User Requirement Specifications
Fermentor

Block Code	Area	Identification #	Quantity(No.s)	Capacity L (W.V.)
B1	Multiple Bacterial Block (Hep – B)	B1-FER-01,02	2	500
B1	Multiple Bacterial Block(Hep – B)	B1-FER-03	1	35
B1	Multiple Bacterial Block(Hep – B)	B1-FV-01,02,03,04	4	150
B1	Multiple Bacterial Block(HIB)	B1-FER-04,05	2	500
B1	Multiple Bacterial Block(HIB)	B1-FER-06	1	35

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URS Annexure List

URS Annex No.	Detail
1	Layout showing location of the Fermentor in the Multiple Bacterial Bulk Block
2	List of preferred MAKE of components

1.0 APPROVAL SIGNATURE

This document is prepared by the Process, Validation and GMP Compliance team of "NNE Pharmaplan India" for the project "Integrated Vaccines Complex, Chengalpattu, Chennai" (project number: 120310) of HLL BIOTECH LIMITED (Chennai) under the authority of their Project Manager. Hence, this document before being effective shall be reviewed by HBL user/s and project/ engineering team, approved by team lead of user department and QA and authorized by the appropriate Project Authority.

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2.0 EQUIPMENT DESCRIPTION

The Equipment described in this URS are " Fermentor" and "Feed Vessels". Fermentor is the reaction vessel that maintains optimal condition (pH, Temp, DO) for the growth of microorganism .The Fermentor will be used for batch operation & it will be installed in grade "C" classified area.

Feed vessel is used for the preparation of feed and it will be fed into the Fermentor during fermentation.

TABLE 1:Basic Specification

SL. No.	Description	Purpose	MOC	Remarks from vendor
1.	Shell	Cylindrical, for fermentor	SS316L	
2.	Top closure	Flat lid with manual lifting device for B1-FER-01,02,04,05 Flat lid for B1-FER-03,06,B1-FV-01,02,03,04	SS316L	
3.	Bottom closure	Torispherical dish	SS316L	
4.	Jacket	For temperature Maintenance	SS304	
5.	Insulation	To avoid heat loss	Chloride free ceramic wool	
6.	Cladding	Cladding shall be used to cover the insulation	SS304	
7.	Bottom Agitator – Production Fermentor	For mixing the process fluid constantly & keep uniform solution and to avoid dead air pocket	SS316L	
8.	Top Agitator –Seed Fermentor	For mixing the process fluid constantly & keep uniform solution and to avoid dead air pocket	SS316L	
9.	Bottom magnetic Mixer-Feed Vessel	Bottom mounted magnetic mixer	SS316L	

TABLE 2:Specific Requirements

S.No.	Description	Fermentor				Feed vessels	Remarks from Vendor
		Hep - B section		HIB section		Hep - B Section	
1	No. of Fermentors/ Vessels	2	1	2	1	4	
2	Type of Vessel	fixed	Fixed	Fixed	Fixed	Fixed	
3	Max. Working volume , L	500	35	500	35	150	
4	Geometric volume, L	Vendor to specify (Head volume should be min 30% of the total height)	Vendor to specify (Head volume should be min 30% of the total height)	Vendor to specify (Head volume should be min 30% of the total height)	Vendor to specify (Head volume should be min 30% of the total height)	Vendor to specify	
5	Minimum operating volume, L	120L	6L	120L	Vendor to specify	Vendor to specify	
6	Operating Temperature	0 - 35 °C	0 - 35 °C	0 - 35 °C	0 - 35 °C	0 - 35 °C	
7	H/D ratio	3:1	3:1	3:1	3:1	2:1	
8	Addition port (TC type)	8	7	7	7	6	
9	Baffles (Fixed type)	4	2	4	2	2	
10	PRV for pure steam line	Yes	Yes	Yes	Yes	NA	
11	Level/Volume Measurement	DP	Potentiometric	DP	Potentio-metric	Potentio-metric	
12	Peristaltic Pumps (Quantity per unit system)	2 nos Portable, Standalone variable speed Pump (1-10l/hr) with display. 3nos fixed speed pump(100ml /min)	3 no.s fixed speed pump (100ml/min)	1 no.s Portable, Standalone variable speed Pump (1-10l/hr) with display. 3nos fixed speed pump(100ml/ min) fixed speed pump(100ml/ min)	3no.s fixed speed pump(100 ml/min)	1 no. Portable, Standalone variable speed Pump (1-10l/hr) with display	

S. No.	Description	Fermentor				Feed vessels	Remark from Vendor
		Hep - B section		HIB section		Hep - B Section	
13	pH sensor	Monitoring controlling and Indication	Monitoring controlling and Indication	Monitoring controlling and Indication	Monitoring controlling and Indication	NA	
14	DO probe	Monitoring controlling and Indication	Monitoring controlling and Indication	Monitoring controlling and Indication	Monitoring controlling and Indication	NA	
15	Temperature Probe	Monitoring controlling and Indication	Monitoring controlling and Indication	Monitoring controlling and Indication	Monitoring controlling and Indication	Monitoring controlling and Indication	
16	Aeration O_2 sparger	Yes	Yes	Yes	Yes	NA	
17	foam Probe	Monitoring controlling and Indication	Monitoring controlling and Indication	Monitoring controlling and Indication	Monitoring controlling and Indication	NA	
18	Agitator Type	3 nos Height adjustable, 6 Blade Rushton turbine. Tip speed 3-5m/s	3 nos Height adjustable, 6 Blade Rushton turbine. Tip speed 3-5m/s	3 nos Height adjustable, 6 Blade Rushton turbine. Tip speed 3-5m/s	3 nos Height adjustable, 6 Blade Rushton turbine. Tip speed 3-5m/s	Bottom mounted magnetic mixer	
19	Sterilization	ESIP FSIP	ESIP FSIP	ESIP FSIP	ESIP FSIP	ESIP FSIP	
20	CIP	Each line of Hep-B (*1no production Fermentor, 1no seed Fermentor, 2nos feed vessel*) should have a centrifugal pump, conductivity sensor and necessary valves .CIP for each line should be done in a fully automated mode.		Each line of Hib (*1no production Fermentor, 1no seed Fermentor*) should have a centrifugal pump, conductivity sensor and necessary valves .CIP for each line should be done in a fully automated mode.			

Note:- Independent SIP shall be provided for sampling, transfer line, Addition port for Acid, Base, Filters line etc.
CIP operation must be possible for each vessel/together with complete skid. Selection of equipment must be available in set parameter.

2.1 General design of Fermentor :

Fermentors are supplied along with all the necessary piping with skid, valves, instrumentation and Control panels.

S No.	Description	Remarks from vendor
2.1.1	**Dosing Unit:** Addition ports shall be of sterile arrangement with four-way valve assembly for SIP, draining and isolation. A temperature sensor shall be provided near the drain point of the four-way valve assembly. All ports shall have a J-tube arrangement facing the interior wall of the vessel. Independent SIP required for all adition assemblies. Sterile valve assembly shall be used for addition of solutions from respective containers in to the Fermentor through peristaltic pump. Dosing pumps shall be controlled by the feedback signals from pH sensors. Also Necessary arrangements like hose nipple should be provided. (As per ASME SEC VIII Div1. & BPE)	
2.1.2	**Gas supply system:** The Fermentors must be provided with a gas supply system for supplying sterile gases as per the process requirement. The air supply line should be equipped with a air-PRV, MFC and Rotameter. Necessary Isolation valves,NRV shall be provided for isolating MFC and rotameter. Mass flow controller should be designed for a flow rate of 1-500 LPM (for Hep-B, 500L Fermentor) and 1-100 LPM (for HIB, 500L Fermentor) and should attain 30 % DO. Ring sparger should be provided for all Fermentor for uniform aeration. Sparger should contain holes facing downwards for better drainability. Sparger should be CIP/SIP able. Separate MFC to be provided for process air and O_2 supply.	
2.1.3	**Gas Inlet Filter:**The system should equipped with a filter and housing for supplying sterile gases into the vessel. Sparger and overlay should supply sterile air to the fermentors. The filter should be hydrophobic in nature with a 0.22 µm pore size. Filter housing should be of SS316L,surface finish equivalent to Fermentor interior and should have necessary drain arrangements for removing condensate during sterilization. Filters should have an independent sterilization.	
2.1.4	**Spray ball:** Fermentor shall have sufficient number of static spray ball(s) to ensure cleaning of the interior surfaces. The vendor shall ensure cleanability of the Fermentor, 360 degree spray coverage should be ensured.	
2.1.5	**Vent/Exhasut Filter:** Fermentor should have a vent filter (Hydrophobic, 0.22 µm pore size) with SS316L Housing, surface finish equivalent to Fermentor interior and should have necessary drain arrangements for removing condensate during sterilization. Filters should have an independent sterilization.	
2.1.6	**Temperature Control:** Temperature during preparation shall be controlled via circulation of utilities (plant steam, cooling water, chilled water etc.) in the jacket or through heat exchanger. Temperature control during fermentation (tolerance limit: ± 0.1°C) & during sterilization the temperature should be 122°C. (Tolerance limit: ± 1°C). Pneumatically actuated valves for steam and cooling water/ chilled water	
2.1.7	**Exhaust Line:** Fermentor vent line shall include a condenser to condense the vapors escaping out of the Fermentor through the vent. Exhaust line also should have a vent heater to prevent the moisture content in the vent filter by non-condensable gases/vapors. The heat exchanger shall use steam as heating medium to raise the temperature of the vapors beyond dew point. It should be comply with ASME BPE 2009; Part SD-4.17.3.	

S No.	Description	Remarks from vendor
2.1.8	**Agitator:** The Fermentor shall have a centric bottom mounted wet double mechanical seal agitator with height adjustable Rushton turbine impellers for production Fermentors(Capacity 500 L) and top driven agitator for Seed Fermentor (capacity 35 L) Agitator should be equipped with an AC motor with VFD which facilitates in controlling agitation speed as per process requirement. Agitator motor should be designed for a tip speed of 3-5m/s in gassed condition.	
2.1.9	**Thermo-siphon:** Thermo-siphon shall be provided for the double mechanical seal. Clean steam and chilled water should be supplied to the thermo-siphon for condensate formation. The thermos-siphon shall be maintained the positive pressure always during the operation. Sterile filter assembly with filter housing to be provided for maintain the positive pressure with SIP arrangement and Selection/change over must be provided either clean steam or process air. Thermo siphon should be an independent steam sterilizable and it should have a view glass, pressure switch [Min. & max. set limit],necessary valve, temp. sensor and steam trap.	
2.1.10	**Back Pressure Control Valve:** Automated control valve shall be provided to control the pressure inside the Fermentor. A needle valve shall be provided as a bypass to the automated valve for the manual control on emergency.	
2.1.8	**Sampling valve:** The Fermentor shall be fitted with a zero dead leg re -sterilizable sampling valve. The diaphragm of this valve is made of EPDM and should be of FDA compliant. Independent sterilization of sampling valve shall be provided. The sampling system must equipped with an autoclavable assembly with disc filter, glass bottle of 100 ml. Extra 5No.s of sampling assemble to be provided for each main fermentor[Total-15No.s]	
2.1.9	**Flush bottom valve:** The Fermentor must be equipped with a zero dead leg re-sterilisable flush Bottom valve. The diaphragm of this valve is made of EPDM and is FDA compliant. Independent sterilization of flush bottom valve shall be provided.	
2.1.10	**CIP (Cleaning – In – Place)**: The Fermentor shall be cleaned by using a CIP recirculation pump and the CIP solution will be from either header or mobile CIP station.The Fermentor shall have spray ball(s) to ensure cleaning of the interior surfaces. The design and location of the spray ball is the vendor's responsibility and will be a part of the Design Qualification. The system shall be tested for clean-ability & drainability and shall pass the spray ball coverage test in accordance with the recommendations outlined in ASME BPE-2012; part SD-4 & 5.The vendor shall ensure the cleanability of Fermentor.	
2.1.11	**SIP (Sterilization – In – Place):** The following principles will be applied for SIP of the system,but not limited to these: • The Fermentor should be provided with ESIP and FSIP features • The exhaust and Inlet filters should be of independent sterilizable. • The Agitator mechanical seal , sampling,harvest and flush bottom valve should also be sterilized independently. • The sensors should be reusable and sterilizable type. • All addition valve groups are sterilized along with the Vessel and independent sterilisation provision.	
2.1.12	Seed Fermentor should have a provision for part transfer to the production fermentor B1-FER01, 02 for Hep-B and production fermentor B1-FER04, 05 for HIB. Harvest transfer line SIP & CIP should be provided with necessary valve arrangement from seed fermentor to main fermentors.	

S No.	Description	Remarks from vendor
2.1.13	**Automation:** Each Fermentor should be controlled by an individual PLC and a not less than 15"HMI screen. • HMI should be of Touch screen type with a provision of manual operation. • All critical alarms, interlocks. • All recipes/sequences • All parameters should be user settable. Each PLC from Hep-B and HIB area is connected to a separate local SCADA located in the Hep-B and HIB fermentation room. [Vendor must provide PC -2No.s & colour Printer-2No.s] Windows based supervisory Control and DATA Acquisition Software for monitoring and control of various process parameters with 21 CFR part11 compliant. The Software capable for remote logging and process control. The system suitable for supervisory control for multiple fermentors. The system, designed for process validation, batch management features, multi-parameter display, time based programming of set points, regulation of process by both measured and calculated variables (by using equations), equation writing and its integration for control of Fermentor parameters, ability to set both high and low limits and alarms, graphic /plotting, off-line data integration (Non-editable data sheet and batch reports). Options for manual override of all values, set-points and process parameters during the process. Spare IOs shall be considered for all the fermentors.	

2.2 General design of Feed Vessel :

Feed Vessel is supplied along with all the necessary piping with skid, valves,instrumentation and Control panels, but not limited to these.

S No.	Description	Remarks from vendor
2.1.1	**Dosing Unit:** Addition ports shall be of sterile arrangement with four-way valve assembly for SIP, draining and isolation. A temperature sensor shall be provided near the drain point of the four-way valve assembly. Independent SIP must be provided. All ports shall have a J-tube arrangement facing the interior wall of the vessel. Sterile valve assembly shall be used for addition of solutions from respective containers in to the feed vessel through peristaltic pump. Also Necessary arrangements like hose nipple should be provided. Peristaltic pump should have totalizer, volume /time options.	
2.1.3	**Spray ball:** Vessel shall have sufficient number of spray ball(s) to ensure cleaning of the interior surfaces. The vendor shall ensure cleanability of the Fermentor, 360 degree spray coverage should be ensured.	
2.1.4	**Vent/Exhaust Filter:** Feed vessel should have a vent filter(Hydrophobic, 0.22 µm pore size) with SS316L Housing[CIP/SIP-able], surface finish equivalent to vessel interior and should have necessary drain arrangements for removing condensate during sterilization.	

S No.	Description	Remarks from vendor
2.1.6	**Mixer:** The vessel shall be designed with bottom mounted GMP magnetic mixer. Motor should have a Variable frequency drive to adjust speed from 50-400 rpm. Suitable for liquids up to pH 1-14 and temperature 130°C.	
2.1.7	**Sampling valve:** The vessel shall be fitted with a zero dead leg re -sterilizable sampling valve. The diaphragm of this valve is made of EPDM and should be of FDA compliant. Independent sterilization of sampling valve shall be provided. The sampling system is equipped with an autoclavable glass bottle of 100 ml.	
2.1.8	**Flush bottom valve:** It is Zero Dead Leg type valve with steam sterilizable. It shall be directly welded to vessel bottom centrally; having a PTFE diaphragm and independent sterilisation shall be provided for flush bottom valve.	
2.1.9	**CIP (Cleaning – In – Place)**: The Vessel shall be cleaned by using a CIP recirculation pump and the CIP solution will be from either header or mobile CIP station. The Vessel shall have spray ball(s) to ensure cleaning of the interior surfaces. The design and location of the spray ball is the vendor's responsibility and will form a part of the Design Qualification. The system shall be tested for drainability and shall pass the spray ball coverage test in accordance with the recommendations outlined in ASME BPE-2012; part SD-4 & 5.The vendor shall ensure cleanability of vessel.	
2.1.10	**SIP (Sterilization – In – Place):** The following principles will be applied for SIP of the system: • The Vessel should be provided with ESIP and FSIP features. • The exhaust/Inlet air filters to be sterilized along with the vessel. • The sampling,Harvest/transfer line and FBV should be sterilized independently. • All addition valve groups are sterilized along with the Vessel and independent also. • The sensors should be reusable and sterilizable type.	
2.1.11	**Automation:** Feed vessels shall be communicated with the production Fermentor. Feed vessel control shall be done by Fermentor PLC, so necessary IO modules shall be considered in the Fermentor PLC.	

Note:

1. HIB, 2 no's of 500L Production Fermentor and 1 no of 35 L seed Fermentor will be mounted on a common skid. Operational accessibility should be provided for all the filters and transfer lines.

2. Hep - B , 2 nos of 500 L production Fermentor , 1 no of 35 L seed Fermentor and 4 nos of 150 L Feed vessel will be mounted on a common skid with platform. Operational Accessibility should be there for all the filters and transfer lines. Each main fermentor should have a 2no.s of 150L feed vessel.

3. All 500L production Fermentors should be provided with a ladder to access the top portion.

2.3 General Requirement for Fermentor

2.3.1 Nozzle schedule for Fermentor of Hep-B 500 L capacity :

2.3.1.1 **Top dish**

- Sight/Light glass
- Spray ball
- Diapharm pressure guage and pressure sensor
- Rupture disc
- Foam sensor.
- Antifoam addition port 0.5" port (TC) -1 no
- Exhaust Line
- Spare port -1 No [TC]

2.3.1.2 **Upper wall side**

- Vertical Glass
- Acid addition port 0.5"port (TC) -1 no.
- Alkali addition port 0.5"port (TC) -1 no.
- Media addition port 1"port (TC) -2 nos.
- Inoculum addition port 1" port (TC) -1 no.
- Feed addition port 1" port (TC) -1 no.
- Jacket outlet
- Aeration Sparger -1 no.
- Aeration-overlay-1 no

2.3.1.3 **Lower wall side**

- Temperature sensor (PT 100) -1 no.
- DO probe -1 no.
- pH probe - 1 no.
- Jacket inlet -1no.
- Sampling Port -1no.
- Spare port -1no.

2.3.1.4 **Bottom dish**

- Flush bottom valve
- Bottom mounted agitator

2.3.2 **Nozzle schedule for Fermentor of HIB 500 L capacity :**

2.3.2.1 **Top dish**

- Light/Sight glass
- Spray ball
- Diapharm pressure guage and pressure sensor
- Rupture disc
- Foam sensor
- Antifoam addition port 0.5" port (TC) -1 no.
- Exhaust port
- Spare port -1 No [TC]

2.3.2.2 **Upper wall side**

- Vertical Glass
- Acid addition port 0.5"port (TC) -1 no.
- Alkali addition port 0.5"port (TC) -1 no.
- Media addition port 1"port (TC) -1 no.
- Inocculum addition port 1" port (TC) -1 no.
- Jacket outlet -1No.
- Aeration Sparger -1 no.
- Aeration Overlay-1no.

2.3.2.3 **Lower wall side**

- Temperature sensor (PT 100) -1 no.
- DO probe -1 no.
- pH probe - 1 no.
- Sampling Port – 1no.
- Jacket inlet – 1no.
- Spare port – 1no.

2.3.2.4 **Bottom dish**

- Flush bottom valve
- Bottom mounted agitator

2.3.3 **Nozzle schedule for seed Fermentor of 35 L:**

2.3.3.1 **Top dish**

- Light/Sight glass
- Foam Sensor port
- Spare port
- Spray ball
- Diapharm pressure guage and pressure sensor
- Rupture disc
- Top driven Agitator
- Antifoam addition port 0.5" port (TC)
- Exhaust port

2.3.3.2 **Upper wall side**

- Vertical view Glass
- Acid addition port 0.5" port (TC)
- Alkali addition port 0.5" port (TC)
- Media addition port 1" port (TC)
- Inoculum addition port 1" port (TC)
- Jacket outlet
- Aeration Sparger
- Aeration-overlay

2.3.3.3 **Lower wall side**

- Temperature sensor (PT 100) -1 no.
- DO probe -1 no.
- pH probe - 1 no.
- Spare port
- Sampling Port
- Jacket inlet

2.3.3.4 **Bottom dish**

- Flush bottom valve

2.3.4 **Nozzle schedule for Feed Vessel of 150 L :**

2.3.4.1 **Top dish**

- Light/Sight glass
- Spare port
- Spray ball port
- Diapharm pressure guage and pressure sensor port
- Rupture disc port
- Vent/Exhaust port

2.3.4.2 **Upper wall side**

- Vertical view Glass
- Addition port 1/2" port (TC) – 2 no.
- Jacket outlet

2.3.4.3 **Lower wall side**

- Temperature sensor (PT 100) -1 no.
- Sampling Port
- Jacket inlet
- Spare port

2.3.4.4 **Bottom dish**

- Flush bottom valve
- Bottom Mounted GMP Mixer

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

- **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 5.6

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. In case of any 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 cost for necessary options becomes 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 vendor's 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 HBL before submitting the quotes.
10.	The makes requested are standard international makes. In case of any deviation, vendor to seek clarification from HBL before submitting the offers.
11.	Refer document "Installation Requirement Specifications and Specific Instructions" with URS NPI_120310_EQP_IRS_S1_01
12.	Refer tender document NPI_120310_EQP_S1_TD_10

Specifications	Remarks
3.0 PROCESS DESCRIPTION	
3.1 Input & Charging method (Fermentor)	
3.1.1 Input & Charging for Seed and Production Fermentor: 3.1.1.1 Media and Inoculum shall be added to the seed Fermentor/Fermentor by using pump/pressure, bottle and sterile valve assembly. 3.1.1.2 Media to the Seed fermentor/production Fermentor shall be added from media preparation vessel with the help of sterile valve assembly. Inoculum shall be added from the seed Fermentor to the production Fermentor by part transfer.	
3.1.2 Acid and Base solution shall be added through fixed peristaltic pump to maintain the pH.	
3.1.3 Components from Feed vessel also shall be added to the production Fermentor (Hep-B) by using peristaltic pump [Variable speed with totalizer] and sterile valve assembly.	
3.2 Brief Process Steps	
The Fermentor has to be designed for microbial fermentation on batch and fed batch mode of operation	
3.2.1 Media shall be transferred to the cleaned and sterilized Fermentor for full vessel sterilization. Design the Fermentor in such a way that charring of media shall be avoided. Media shall be cooled by using cooling water/chilled water upto 35°C.	
3.2.2 Process parameters like agitator speed, pH, pressure, DO, air-flow and temperature are controlled, during the process.(Auto mode, Cascade mode and Manual mode options for controlling should be provided)	
3.2.3 For Hep-B, feed shall be added in the specified intervals from the feed vessels. Variable speed pump with totalizer shall be provided for the accurate transfer of feed to the Fermentor. The same should be recorded in the respective Fermentor PLC.	
3.2.4 Samples can be drawn through sampling valve.	
3.3 Output & Discharging method	
3.3.1 Process fluid is harvested and transferred for further processing.	
3.4 Input & Charging method (Feed Vessel)	
3.4.1 The components for the preparation of feed shall be added in the vessel.	
3.4.2 WFI is added in to the feed vessel.	
3.4.3 After FSIP, component will be added through sterile addition port by using peristaltic pump. [Variable speed with totalizer]	
3.5 Brief Process Steps	
3.5.1 Components are mixed with WFI at required temperature.	
3.5.2 Samples can be drawn through sampling valve.	

Specifications	Remarks
3.6 Output & Discharging method	
3.6.1 The feed shall be charged to the Fermentor as per process requirement.	
4.0 PRODUCTIVITY REQUIREMENT	
4.1 Change Over Time	
Not Applicable	
4.2 Others(If any)	
Not Applicable	
5.0 CONTAINMENT	
Not Applicable	
6.0 GMP REQUIREMENTS	
6.1 Process control	
The equipment must operate and control the following process parameters.	
6.1.1 Temperature and pressure control(for Fermentor/Feed vessel)	
6.1.2 Speed of the agitator during process (for Fermentor)	
6.1.3 Speed of the mixer during the process(for feed vessel)	
6.1.4 DO for control and monitor (only for Fermentor)	
6.1.5 pH for control and monitor.(During fermentation)	
6.1.6 Rate of flow of process Air Overlay and sparger.	
6.1.7 Pneumatically actuated individual valves for the clean utilities like pure steam, CIP, PW and WFI at the header.	
6.2 Failure mode detection	
Equipment shall be capable to detect the following failure, notify the operator with alarm and shutdown the process: (if it exceeds by 0-10% (i.e. tolerance limit) of the set point value):	
6.2.1 Agitator RPM is out of set range(for Fermentor)	
6.2.2 Mixer RPM is out of set range(feed vessel)	
6.2.3 pH is out of set range	
6.2.4 Temperature is out of set range	
6.2.5 Low/high pressure	
6.2.6 Air flowrate out of set range (only for Fermentor)	
6.2.7 Low/high volume	
6.2.8 Abrupt change in temperature in a particular time (at constant operating temperature)	

Specifications	Remarks
6.3 In – Process control	
6.3.1 DO cascade control should be provided with agitation and aeration.	
6.3.2 During fermentation, it should have provision for sampling of product solution.	

6.4 Level of instrumentation

Sufficient and suitable instrumentation for the process, safety and productivity control as indicated in the following table,but not limited to these:

Parameter	Purpose	Type of control and Instrumentation	Remarks
Fermentor			
Speed	To control,monitor,indicate and record agitator speed	Variable frequency drive with indicator	
Temperature	To monitor, indicate,record and control the temperature	Temperature sensor and transmitter	
Pressure	To monitor, indicate,record, and control the pressure	Pressure sensor and transmitter	
pH	To control ,monitor,record and indicate the product pH	pH sensor	
Level/Volume measurement	To monitor,indicate,record & control the level of the product in the vessel	DP sensor-for production Fermentor	
		Potentiometric level sensor-for seed Fermentor.	
Dissolved oxygen	To control ,monitor,record and indicate the dissolved Oxygen (0-100%)	Amperometric pO_2 electrode	
Process Air	Air flow to monitor, indicate,record and control	Mass Flow controller	
Peristaltic Pump	To dose inoculum, media, acid, alkali,feed, Antifoam etc.	Peristaltic pump	
Feed Vessel			
Mixing Speed	To control mixer speed	Variable frequency drive with display	
Temperature	To monitor, indicate and control the temperature	Temperature sensor and transmitter	
Pressure	To monitor, indicate and control the pressure	Pressure sensor and transmitter	
Level/Volume measurement	To monitor the level of the product in the vessel	Potentiometric level sensor	

Specifications	Remarks
6.5 Batch data display and record printing	
6.5.1 Batch data printing should include these parameters, but not limited to these, • Time, Temperature, Volume • Operator name and space for signing 6.5.2 SS 304 Control panel (HMI) with the following (not limited to these) • Display of temperature, DO, pressure, pH, Volume and RPM • Provision for manual operation, CIP/SIP time duration, Emergency stop Button Also refer IRS	
6.6 GMP requirements (Others)	
6.6.1 All nozzle connection shall be sanitary type and special attention shall be given in shape and dimension of the nozzle and connection to realize efficient cleaning and steaming process. All nozzle connection should comply with dead leg requirement.	
6.6.2 All nozzles shall be flushed to the wall on closure.	
6.6.3 Steam traps shall be provided where ever required at the system.	
6.6.4 Isolation valves should be provided wherever necessary	
6.6.5 All valves in the sterile part of the Fermentor /vessel should be of sanitary Diaphragm valves	
6.6.6 All gaskets should be made up of food grade/Silicone/EPDM	
6.6.7 Fermentor should meet ASME pressure vessel standards, ASME section VIII,DIV.1,ASME BPE 2012,bio-procecessing equipment, GAMP 5, a risk based approach to compliant ,US FDA 21 CFR part 11 for electronic records and electronic signatures, GAMP for validation of automation system, IEC 60529 standards for protection of panel enclosure.	
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 Separate drain for Biowaste and condensate shall be provided with necessary isolation valves & NRV.	
6.7.2 Nozzle shell shall be seamless.	
6.7.3 Nozzles, adaptors, instrument shall comply with ASME BPE 2012 compliant.	
6.7.4 Total motor drive assembly with SS304 cover with TEFC eff 1.	
6.7.5 Feed addition peristaltic pump must be in-line sterilisable.	

Specifications	Remarks
6.7.6 **Design Parameters:** 6.7.6.1 Shell working Pressure- FV to 2.5 bar(g) 6.7.6.2 Shell working Temperature- 2-140°C 6.7.6.3 Shell sterilization Temperature- 121°C 6.7.6.4 Shell design Pressure- Vendor to specify 6.7.6.5 Shell design Temperature- Vendor to specify 6.7.6.6 Jacket working Pressure- FV to 4 bar(g) 6.7.6.7 Jacket working Temperature- 140°C 6.7.6.8 Jacket design Pressure- Vendor to specify 6.7.6.9 Jacket design temperature- Vendor to specify	
6.7.7 The equipment shall be easily accessible for cleaning the product non-contact part at maintenance side of the equipment.	
6.7.8 Fermentor & its vessels shall be on 4 legs with pad plates MOC: SS 304	
6.7.9 **Performance criteria during FAT/SAT, but not limited to these:** • Pressure hold test should be performed during FAT • Thermal Mapping of Fermentor and Vessel. • Spray ball coverage test during FAT • All FAT/SAT IQ,OQ as per IRS	
7.0 CONSTRAINTS	
7.1 Equipment location and available space	
a) B1-FER-01, B1-FER-02 ,B1-FER-03 and B1-FV-01,02,03,04 will be installed in the **Multiple Bacterial Bulk Block** of IVC Vaccines manufacturing facility at HLL BIOTECH LIMITED,Chengalpattu as follows: **Floor:** Ground floor Multiple Bacterial Bulk Block **Section :** Hepatitis – B (Hep – B) **Room No. :** B1G007 **Room dimension :** 10700 X 12105 mm **False ceiling height:** 4000 mm **Equipment ID:** B1-FER-01, B1-FER-02, B1-FER-03,B1-FV-01,02,03,04 **Floor:** Ground floor Multiple Bacterial Bulk Block **Section:** Haemophilus Influenza type – B (HIB) **Room No. :** B1G106 **Room dimension :** 10230 X 12869 mm **False ceiling height:** 4500 mm **Equipment ID:** B1-FER-04, B1-FER-05, B1-FER-06 The equipment location is indicated in the relevant block of the layout enclosed as **URS Annex 1.**	

Specifications	Remarks
7.2 Available Utility	
7.2.1 Cooling Water @25-30°C,3 bar _____ (Report requirement)	
7.2.2 Chilled Water @6-12 °C _____ (Report requirement)	
7.2.3 Purified Water @ 30 °C _____ (Report requirement)	
7.2.4 Compressed Air @ 8 bar _____ (Report requirement)	
7.2.5 O_2 @ 3 bar _____ (Report requirement)	
7.2.6 WFI (Hot loop) @ 2 bar [80-90 °C] _____ (Report requirement)	
7.2.7 Plant Steam @ 3-8 bar _____ (Report requirement)	
7.2.8 Pure steam @ 2.5 bar _____ (Report requirement)	
7.2.9 Electricity : (Report requirement)	

8.0 ABBREVIATION

Abbreviation	Definition
cGMP	current Good Manufacturing Practices
CIP	Clean In Place
DO	Dissolved Oxygen
EPDM	Ethylene propylene diene monomer (M-class) rubber
FAT	Factory Acceptance Test
FER	Fermentor
FSIP	Full vessel sterilisation in place
GMP	Good Manufacturing Practices
HBL	HLL Biotech Limited
HMI	Human machine interface
IRS	Installation Requirement Specification
LPM	Litre per minute
NA	Not Applicable
NPI	NNE Pharmaplan India Ltd
O_2	Oxygen
PRV	Pressure Reducing Valve
SAT	Sight Acceptance Test
SIP	Sterilization In Place
TBD	To be discussed
TC	Tri-clover Clamp
TEFC	Totally Enclosed and Fan cooled
URS	User Requirement Specification

9.0 REVISION INDEX

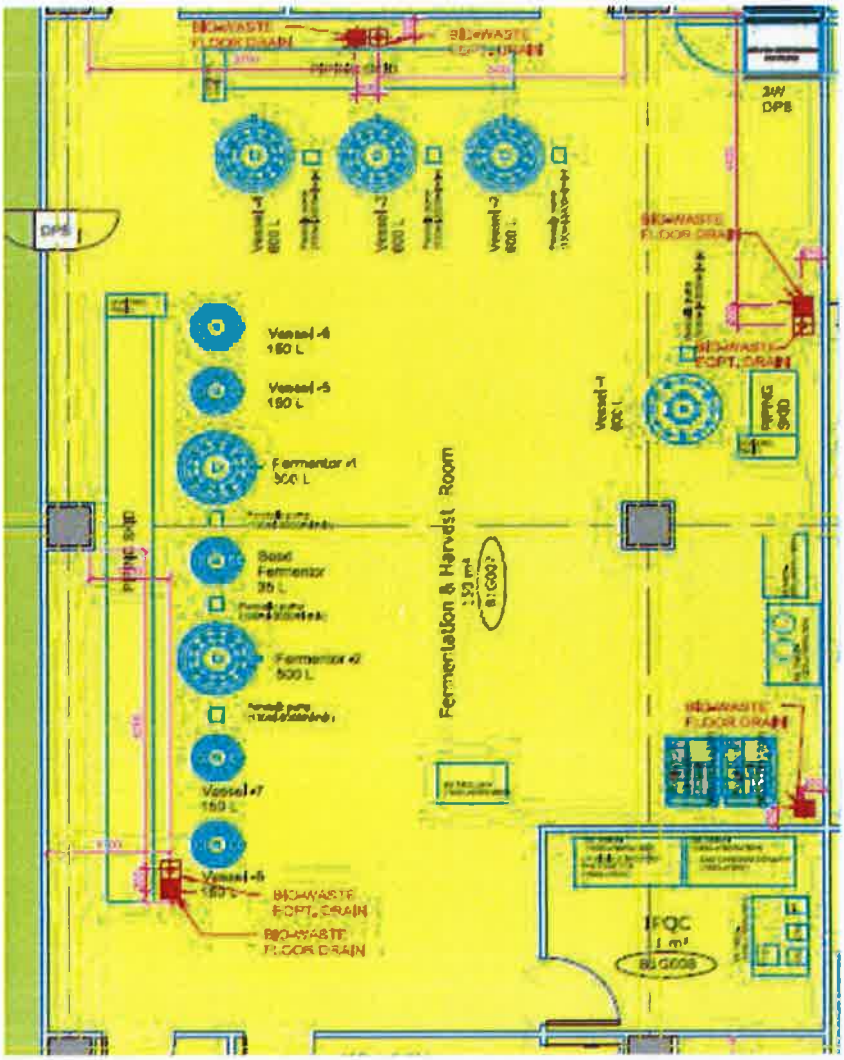
Revision	Date	Reason for Revision
00	22.01.2015	New Document
01	09.04.2015	Updated as per comments received on 30.03.2015 and Telecom on 08.04.15 and 09.04.15

URS Annexure 1: LAYOUT A

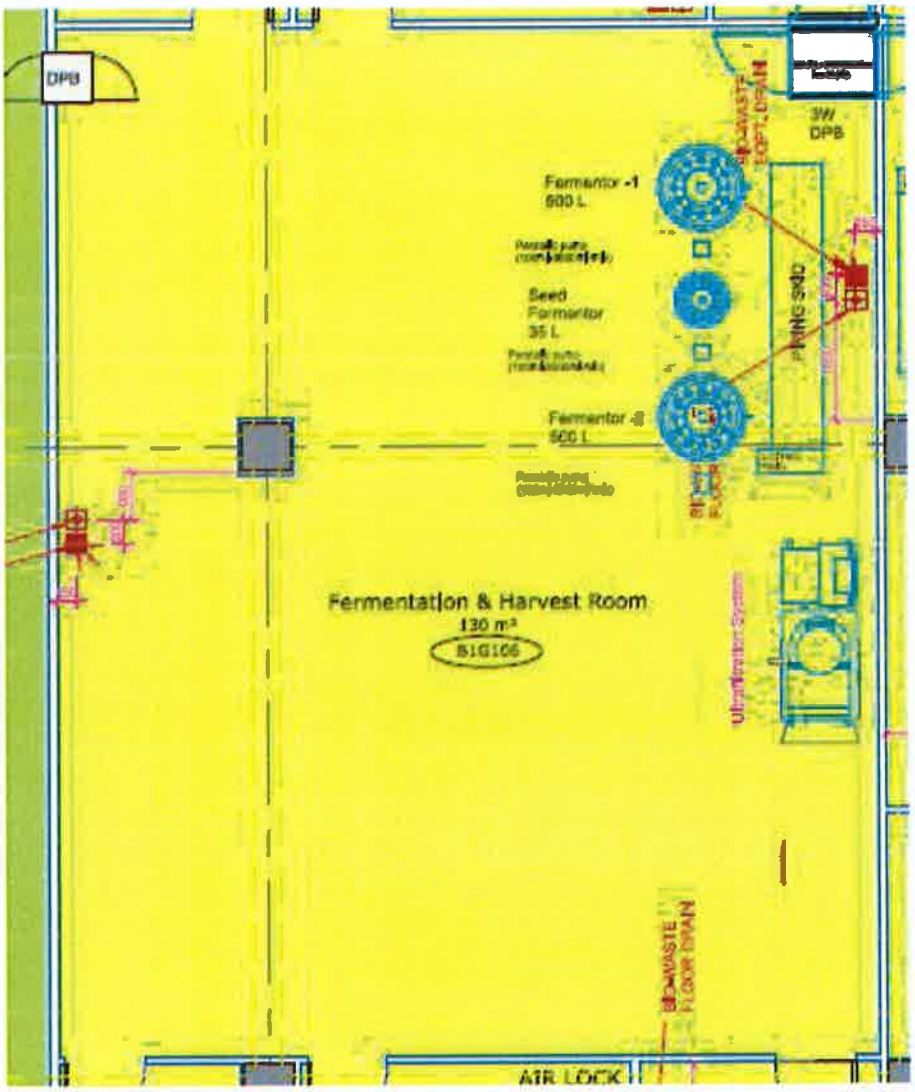
MULTIPLE BACTERIAL VACCINE BLOCK

Hepatitis - B

Fermentation & Harvest (B1G007)



Haemophilus Influenza type - B (HIB)
Fermentation & Harvest (B1G105)



URS Annexure 3: 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/E&H
4	Temperature sensor	Negele/ Radix/E&H
5	p H sensor	Mettler Toledo/E&H
6	Pressure transmitter	Wika /Dwyer/Sensocon
7	Pressure regulator	Festo/SMC
8	DO sensor and transmitter	Mettler Toledo/E&H/Hamilton
9	Mass flow controller	Burkert / Bronkhorst/E+H
10	Rotameter	Gemu/Burkert
B	MECHANICAL	
9	Pressure gauges	Wika/waree/Denver/Negele
10	Vent filter cartridge	Sartorius/Pall/ Millipore
11	Filter housing	Sartorius/ Pall/Millipore
12	Spray ball	Hake/Lechler/Alfa laval
13	Diaphragm valve(Manual)	Gemu / SED
14	Ball valve(Manual)	Modentic/Saunders/Alfa laval
15	Sampling valve	Novaseptic/GEMU
16	Flush bottom valve	Novaseptic/GEMU
17	Safety relief valve	Herose/SS Spirax /Amtech valves
18	Rupture disc	Zook/Elfab/ Fike
19	Peristaltic pump	Watson Marlow/Masterflex
20	Mixer	Novaseptic/Roplan
21	Agitator	PRG
22	Steam trap	Steriflow/Spirax
23	Back pressure Control valve	GEMU/SED/Burkert
24	Clean steam PRV	Spirax/Forbes marshall
C	PNEUMATIC	
25	Diaphragm valve(Automatic)	Gemu / SED/Burkert
26	Angle seat valve(Automatic)	Gemu / SED/Burkert
D	ELECTRICAL	
27	Lamp	Papenmeier