

# HLL LIFECARE LIMITED, CHENNAI

## Revival of DPT Vaccine Manufacturing Facility, PII, Coonoor

nne pharmaplan®

### User Requirement Specifications

**Equipment/System**

Microbial Seed Fermentor

**Identification #**

D-SFR 01

**Document#**

URS/ D-SFR 01

**Effective Date #**

2013-08-26

**Revision#**

06

## User requirement specifications Microbial Seed Fermentor

| Process Code | Area       | Equipment code | Qty(Nos) | Capacity |
|--------------|------------|----------------|----------|----------|
| D            | DIPHTHERIA | D-SFR 01       | 1        | 15L G.V. |

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### URS Annexure List

| URS Annex No. | Detail  |
|---------------|---|
| 1.            | Layout showing the location of the Seed Fermentor in Diphtheria Block |
| 2.            | List of Preferred make for Major 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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| Name/ Designation   | Signature | Date |
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| Name/ Designation  | Signature | Date |
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| Name/ Designation   | Signature | Date |
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| Pasteur Institute of India  |           |      |

### Authorized by

| Name/ Designation                               | Signature | Date |
|---|-----------|------|
| Project Authority<br>Pasteur Institute of India |           |      |

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## 2.0 EQUIPMENT DESCRIPTION

The equipment described in this URS is a “**Seed Fermentor**”. A seed fermentor is a vessel that is designed for growing the inoculums seed which will be used to seed the production scale fermentor. The Fermentor including control panel will be installed in a clean room of Class “C”.

This Inoculum is for batch operation.

The equipment should have the following specifications to run the operation smoothly.

**2.0.1. TABLE 1**

| S. No. | Description            | Purpose  | MOC          |
|--------|------------------------|--|--------------|
| 1.     | Shell                  | Cylindrical, for fermentation  | SS316L       |
| 2.     | Top closure            | Flat Lid   | SS316L       |
| 3.     | Bottom closure         | Torispherical dish   | SS316L       |
| 4.     | Jacket                 | Hollow type; For temperature control   | SS304        |
| 5.     | Insulation             | To avoid heat loss   | Mineral wool |
| 6.     | Cladding               | Outer cover to insulation  | SS304        |
| 7.     | Agitator (top mounted) | For mixing the process fluid constantly & keep uniform solution and to avoid dead air pocket | SS316L       |
| 8.     | Height/Diameter Ratio  | 3.0:1  | -            |


**2.0.2. TABLE 2**

| SI.NO | Description                            | Specification |
|-------|--|---------------|
| 1.    | Geometric volume                       | 15L           |
| 2.    | Maximum working volume                 | 10L           |
| 3.    | Quantity                               | 1 No          |
| 4.    | Min mixing volume                      | 3.5L          |
| 5.    | Fermentation temperature range         | 35±1°C        |
| 6.    | Rise in temperature (heating capacity) | 2 deg C/min   |
| 7.    | Fall in temperature (cooling capacity) | 2 deg C/min   |
| 8.    | Temperature control deviation          | ±0.1°C        |

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|    |                |  |
|----|----------------|--|
| 9. | Surface Finish | Internally Electro polished Ra ≤ 0.6 μm, according to ASME BPE   |
|    |                | Externally Mechanically polished up to Ra <1.2μm matt finish for the jacket.<br>Top and bottom dish - mirror finish. |
|    |                | Stainless steel piping interior Ra≤ 0.6μm, according to ASME BPE   |
|    |                |  |

**2.0.3.** The Seed fermentor shall be skid mounted which should be supplied along with all the necessary piping, valves and instrumentation. The equipment must be designed for closed operation with the following specifications:

- Dosing Unit for Inoculum:** Inoculum will be added to the seed fermentor by flexible hose through the sterile valve assembly and individual Peristaltic pump .
- Dosing unit for Media:** The pre-filtered Media will be added to the seed fermentor by sterile flexible hose through the sterile valve assembly using Peristaltic pump.
- The DO is monitored by:
  - In-situ amperometric DO probe
- Dosing Unit for Antifoam:** Antifoam will be added to the seed fermentor by flexible hose through the sterile valve assembly and individual Peristaltic pump. The Foam shall be controlled by using the
  - Foam sensor
  - By the addition of Antifoam
- Aeration Supply System(Sparger):** Aeration system for sparger consists of ring sparger. The air inlet Process air requirement for sparger is 5 LPM.


The Fermentor is having facility for supplying of process air during process. Process Air addition line is provided with:

- Pressure control valve
  - Sterilizable SS housing with 0.2/0.22 micron sterile filter, which is to be sterilized along with vessel.
  - Rotameter for sparger
- Aeration Supply System(Overlay):** Aeration system consists for Overlay :  
Process air requirement for overlay is 4 LPM  
The Fermentor is having facility for supplying of process air during process . Process Air addition line is provided with:
    - Pressure control valve
    - Rotameter for Overlay
  - Temperature Control:** The temperature during fermentation shall be controlled via circulation of utilities (plant steam, Cooling water, Chilled water, etc) in the jacket with electric heater or steam and a circulation pump. Temperature control during cultivation 35-37°C (tolerance limit: ±0.1 °C) & during sterilization (tolerance limit: ±0.1 °C)
    - The system consists of closed loop pressurized thermostat system with recirculation pump 2 heat exchangers for heating and cooling alternatively which provides a high flow through the hollow vessel jacket and ensures fast temperature control at high accuracy with PT 100 probe (sterilizable).
    - Electrical heater ,Heat exchanger and steam for cooling water & chilled water for operation

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temperature

- Safety relief valve for jacket
- Bourdon type pressure gauge for jacket utility
- Pneumatically operated valves for steam and cooling water/ chilled water

**h. Pressure control:** Pressure of the vessel and CIP/SIP steps shall be controlled by the following:

- Compound Pressure gauge for vessel and Pressure transmitter
- Pressure reducing valve for pure steam lines
- Back pressure control valve in the exhaust line

**i. Agitator:** The vessel shall be designed with top driven agitator. Mechanism should provide minimum shear even at high speeds and maintenance. The agitator shall have shaft with 1 height adjustable Rushton type impeller with speed control from 20-1000 rpm (approx. 500 rpm will be the operating speed). The specifications of the agitator are as follows:

- The agitator shaft to be provided with 6 bladed Rushton turbine type impellers.
- Bearing frame and direct motor drive arrangement
- Shaft seal: Double mechanical seal with thermosyphon should have the sterile air inlet connection for pressurization during operation. During seal SIP, pure steam shall be used.
- Shaft, length shall be decided by the vendor according to the height of the vessel
- VFD should be provided to control the RPM
- Vendor shall specify the following:
  - SS316 L, 6 Bladed Rushton turbine type shall be provided
  - Shaft diameter
  - Width of the blade
  - Height of the blade
  - Diameter of the disc
  - Tip speed
  - RPM: 20 to 600
- Interconnection shall be provided with the sensoric arrangement (eg. DO sensor) of the system.
- Thermosyphon shall be provided with the utility connection and CIP/SIP.
- MOC:
  - SS 304 bearing frame
  - SS 316L shaft of the agitator
  - SS 316L disc
  - SS316L Impeller

**j. Vent Line/Exhaust Line:** Fermentor vent line includes:

- an exhaust condenser,
- a sterile hydrophobic vent filter.
- A Rupture disc is mounted on Fermentor vessel to relieve excess pressure during operations.

**k. Flush Bottom Valve/Sampling valve:** It should be zero dead leg type valve attached directly to the bottom of the vessel, with a provision for sterilization. The diaphragm shall be of PTFE type.


**l. CIP (Cleaning – In – Place):** CIP shall be done manually using the CIP solution.

- SS 316L Spray ball shall be provided for the cleaning of the interior of the vessel and all the

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nozzles on the top lid and nozzles, ports on the vessel.

**m. SIP (Sterilization – In – Place) :** The following principles will be applied for SIP of the system:

- The vessel should be provided with ESIP/FSIP features
- The exhaust air filters to be sterilized along with the vessel.
- The sampling valve and Flush bottom valve can be sterilized independently.
- All addition valve groups for media, inoculum, antifoam are sterilized along with the vessel.
- The sensor ports should be reusable and sterilizable type.
- Manifold shall be provided at the top so as to connect SIP recipe clean steam along with the pneumatic diaphragm valve operated directly through HMI.

**n. Controller:** - PLC Based Controller(Non-editable data format to be obtainable)with a 15" industrial touch screen HMI (Displaying data trends as Graphs, synoptic view of running parameters etc).

**o. The HMI shall be touch screen type (Provision for manual operation also to be provided). All setting shall be user adjustable.**

- HMI screen size shall be of 15 inches
- 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 inoculum, media and antifoam
- All Recipes/ sequences (Process, CIP , SIP, transfer etc)
- P&ID of the vessel along with instrumentation details
- Login details
- HMI screen showing simulation of valves

### 2.0.4. Nozzle schedule :

#### 1. Top Lid:


The Fermentor Head Plate will have:

- Port for addition of Anti foam with sterile valve assembly-1 No
- Port for Foam sensor-1 No
- Port for Rupture disc-1 No
- Port for Compound Pressure Gauge-1 No
- Port for Pressure transmitter-1 No
- Port for Spray ball- TC clamps with gasket-1 No
- Port for exhaust Outlet exhaust Condenser with reusable & sterilizable Filter (hydrophobic vent filter 0.22µm) - TC clamps with gasket-1 No
- Port for Light glass-1 No
- Port for Agitator-1 No
- 19 mm spare port with septum-1 No



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### 2. Upper wall side:

The fermentor's upper wall side normally will have :

- Port for Addition of inoculum with sterile valve assembly-1 No
- Port for addition of pre-filtered media-1 No
- Vertical view Glass –Bolted with gasket-1 No
- Port for sparger -1 No
- Port for overlay air -1 No

### 3. Lower wall side:

The fermentor lower wall side shall have the following ports and elements shall be placed and fastened there:

- Ports for sensors:
  - 25 mm Temperature sensor-1 No
  - 25 mm pH sensor-1 No
  - 25 mm DO sensor-1 No
  - 25 mm Spare port-1 No
- Port for Sampling valve, sterilizable -1 No

### 4. Bottom Connections

- Port for Flush bottom valve ,sterilizable-1 No

### 5. Jacket Connection


- Jacket Bottom: Jacket Inlet port, jacket drain
- Jacket Upper side: Jacket outlet port, Safety relief valve

**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**
    - **SI.NO 2 and 3** :FDA guidance for industry
    - SI.NO 5 CE Conformity,
    - SI.NO 7 ANSI/NSF 49-2008, ISO 14664, ISO 8362
    - SI.NO 8 ISO 14664
    - SI.NO 9 ISO 8362
  - Sec 5.4.1 All metallic product contact / critical surfaces should be constructed of SS316 L grade with internal mirror finish (< 0.5µm Ra for filling line and < 0.8µm Ra for lyophiliser) and external surface matte finish (< 1.2µm Ra).
- For surface finish values refer the point 9 under Sec 2.0.2 Table 2 mentioned in the URS
- Sec 5.6

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### 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 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 cost for necessary options become necessary the item must be clearly stated.   |
| 4.  | In case that the requirement includes a question or request or an 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.  | <b>Special Instruction</b> <ol style="list-style-type: none"> <li>If no comments against any specification shall be considered as "NO" and</li> <li>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.</li> </ol>  |
| 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/01  |

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| Specifications | Remarks |
|----------------|---------|
|----------------|---------|

### 3.0 PROCESS DESCRIPTION

#### 3.1 Input & Charging method

*Note: This section also includes the charging method of process media along with charging method for material input.*

- 3.1.1 Inoculum from flasks shall be transferred to the seed fermentor through sterile flexible piping the help of peristaltic pump.
- 3.1.2 Pre filtered media shall be fed into the seed fermentor through sterile valve assembly and sterile flexible hose using fixed speed peristaltic pump
- 3.1.3 Temperature of the microbial biomass shall be adjusted to the working temperature with the help of utilities.

#### 3.2 Brief Process Steps

##### A) The tanks have to be designed for the preparation of media and Propagation of microbial organisms respectively.

- 3.2.1 Transfer of inoculums, media to the fermentor.
- 3.2.2 Antifoam is added into the vessel, whenever the foam to be controlled.
- 3.2.3 The temperature of the media is maintained by circulating the utilities in the jacket using electrical heater, appropriate circulation pump and temperature sensors.
- 3.2.4 Process parameters like agitator speed, temperature, pressure, pH & DO(only monitoring), air-flow are measured, during the process, samples can be taken through sampling ports.

#### 3.3 Output & Discharging method

- 3.3.1 The fermentation broth after the completion of fermentation cycle is transferred to production scale fermentor with the help of flexible hose aseptically

### 4.0 PRODUCTIVITY REQUIREMENT

#### 4.1 Desired/ suggested capacity

Min: 3.5L  
Max: 10L  
GV: 15L

#### 4.2 Standard batch size

Not-applicable

#### 4.3 Change over time


Not Applicable

#### 4.4 Others(if any)

Not Applicable

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### 5.0 CONTAINMENT

Not Applicable

### 6.0 GMP REQUIREMENTS

#### 6.1 Process control

6.1.1 The fermentor shall essentially have the necessary provisions for adjustment / control for the following critical process parameters:

i) Temperature of the process

ii) Pressure within the vessel

iii) Foam

iv) DO(Only monitoring)

v) pH(Only monitoring)

vi) Rate of flow of process Air (Overlay and Sparger)

vii) Duration of CIP and temperature ,pressure during CIP

viii) Duration of SIP and temperature ,pressure during SIP

ix) RPM of agitator

x) Pneumatically actuated individual valves for the clean utilities like Pure steam, CIP,PW and WFI at the header.

#### 6.2 Failure mode detection

**A. The equipment shall be capable to detect the failure, notify the operator with audio / video alarm and shut down the process.**

a) Agitator RPM is out of set range

b) pH is out of set range

c) Temperature is out of set range

d) Low/high pressure

e) Air flow being out of range

f) Low/high volume


g) Abrupt change in temperature in a particular time (at constant operating temperature)

**B. Equipment shall shutdown the process (if it exceeds tolerance limit of the set point value)**

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### 6.3 In – Process control

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:

| Parameter                           | Purpose   | Type of control and Instrumentation                      |
|-------------------------------------|---|--|
| Temperature vessel                  | To monitor, indicate and control the fermentation temperature.    | Temperature probe with indicator and controller (PT 100) |
| Temperature of the Jacket           | To monitor, indicate and control the jacket temperature.          | Temperature probe with indicator and controller          |
| pH                                  | Monitoring of pH (2-12)   | pH probe/transmitter                                     |
| Dissolved oxygen                    | To monitor and indicate the dissolved oxygen (0-100%)             | Amperometric pO <sub>2</sub> electrode                   |
| Anti-Foam                           | To control and remove the foam in the vessel                      | Foam sensor  |
| Agitation                           | To monitor, control and indicate agitator speed                   | Variable frequency drive with indicator                  |
| Pressure                            | To monitor, indicate and control the vessel pressure and for SIP. | Pressure transmitter with indicator and controller       |
| Time                                | Timer control of process and monitoring SIP process               | Timer (HMI)  |
| Process Air for Sparger and Overlay | To monitor, control and indicate Air flow                         | Rotameter  |
| Dosing                              | To dose Media , inoculum and Antifoam                             | Peristaltic pump(2 Nos)                                  |

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### 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.  
Realtime online printing shall be available for batch report

### 6.6 GMP requirements (Others)

- 6.6.1 The air housings in the vessel shall be provided with Staubli connectors for in-situ integrity testing of the vent filters.
- 6.6.2 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.
- 6.6.3 All nozzles shall be flushed to the wall on closure.
- 6.6.4 Nozzle length shall be minimized (less than 2D) to avoid cold spot during steam sterilization.
- 6.6.5 Bottom discharge and sampling valve shall be zero dead leg type.
- 6.6.6 Utility operation shall be preferably automatic and valves shall be placed inside of aseptic area.
- 6.6.7 Steam traps shall be provided where ever required at the system.


### 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 .
- 6.7.2 Nozzle shell shall be seamless.
- 6.7.3 Nozzle connection to be Triclover.
- 6.7.4 Nozzles, adaptors, instrument shall comply to ASME BPE compliant.
- 6.7.5 Total motor drive assembly with SS304 cover with TEFC eff 1.
- 6.7.6 Instrumentation and control for Automatic operation of the unit (PLC).
- 6.7.7 **Design Considerations:**
- 6.7.7.1 Vessel working Pressure: Full Vacuum to 2.5 bar(g)
  - 6.7.7.2 Vessel working Temperature: 25 °C to 134 °C.
  - 6.7.7.3 Vessel design Pressure: Vendor to specify
  - 6.7.7.4 Vessel design Temperature: Vendor to specify
  - 6.7.7.5 Vessel sterilization Temperature: 121 °C
  - 6.7.7.6 Jacket working Pressure: Full Vacuum to 4 bar(g)
  - 6.7.7.7 Jacket working Temperature: 2 °C to 135 °C.
  - 6.7.7.8 Jacket design Pressure: Vendor to specify
  - 6.7.7.8 Jacket design Temperature: (Vendor to specify)

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| Specifications | Remarks |
|----------------|---------|
|----------------|---------|

|       |  |  |
|-------|--|--|
| 6.7.8 | 1 No of fixed speed Peristaltic pump is required for the addition of Media, Inoculum addition and 1 No of fixed speed Peristaltic pump is required for the addition of Antifoam. |  |
|-------|--|--|

|       |   |  |
|-------|---|--|
| 6.7.9 | <b>Cabling</b><br>All cabling and pneumatic tubing within the individual skid will be performed by Vendor.<br>Cabling and pneumatic tubing is routed via stainless steel protective pipes with open ends.<br>Segregation between power cables and signal cables will be provided.<br>Motor cabling between the individual skids and the MCC's in the technical area will be performed by vendor, however cable ways and wall penetrations will be provided by the Customer.<br>Ethernet cabling for the dedicated Control Network will be provided by Vendor, however cable ways and wall penetrations will be provided by the Customer.<br>Line voltage supply for the individual cabinet will be provided by the Customer as follows: <ul style="list-style-type: none"> <li>• 230 V AC and 230 V UPS (for controls) for each Local Control Cabinet</li> <li>• 415VAC for each Motor Control Cabinet</li> </ul> |  |
|-------|---|--|

|        |   |  |
|--------|---|--|
| 6.7.10 | <b>Performance Criteria Required for FAT/SAT</b> <ul style="list-style-type: none"> <li>• Pressure hold test to be performed before every SIP</li> <li>• Spray ball coverage test during FAT</li> <li>• All FAT/SAT,IQ,OQ as per IRS</li> </ul> |  |
|--------|---|--|

## 7.0 CONSTRAINTS

### 7.1 Equipment location and available space


|   |  |
|---|--|
| This equipment will be installed in the <b>DPT vaccine manufacturing Facility at PII, Coonoor.</b><br><b>Equipment Location:</b><br><u>Fermentation room (B1G048)</u><br><b>Block:</b> Diphtheria Block<br><b>Floor:</b> Ground Floor<br><b>Room Size:</b> 65 sq.m<br><b>Room No:</b> B1G048<br><b>False Ceiling height:</b> 3000 mm<br><b>Physical condition of the rooms:</b> <ol style="list-style-type: none"> <li>1. Room will be BSL 2</li> <li>2. Class: EU Class "C"</li> <li>3. Differential Pressure: 5 Pa (Absolute)</li> <li>4. Temperature maintained: 22±2 °C</li> <li>5. Relative Humidity: NMT 55 % RH</li> </ol> The equipment location is indicated in the relevant block of the layout enclosed as <b>URS Annex-1.</b> |  |
|---|--|

### 7.2 Available Utility

|    |   |  |
|----|---|--|
| a) | Plant steam @ 3–3.5 bar (g) and 130°C-150°C------(Report requirement) |  |
|----|---|--|

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| Specifications   | Remarks |
|--|---------|
| b) Pure steam @2.4 bar (g) and 121 <sup>0</sup> C-130 <sup>0</sup> C------(Report requirement)                                   |         |
| c) WFI (Hot loop) @2 bar(g) and 80 <sup>0</sup> -85 <sup>0</sup> C ------(Report requirement)                                    |         |
| d) Cooling water @3 bar(g) and 28 <sup>0</sup> C-30 <sup>0</sup> C ------(Report requirement)                                    |         |
| e) Chilled water @ 7°C to 12°C------(Report requirement)   |         |
| f) Electricity – 415V/3ph/50Hz, 240V/1ph/50Hz  |         |
| g) Compressed air @ 6.0– 8.0 bar (g)   |         |
| <b>Note: Utility consumption to be specified by the vendor, in case if there is any deviation in the values mentioned above.</b> |         |



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## 8.0 ABBREVIATION

| Abbreviation | Definition                           |
|--------------|--------------------------------------|
| °C           | Degree Centigrade                    |
| SFR          | Microbial Seed fermentor             |
| HMI          | Human Machine Interface              |
| ISO          | International Standards Organization |
| MOC          | Material Of Construction             |
| NPI          | NNE Pharmaplan India Ltd             |
| PII          | Pasteur Institute of India           |
| PLC          | Programmable Logic Controller        |
| QA           | Quality Assurance                    |
| RPM          | Revolutions Per Minute               |
| SS           | Stainless steel                      |
| NMT          | Not More Than                        |

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### REVISION INDEX

| Revision | Date       | Reason for Revision  |
|----------|------------|--|
| 00       | 2012-09-12 | 1 <sup>st</sup> draft for client's review  |
| 01       | 2012-10-18 | Format changed as per HLL requirement  |
| 02       | 2013-01-24 | HLL comments incorporated, received during the workshop dated 22 <sup>nd</sup> and 23 <sup>rd</sup> January 2013   |
| 03       | 2013-02-26 | PIIC comments incorporated received on 26 <sup>th</sup> Feb 2013   |
| 04       | 2013-04-26 | As per HLL comments dated 25.04.2013 by email  |
| 05       | 2013-05-14 | <p>As per the Telephonic discussion with HLL on 2013.05.13. Following major changes are incorporated:</p> <ul style="list-style-type: none"> <li>Jacket MOC changed to SS304</li> <li>Ports for acid and alkali addition and dosing pumps for the same are deleted</li> <li>1 peristaltic pump is required for the addition of inoculum, media and 1 peristaltic pump for antifoam.</li> <li>Mass Flow Controllers are deleted from overlay and sparger lines</li> <li>Electrical heater, heat exchanger and steam required for temperature control. Bourdon type pressure gauge for jacket is included under temperature control.</li> <li>Only single PLC is required for seed fermentor</li> <li>HMI screen size changed as 15"</li> <li>Repeated points under SIP details are deleted</li> <li>No. of cycles for CIP, SIP deleted under process control</li> <li>19 mm port with septum -1 No is added at the top lid</li> <li>Port for addition of inoculum provided on the upper wall side</li> <li>Input and charging of media modified in sec 3.1</li> <li>Sec 6.1 Under process control, No. of cycles(CIP,SIP) deleted</li> <li>Sec 6.4 Level of instrumentation                             <ul style="list-style-type: none"> <li>➤ Second line Temperature of the vessel changed to jacket</li> <li>➤ Pressure transducer changed to transmitter</li> <li>➤ Mass flow controllers deleted</li> <li>➤ No. of pumps changed to 2</li> </ul> </li> <li>Point 6.7.8 Peristaltic pump specifications modified as 1 No. of fixed speed peristaltic pump for the addition of inoculum and media with size:3.8/7 mm and 1 No. of Peristaltic pump for the addition of antifoam with tube size:3.8/7 mm</li> <li>➤ URS Annex 3: List of preferred MAKE of components modified</li> <li>➤ SI.No 3 Agitator removed</li> </ul> |

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|----------|------------|---|
|          |            | <ul style="list-style-type: none"> <li>➤ SI.No 6 Pressure sensor deleted</li> <li>➤ SI.No 9 pressure regulator-FESTO retained</li> <li>➤ SI.No Prefilter cartridge and vent filter cartridge: PALL to be included , Airtech and Fine airsys removed</li> <li>➤ SI.No 17 Filter housing: PALL included</li> <li>➤ SI.No 19 Diaphragm valve(manual): Avcon and Saunders deleted</li> <li>➤ SI.No 22 and 23: Sampling valve and Flush bottom valve: GEMU included</li> <li>➤ SI.No 31 Control panel deleted from the list</li> <li>➤ SI.No 34 Electrical motor deleted</li> </ul>  |
| 06       | 2013-08-26 | <p>As per the comments from HLL by email dated 2013-06-12, the following comments are incorporated:</p> <ul style="list-style-type: none"> <li>➤ 2.0.3 i) Shaft seal: Double mechanical seal with thermosyphon should have the sterile air inlet connection for pressurization during operation. During seal SIP , pure steam shall be used.</li> <li>➤ <b>URS Annex 2: List of MAKE</b> <ul style="list-style-type: none"> <li>• 1 -PLC: Mitsubishi deleted</li> <li>• 2 – Operator interface /HMI : Mitsubishi deleted</li> <li>• 18-Diaphragm valve(manual): Burkert deleted</li> <li>• 24-Sanitary rupture disc- Fike added</li> <li>• 28-Diaphragm valve(automatic): ITT added</li> <li>• 29-Angle seat valve(automatic): ITT added</li> <li>• Agitator- Make PRG added</li> </ul> </li> </ul> |

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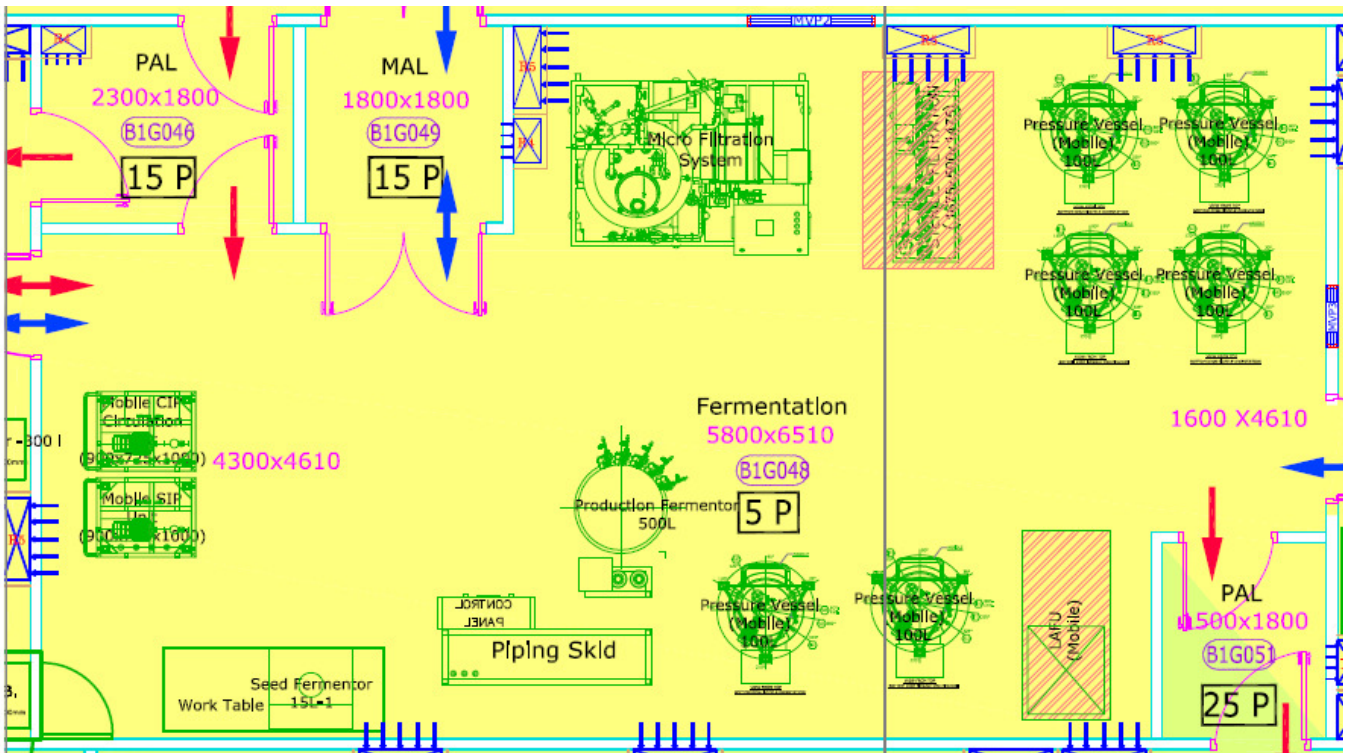
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### URS Annexure 1: LAYOUT OF DIPHTHERIA BLOCK

#### Room No : B1G048



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### URS Annexure 2: List of Preferred Make of components

| SL.NO    | DESCRIPTION              | MAKE                               |
|----------|--------------------------|------------------------------------|
| <b>A</b> | <b>INSTRUMENTATION</b>   |                                    |
| 1        | PLC                      | Allen Bradley/ Siemens             |
| 2        | Operator Interface/HMI   | Allen Bradley/ Siemens             |
| 4        | Temperature transmitter  | Radix/ Yokogawa/Emerson            |
| 5        | Temperature sensor       | NEGELE                             |
| 6        | p H sensor               | METTLER<br>TOLEDO/E&H/Hamilton     |
| 7        | Pressure transmitter     | Wika /Dwyer/Sensocon               |
| 8        | Pressure regulator       | FESTO                              |
| 9        | Temperature indicator    | Radix/ Wika/ Waaree<br>instruments |
| 10       | Steam trap               | STERIFLOW/ITT                      |
| 11       | Printer                  | Epson/ HP/ Canon                   |
| 12       | DC source                | Shavision/ Yokogawa/ Emerson       |
| <b>B</b> | <b>MECHANICAL</b>        |                                    |
| 13       | Pressure gauges          | WIKI/Denver/Negele                 |
| 14       | Pre air filter cartridge | Sartorius/PALL / Millipore         |
| 15       | Vent filter cartridge    | Sartorius/PALL / Millipore         |
| 16       | Filter housing           | Sartorius/PALL/ Millipore          |
| 17       | Spray ball               | HAKE                               |
| 18       | Diaphragm valve(Manual)  | GEMU                               |
| 19       | Ball valve(Manual)       | Modentic/Saunders/Alfa laval       |
| 20       | Non return valve         | Modentic/Saunders/Alfa laval       |
| 21       | Sampling valve           | Novaseptic/GEMU                    |
| 22       | Flush bottom valve       | Novaseptic/GEMU                    |
| 23       | Safety relief valve      | HEROSE/SS Spirax /Amtech<br>valves |
| 24       | Sanitary Rupture disc    | ZOOK/Elfab/Fike                    |
| 25       | Flow switch              | Orion/ Wika/Emerson                |
| 26       | Rotameter                | GEMU/Allborg                       |
| 27       | Peristaltic pump         | Watson Marlow/Masterflex           |
| 28       | Agitator                 | PRG                                |

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| C  | PNEUMATIC                   |               |
|----|-----------------------------|---------------|
| 29 | Diaphragm valve(Automatic)  | GEMU / ITT    |
| 30 | Angle seat valve(Automatic) | GEMU / ITT    |
| D  | ELECTRICAL                  |               |
| 31 | Lamp                        | PAPENMEIER    |
| 32 | Heater                      | Common wealth |