S. No.	Description	Purpose	MOC	Capacity/Size
1.	System frame	To hold cassette holder	SS304	Vendor to specify
2.	Cassette holder	To hold cassettes	SS316L	5 m^2 with a provision to increase the filter area to 10m^2
3.	Recirculation pump	To recirculate the permeate and retentate	Sanitary type-SS316L	Vendor to specify according to membrane area
4.	Flow path	For the circulation of feed, permeate and retentate	SS316L	Vendor to specify
5.	Pressure transmitter in the feed, permeate and retentate lines	To measure Pressure differential (ΔP) and trans membrane pressure (TMP)	Sanitary type with SS316L diaphragm	NA
6.	Surface Finish	System should be Internally Electro polished and passivated Ra≤0.6 µm, according to ASME BPE guidelines (2009)		
		Externally Mechanically polished and passivated up to Ra<1.2 µm		
		Stainless steel piping interior Ra≤ 0.6 µm, , according to ASME BPE guidelines (2009)		

System should be provided with rotary lobe pump proven to handle shear sensitive biomolecules with suitable flow rate and pressure with variable speed control and auto cut off of the pump at dry condition of the tank.

All pressurized parts of the system should be piped and connected via sanitary connections.

2.3 Vessel Specifications

TABLE 2

S. No.	Description	Purpose	MOC
1.	Shell	Cylindrical	SS316L
2.	Top closure	Flat Lid	SS316L
3.	Bottom closure	Torispherical dish	SS316L
4.	Spray Ball	For the cleaning of the interior of the vessel.	SS 316L
5.	Cladding	Cladding is welded to jacket around the insulation	SS304

2.4 Vessel design specification

TABLE 3

Sl.NO	Description	Specification
1.	Maximum working volume	150L
2.	Quantity	1 No
3.	Working temperature range	25 °C-134 °C
4.	Surface Finish	Internally Electro polished Ra ≤ 0.6 µm, according to ASME BPE guidelines
		Externally Mechanically polished up to Ra <1.2µm mirror finish.
		Stainless steel piping interior Ra≤ 0.6µm, according to ASME BPE guideliness

2.4.a **The Chassis mounted system (with castor wheel) with One Ultrafiltration unit, Semi-Automatic System and intermediate feed tank**. The following main features:

A. Dosing unit for feed: The feed (from Nalgene bottles of 50 L) shall be fed into the feed tank of the filtration unit using the feed pump.

B. Air Filters

- Inlet Air filters:
  - Reusable SS housing with 0.2/0.22 µm sterile filter (code 7) with manual diaphragm valve, which is to be sterilized along with vessel.

C. Pressure Indication:

- Pressure of the vessel
  - Compound pressure gauge for vessel
  - Rupture disc to release the excess pressure in the vessel

D. Flush bottom valve: It should be zero dead leg type valve attached directly to the bottom of the vessel. The diaphragm shall be of PTFE type

E. Feed Line:

- Pressure transmitter

F. Permeate Line:

- Pressure transmitter
- Electromagnetic Flow Measuring System , for measuring the flow of conductive fluids in process applications
- Sampling valve

G. Retentate Line:

- Pressure transmitter
- Electromagnetic flow meter
- Retentate Sampling
- Control Valve for ΔP and TMP

H. CIP (Clean in Place):

- Manual CIP of the system must be made possible

I. General characteristics of the Ultrafiltration membrane:

- Filter area of 5 m2 with a provision to increase the filter area to 10m2
- Membrane with 30 KD Molecular Weight cut off.
- Membranes to be CIPable only (No SIP for membranes)
- Hydrophilic in nature.
- High velocity and high particulate level capability.
- Maximum containment of hazardous fluids.
- Low hold-up volume
- Low protein binding.
- Good compatibility with most of the cleaning, sanitizing, depyrogenation and storage agents
- Void free composite PES membrane with 0.5M caustic compatibility.
- Capable of withstanding 100 psi forward pressure at 25degC.
- Should meet USP class VI biological tests invivo

J. 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.

K. Controller: PLC Based Controller (Semi- Automatic operation) with a 10" industrial touch screen large HMI (Displaying data trends as Graphs, synoptic view of running parameters etc).

L. The HMI shall be touch screen type (Provision for manual operation also to be provided)

- HMI screen size shall be of 10" with resolution of 1200 x 800 pixels
- Human machine interface must be used to enter the process details, which should appear in the print out.
- All critical alarms
- All critical parameters & interlocks
- Addition of the buffer
- All Recipes/ sequences (process, CIP, transfer etc)
- P&ID of the vessel along with instrumentation details
- Login details
- HMI screen shots shall be available

M. Nozzles Schedule :
Top Head Plate *(design of shell to be provided by the vendor)*

- GMP type Spray ball assembly with 360ospray(design of the same shall be submitted by the vendor)
- Sterilizing grade hydrophobic inlet and vent filter (0.2/0.22µ filter) with SS housing and manual diaphragm valve with connection to drain line
- Rupture disc – NA connector with connection the drain line
- Port for Light/Sight Glass –Bolted with gasket.
- Port for Spare port- TC clamps with gasket
- Port for Pressure gauge
- Port for inlet of retentate with "J" type nozzle
- Port for level sensor-accuracy of ± approx. 0.1% of the total range

Upper wall side:

The feed vessel upper **wall** shall normally have :

- Port for the addition of feed/ buffer with peristaltic pump
- Permeate recirculation port with "J" type nozzle

Lower wall/Bottom connections:

- Port for temperature transmitter
- Port for conductivity meter

N. All points of the IRS except the below mentioned would be applicable for the equipment

- 4.1.10, 4.1.11, 4.1.13, 4.1.17
- FDA Guidance for industry, CE Certification,
- ANSI/NSF 49-2008, ISO 14664, ISO 8362

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. In case of a 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 become necessary the item must be clearly stated.
IV.	In case the requirement includes a question or request or an 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 vendors' 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_110831_IRS_PII_01
XII.	Refer Tender document with URS; NPI/110831/EQP/TD/04

Specifications	Remarks
3.0 PROCESS DESCRIPTION	
3.1 Input & Charging method	
3.1.1 The feed (from Nalgene bottles of 50 L) shall be fed into the feed tank of the filtration unit using the feed pump.	
3.2 Brief Process Steps	
3.2.1 The equipment will be used for concentration of toxoid a) The toxoid shall be directly fed into feed tank with peristaltic pump. b) The flow-rate of the toxoid into the system and the feed pump shall be controlled by a control panel. ***(Basic Requirement: Concentration factor: 100X)*** The required number of filtration modules shall be installed as per the required filtration area in single or in multiple membrane cassettes. c) Permeate and retentate will be recirculated into the vessel until the equilibrium is achieved. d) After achieving the equilibrium, permeate is collected separately and retentate shall be recirculated in the vessel e) System to be designed to process simultaneously product feed inlet and concentration operation. f) A separate provision to be made for product recovery to flush the module.	
3.3 Output & Discharging method	
a) After diafiltration the retentate (50 L) shall be collected in the 100 L (WV) mobile pressure vessel which will serve as feed tank to sterile filtration system.	
b) Permeate is collected separately and sent to the bio waste inactivation system.	
4.0 PRODUCTIVITY REQUIREMENT	
4.1 Desired/ suggested capacity	
a) Ultrafiltration Poly Ether Sulphone membrane to handle toxiod fermentation broth with low protein binding.	
b) Feed Vessel: 5L (Minimum) and 150L (Maximum working Volume)	
4.2 Standard batch size	
Feed: 16 nalgene bottles of 50L (G.V.)	
4.3 Other Productivity Requirement	
Not Applicable	
5.0 CONTAINMENT	
Not Applicable	

6.0	**GMP REQUIREMENTS**	
6.1	**Process control**	
6.1.1	The Ultrafiltration unit should essentially have the necessary provisions for adjustment / control of the following critical process parameters:	
6.1.2	Following parameters shall be controlled by the equipment	
	a) Pressure (trans membrane pressure (TMP), differential pressure (ΔP)	
	b) Temperature of the product	
	c) Flow of the permeate	
	d) NWP stabilization and measurement time	
	e) Duration of the cycle	
	f) The drain valve position and control.	
	g) Parameters during CIP	
	h) Conductivity	
	i) Variable frequency drive	
	j) Level/Weight of the product	
6.1.3	Following conditions need only notification to operator for procedural control:	
	k) Emergency stop activated.	
	l) Power failure.	
	m) Malfunction of sensors of temperature, pressure, flow and conductivity	
6.2	**Failure mode detection**	
6.2.1	**Equipment shall be capable to detect the following failure, notify the operator with alarm and shutdown the process:**	
	a) Pressure level low / high	
	b) Alarm is activated in case Temperature is out of range	
	c) Emergency stop activated	
	d) Alarm in case of not reached pre-set value. (TMP, ΔP)	
6.3	**In –Process control**	
6.3.1	TMP, ΔP	
6.3.2	Temperature measurement and control of the product.	

6.3.3	Measurement and control of fluid level in the tank.	
6.3.4	Flow measurement on the feed inlet line	
6.4	**Level of instrumentation**	

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

Parameters	**Purpose**	**Type of control and Instrumentation**
Temperature	Monitor and control the temperature	RTD sensor and temperature indicator & controller on the tank
Pressure	Monitor and control the pressure(TMP&Δ P)	Pressure gauge for vessel and Pressure transmitter for the skid
Flow rate	Monitor the rate of flow of permeate	Mass Flow rate indicator and flow meter
Conductivity	To measure the conductivity during CIP	Conductivity sensor
Level of the volume/Weight	To maintain the correct volume/weight of the product	With the accuracy of 0.1% of the completed range.

6.5	**Batch data display and record printing**	
	Refer IRS (Installation Requirement Specification and Specific Instruction) Non editable data shall be available / transferred to USB Drive for printing the batch report, alarm log. Real time online printing shall be available for batch report	
6.6	**GMP requirements (Others)**	
6.6.1	Equipment design must be designed for aseptic processing (zero contamination).	
6.6.2	All process relevant wiring has to be executed in fail safe manner.	
6.6.3	All parts of the machine exposed in A/C area must be resistant to standard disinfectants or vendor shall provide the name of specific disinfectants.	
6.7	**Specific requirements**	
6.7.1	In general the equipment has to be designed in a way to get easy and quick access to all necessary maintenance points e. g. Motors, etc.	
6.7.2	All ports should be attached with Sanitary connections	
6.7.3	All diaphragm valves to be sterile type	
6.7.4	Make of level sensor. ***(vendor to specify with technical data sheet)***	
6.7.5	All setting should be user adjustable.	

6.7.6	Automated Temperature control during clarification process **(tolerance limit: ±0.2 degree Celsius)**	
6.7.7	Nozzle shell shall be seamless.	
6.7.8	Nozzle connection to be Triclover.	
6.7.9	Nozzles, adaptors, instrument shall comply with ASME BPE compliant.	
6.7.10	Flexible hose with TC end of 2m length to be provided for connections between the Utility header and the system	
6.7.11	Flexible hose with TC end of 2m length to be provided for connections between system and drain point.	
6.7.12	Total motor drive assembly with SS304 cover with TEFC eff 1.	
6.7.13	All process Utility piping from header to the vessel skid: SS 316L. Ra < 0.6µm	
6.7.14	**Pump specification: Sterile Sanitary design** **CIP :** Yes **Surface finish**: Ra <0.6 µm (electropolished) **MOC:** SS316L **Seal:** Single mechanical seal **Elastomers:** EPDM – FDA/ USP	
6.7.15	The filtration system should have provision for filer integrity tests system, for filter integrity test done pre and post filtration.	
6.7.16	Design Considerations: • Vessel working Pressure: -1 to 3 bar(g) • Vessel working Temperature: 0℃ to 134℃. • Vessel design Pressure: 4 bar or (vendor to specify) • Vessel design Temperature: 0-1500 C or (vendor to specify) • Design pressure for safety release valve: 4.9 bar or (vendor to specify)	
6.7.17	Performance Requirements: Vendor to demonstrate the following during FAT/SAT • Sterility of the complete system • Flux- to be demonstrated with model solution • CIP- effectiveness to be demonstrated and spray ball coverage. • Temperature Control along with the level accuracy to be demonstrated.	
7.0	**CONSTRAINTS**	
7.1	**Equipment location and available space**	
	This equipment will be installed in the area of **DPT Vaccine Manufacturing Facility, PII, Coonoor.** **Equipment Location:** **Concentration &Purification Room (B2G039)** Block: Tetanus Block	

Floor: Ground Floor
Room Size: 7225 x 6175 m^2
False Ceiling: 3000 mm

Physical condition of the rooms:

1. Room will be non-hazardous
2. Class: EU Class “C”
3. Differential Pressure: 30 Pa Absolute
4. Temperature maintained: 22±2 ºC
5. Relative Humidity: <55% Rh

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

7.2	**Available Utility**	
7.2.1	Electricity: 3 ph, 415V AC, 50Hz	
7.2.2	Pure Steam: 3 bar	
7.2.3	Plant steam: 3 - 3.5bar g	
7.2.4	Plant steam: 3 - 3.5bar g	
7.2.5	Compressed air: 8 - 10 bar g	
7.2.6	Chilled Water Supply: 6-7degC,	
7.2.7	***Vendor need to take care the utility requirement as desired for the system. As per the system if changes required in the utility pressure vendor should consider within the package.***	

8.0 ABBREVIATION

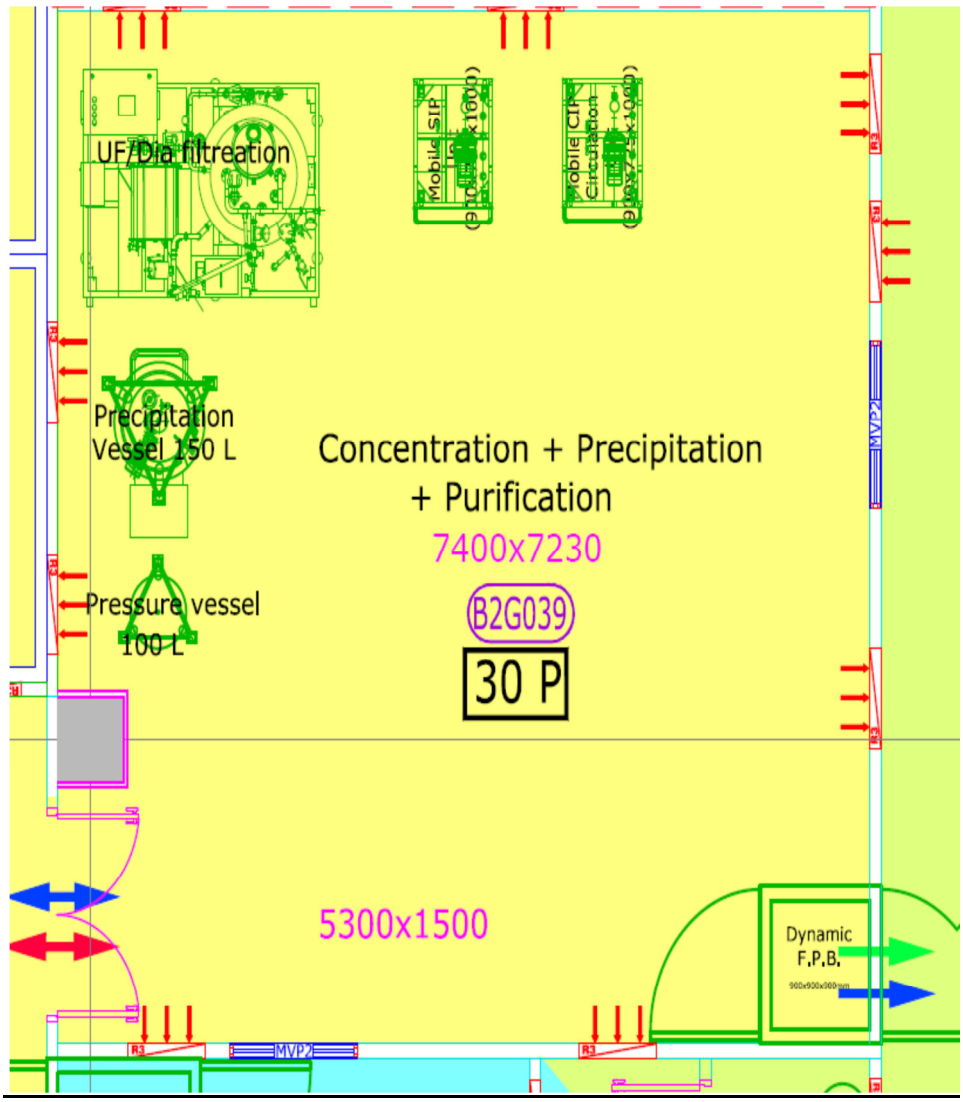
Abbreviation	Definition
ΔP	Differential Pressure
^{0}C	Degree Centigrade
db	Decibel
HMI	Human Machine Interface
MOC	Material Of Construction
NNE	Novo Nordisk Engineering
NPI	NNE Pharmaplan India Ltd
PID	Proportional Integral Derivative
NWP	Nominal Water Permeability
PII	Pasteur Institute of India
PLC	Programmable Logic Controller
RPM	Revolutions Per Minute
SS	Stainless steel
TMP	Trans membrane Pressure
UFS	Ultra Filtration System

REVISION INDEX

Revision	Date	Reason for Revision
00	12.12.2011	1st draft for client's review
01	18.05.2012	Client's Comment Incorporated
02	2012-10-22	Format changed as per HLL requirement
03	2013-01-23	HLL comments incorporated, received during the workshop dated 22nd and 23rd January 2013
04	2013-02-21	PIIC comments incorporated, received on 2013-03-18
05	2013-05-14	Format internally revised
06	2013-11-11	Updated as per Telecon dated 2013-11-08
07	2013-12-18	Updated as per commented URS received from HLL on e-mail dtd 2013-12-17

URS Annexure 1: LAYOUT OF TETANUS BLOCK

Room No: B2G039



List of Preferred Make of components

SL.NO	DESCRIPTION	MAKE
A	**INSTRUMENTATION**	
1	PLC	Allen Bradley/ Siemens
2	Operator Interface/HMI	Allen Bradley/ Siemens
3	Temperature transmitter	Radix/ Yokogawa/Emerson
4	Temperature sensor	NEGELE/E&H
5	pH sensor	METTLER TOLEDO/E&H
6	Pressure transmitter	Wika /Dwyer/labom
7	Pressure regulator	FESTO
8	Flow meter	E&H / Khrone Marshall/ Rosemount
9	Temperature indicator	Radix/ Wika/ Waaree instruments
10	Steam trap	Spirax Marshall
11	Rupture Disc	Fike
12	Printer	Canon/Epsilon/HP
B	**MECHANICAL**	
13	Pressure gauges	WIKA/Denver/Negele
14	Vent filter cartridge	Sartorius/PALL/Millipore
15	Filter housing	Sartorius/ PALL/Millipore
16	Spray ball	HAKE/LECHLER
17	Diaphragm valve(Manual)	GEMU/ITT/Novaseptic
18	Ball valve(Manual)	Modentic/Alfa laval
19	Flush bottom valve	Novaseptic/GEMU
20	Sampling Valve	Novaseptic/GEMU
21	Flow switch	E&H/ Wika/Emerson
22	Recirculation Pump	Johnson/ Alfa Laval
C	**PNEUMATIC**	
23	Diaphragm valve(Automatic)	GEMU/ Novaseptic
24	Angle Seat valve	GEMU/Spirax/Sarco
D	**ELECTRICAL**	
25	Lamp	PAPENMEIER