User Requirement Specifications
Vial Filling and Stoppering Machine

Process Code	Area	Equipment ID	Quantity	Capacity
F2	Bacterial vaccine formulation area	F2-VFS 01	1	200 Vials/Minute

URS Annexure List

URS Annex No.	Detail
1.	Layout showing location of the installation of Vial filling and Stoppering Machine
2.	List of components and make
3.	Transfer philosophy showing transfer of formulated vaccine from blending vessel to the buffer vessel of filling machine
4.	Data sheet for buffer vessel of filling machine.

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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 "Integrated Vaccine 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 approved by the QA team of HLL BIOTECH LIMITED, and authorized by the appropriate Project Authority

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2.0 EQUIPMENT DESCRIPTION

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

S. No.	Description	Purpose
1.	In feed Turn Table	To feed vials for filling machine integrated /synchronized with depyrogenation tunnel
2.	Infeed starwheel, turret/screw	For uniform spacing
3.	Filling Machine	Filling of product in vials
4.	Rubber Stoppering Machine	Rubber stopper placement
5.	Hopper with vibration unit	Used for feeding the rubber stoppers to the stoppering unit.
6.	Star wheel	This indexes the vial into and out of the pocket on the conveyor belt
7.	Out-feed star wheel/ turret / screw	Transfer from stoppering machine to sealing turntable

Machine should have all operation automatic with minimum manual intervention with specified accuracy of ± 1% for all fill volume. The turn-table should have provision for attachment with out-feed system of tunnel so that smooth transfer of vials takes place from tunnel to turn table with interlocking.

Stoppering should takes place automatically with the help of vacuum release system. All operation should take place in aseptic condition under laminar air-flow (class A zone) i.e **Open RABS (active)** with background of Grade B.

All the points in the IRS would be applicable for the equipment except below mentioned points:

- 4.1.11
- FDA Guidance for industry, ANSI/NSF 49-2008,

Note:

I.	This Technical Specification is the basis for an inquiry to a vendor and therefore the basis for the vendor's proposal.
II.	The vendor is asked to state in "REMARKS" column with "yes" if the described requirement will be completely fulfilled and with "no" in case the requirement will not or cannot be fulfilled with the proposed equipment. I n case of an deviation a comment must be inserted or enclosed as a separate annexure by referring to the respective URS specification number.
III.	The vendor must clearly comment each item of the Technical Specification. The comments must be in English language. If extra cost for necessary options becomes necessary the item must be clearly stated.
IV.	In case that the requirement includes a question or request or information from the vendor, the answer / information should be stated in the "REMARKS" column.
V.	The final version of this document including the vendor's comments will become basis of a potential purchase order or contract.
VI.	The Technical Specification serves to define a summary of all vendor's requirements concerning scope of delivery and services.
VII.	The vendor is responsible for technically unobjectionable function of the equipment. This TS is not intended to dictate a technical design to the vendor. If agreed upon with the vendor, the vendor can apply his practically proven design.
VIII.	Special Instruction a. If no comments against any specification shall be considered as "NO" and b. If there is no reply / comments against the complete URS by the vendor then it shall be treated as unresponsive / technically non-compliant and rejected.
IX.	All the instruments and controls mentioned in the URS(s) are expected to be standard supply and part of your standard equipment model. In case of any deviation or redundancy or additional scope of supply is noticed, vendor is required to obtain clarification from HBL before submitting the quotes.
X.	The makes requested are standard international makes. In case of any deviation, vendor to seek clarification from HBL before submitting the offers.
XI.	Refer document Installation Requirement Specification and Specific Instructions with URS; NPI-120310-IRS-S1-01
XII.	Refer Tender document with URS; NPI-120310-EQP-S1-TD-01

Specifications	Remarks
3.0 PROCESS DESCRIPTION	
3.1 Input & Charging method	
a) **Sterilized and Depyrogenated vials from depyrogenating tunnel**: The depyrogenated vials **(6Rand 2R size according DINISO standard 8362-1)** after cooling cycle in the tunnel shall enter into filling room. The vial shall be collected in a turntable. From the turn table vials should be singled on to a positive transport toreach filling stationand this operation should conform to GMP guidelines.	
b) **Sterilized rubber stoppers (siliconized / non-siliconized) (according DIN ISO 8362-2 for liquid vials):** The sterilised rubber stoppers in the tyvek bag will be charged within hopper manually under RABS with the help of glove arrangement. The machine shall have the capability to operate with siliconized / non siliconized. ***Format : 20mm Nominal Size (for 6R) and 13mm Nominal size (for 2R)***	
c) **Buffer Vessel:** Vendor to provide the buffer vessel having the capacity of 10L (working volume), which will be placed outside the RABS with dedicated skid arrangement under LAF and connected to the manifold. This will be connected to the Blending vessel aseptically (S2S connection). The product will be recirculated between manifold and buffer vessel using peristaltic pump as the product has the tendency of sedimentation. **Note:** Vendor shall provide buffer vessel with load cell and recirculation pump. Load cell shall have interlock for the controlled flow and transfer of bulk from blending vessel to buffer vessel (sanitary port). ***Refer URS annexure-4 for detailed technical specifications of buffer vessel.***	
d) **Bulk Product Transfer Philosophy:** Bulk is formulated in the Blending vessel. The blended bulk in the blending vessel will be transferred to filling area through hard piping and connected aseptically with buffer vessel. The product will be transferred from blending vessel to buffer vessel using peristaltic pump. The level in the buffer vessel will be controlled by load cell of buffer vessel. Then product is recirculated between the buffer vessel and the manifold with the help of a recirculation pump. ***Refer URS Annexure-3 Schematic of Transfer philosophy***	
e) **Outfeed System:** Turntable shall be provided to singularise the vials before the starwheel. In turn the starwheel will pick the vials from the turntable and transport it to turret / screw for further movement of the vial. The filled and stoppered vials from the collection table / conveyor shall be collected and sent through conveyor to vial sealing machine for vial sealing.	
3.2 Brief Process Steps	
Filling and stoppering machine is to perform following process steps: a) Transportation of depyrogenated vials synchronized with turntable with dead plate in between to provide buffer time. b) Transportation of singularise vial from turntable to infeed starwheel. c) Transportation of vials from star wheel to infeed turret/ screw will transport the vial on filling station. d) Dosing of product liquid within vial of 2R or 6R with the help of rotary piston pump with a filling of 0.65ml or 6.0 ml respectively with a minimum accuracy of ± 1% for all fill volume within a 3 sigma range. e)Transportation of filled vial to stoppering station.	

Specifications	Remarks
f) There shall be provision of rejecting unstopperred vials. g) The outfeed of the vial filling and stoppering machine is attached with vial sealing machine through transfer conveyor/ turret/ screw. ***Note: No vial rejection (like breakage) shall occur during the process. No vials shall be scratched by the machine during processing***	
3.3 Output & Discharging method	
a) The stoppered vials shall then be transferred through transfer conveyor/ turret to vial sealing machine turntable.	
4.0 PRODUCTIVITY REQUIREMENT	
4.1 Desired / suggested capacity	
The filling line should be suitable for line output of 200vial/min of 2R &6R vials respectively to produce filled and stoppered vials at the rate of: 2R: 200 vials/min with fill vol of 0.65ml 6R: 200 vials/min with fill vol of 6.0ml ***Vendor shall consider ISO 6R and 2R vials.*** ***Efficiency: Overall line efficiency of the filling & stoppering machine shall be 99%.***	
4.2 Standard batch size	
Standard batch size shall vary ranging from 40000 to 90000 vials / shift of 8hrs based on the 2R &6R vials.	
4.3 Change Over Time	
Change part replacement should not take more than 30 minutes.	
4.4 Other Productivity Requirement	
a) Hold-up volume should be less than the 1% of the 10 L Buffer vessel.	
b) Any single change part should be not more than 5kg.	
5.0 CONTAINMENT	
Vial filling & stoppering machine to be executed with ***active O-RABS*** with a provision to accommodate LAF.	
6.0 GMP REQUIREMENTS	
6.1 Process control	
a) The equipment control system should be suitable to adjust and maintain the rate of filling (number of vials/ minute)	
b) Stoppering heights has to be adjustable and to be controlled.	
6.2 Failure mode detection	
A. Equipment shall be capable to detect the following failure, notify the operator with alarm and shutdown the process:	

Specifications	Remarks
a) Emergency stop activated	
b) Opening of the RABS door of filling unit & stoppering unit, stop the machine.	
c) Alarm notification and process trip in case of infeed is empty	
d) Maximum infeed condition in turn table should notify the operator with alarm and stops the tunnel out feed. ***Note: interconnection between filling, depyrogenating tunnel and washing machine is required.***	
e) Maximum out feed condition reached.	
f) Less than 1% volume of product in buffer vessel.	
g) Continuous detection of missing vial on filling station.	
h) Rotary piston pump not working.	
i) The rubber stopper bowl runs only on machine stopper request. Bowl stops when machine is not working.	
j) Continuous detection of missing stoppers on stoppering station.	
B. Following condition (not limited to the mentioned below) need only notification to operator for procedural control	
a) Compressed air pressure low for instrument.	
b) Vacuum pressure low.	
c) Rejection of vial, notify the operator with alarm.	
d) Any toppled vial on transport conveyor.	
C. Following Interlocks with alarm for procedural control	
e) No vial no fill	
f) No vials no stoppering	
g) Jamming of the stoppers in the transport chute	
6.3 In – Process control	
a) Provision to be provided for continuous monitoring of particulate at different locations over filling and stoppering machine and conveying system to demonstrate Class A condition. Therefore machine table should have proper sampling nozzle connection to connect the air sampling system for both viable and nonviable particulate. The exact position and number shall be decided on receipt of the GA drawing of the equipment and in a direct meeting with vendor.	
b) Isokinetic sampling system for plate exposure and for particle count of Class A condition. Port to accommodate for the following environmental monitoring system have to be supplied and integrated within the filling machine: - 3 x particle count isokinetic funnel - 3 x viable microbiological air sampling	

Specifications	Remarks
- 3 x holders for settle plates (surface germs)	

6.4 Level of instrumentation

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

Type of control	Purpose	Instrumentation
Filling machine		
Speed	To monitor and control filling speed with recording	Variable frequency drive
Quantity of vials	To count, indicate and record the number of vials (Filled /rejected)	Digital counter
Infeed/ outfeed sensor	To monitor the jamming or accumulation of the vials.	Optical sensor
Volume of product in buffer vessel	To maintain level in the buffer vessel	External Level sensor
Pumps	To fill the product into the vials	Piston pump with PLC control
Sensors	• No vial no fill • No vial no stoppering • No stoppering reject • Jamming of the stoppers in the transport chute	Optical sensor
Differential pressure	To monitor and indicate differential pressure across the HEPA filter	Magnehelic gauges/Photohelic gauges
Stoppering Machine		
Vacuum	To monitor the vacuum for stopper placement.	Vacuum indicator and controller
Quantity of vials	To count and indicate the number of vials.	Digital counter
Hopper Vibration	To monitor, indicate and control the vibration speed.	Vibration indicator with controller.

Specifications	Remarks
6.5 Batch data display and record printing	
Batch data printing shall be provided for basic / standard data acquisition. This shall be mainly to collect and store the data in industrial PC. Data output should be in non-editable format with print out option. PC and printer in vendor scope.	
6.6 GMP requirements (Others)	
6.6.1 All parts of the filling machine exposed in A/B area must be resistant to standard disinfectants and vendor should provide the name of specific disinfectants.	
6.6.2 The internal vibration of the equipment should be considered in installation of the equipment.	
6.6.3 After every stoppage of the filling machine “Home positioning” of the filling with the centering of the filling needle into the vials to be provided.	
6.6.4 The vial filling line has to be controlled via the PLC. Data collecting of critical parameters shall be done by paperless recorder.	
6.6.5 All sensoric, controls, PLC, HMI, all LAF, RABS, Differential cascades, shall be have provision for UPS connection.	
6.6.6 Two power supply entry shall be provided, the wiring of all mentioned above components shall separate than the other components wiring i.e. one for UPS and one for main power supply	
6.6.7 Required support services, like cable tray/SS conduits/pendants outside the complete machine will be in client’s scope.	
6.6.8 **GMP Requirements for RABS**	
a) Machine shall be equipped with RAB system and all the operation should be through glove ports. All doors made of security glass (toughened and shatter proof)	
b) RAB system shall have three sections for in feed table, filling station and capping station separated by partitions (security glass) with a mouse hole for movement of vials	
c) The Mock up test shall be done jointly by the vendor and client for the proper positioning of gloves.	
d) Pressure across the HEPA filters shall be indicate, Vendor to provide provision for the pressure measurement.	
e) Machine shall have provisions in RAB system for facilitating utilities and product connections	
f) Illumination within the RABS to be min 500 lux	
g) Suitable provisions for transfer chutes to be made to ensure the movement of material inside (example: Bags with sterilized filling arrangement, bags with sterilized stoppers) and outside the RABs.	
h) Equipment parts requiring aseptic cleaning shall be designed suitably for handling them inside the RAB system using glove port. Handles of appropriate size to be provided wherever necessary with door interlocking.	
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	

	Specifications	Remarks
	necessary maintenance points e. g. pumps, motors, filters, etc.	
6.7.2	All open doors should be under LAF, so vendor shall provide the extended LAF till that point. Note: Vendor to provide dimensions of the LAF in the technical bid with top view. At DQ stage the vendor to provide accurate drawings with dimensions. The supply of LAF is not under the scope of the vendor.	
6.7.3	Operating height: must be 900± 30 mm (to be finally decided during mock-up of filling machine). The height of the machine has to be adjustable by means of adjustable legs and clearance from the bottom shall be 200mm.	
6.7.4	Mock up test shall be conducted for the filling accuracy & line output during FAT.	
6.7.5	Support during initial product runs at SAT	
6.7.6	All RAB doors have to be supervised by security switches. In case of opening the machine must stop immediately	
6.7.7	CE certification for the filling line is mandatory and would be part of user requirements.	
6.7.8	Product contact parts should be easily dismantle able and cleanable e.g. buffer vessel, manifold, nozzle heads.	
6.7.9	The dosing nozzles should be constructed of SS 316L with Ra = 0.38	
6.7.10	Conveyor should be constructed with material which will be easy to clean. The resistant to disinfectants and low particle emitting comply to Grade A and shall be designed for minimum friction and also ensure that the conveyor belt shall be cleaned automatically towards the end/bottom of the conveyor.	
6.7.11	The MOC of safety cabinet and safety glass shall be compatible with the different disinfectants used.	
6.7.12	The RAB should be constructed of SS 304 frame with transparent safety glass (antistatic type)	
6.7.13	**Turntable**	
a)	Turntable should have a barrier plate between filling and tunnel to maintain positive pressure between filling and tunnel.	
b)	The bio seal between the turn table and the tunnel should be designed suitably to transfer depyrogenated vials onto turn table of filling machine.	
c)	Turntable shall be integrated within the RABS with ergonomic glove port.	
6.7.14	**Transport Belt/ turret/ screw**	
a)	Frictionless, continuous motion shall be provided and driven by programmable servo motor drive.	
6.7.15	**Filling Station**	
a)	**Buffer Vessel, manifold** – Capacity of the vessel shall be 10 L.	

Specifications	Remarks
– Level control using load cell with high accuracy connected to PLC of the machine. – Buffer vessel to be placed on the top of the manifold. – Manifold should be slightly inclined at one end with recirculation provision in between buffer vessel and manifold.	
b) Dosing Nozzle – Movement of nozzle shall be programmable. – Nozzle shall be dripping proof (suck back mechanism) to avoid wastage of the product and spilling of the product. – All parts and components shall be sterilizable by autoclaving at 121℃. – Proper transfer of buffer vessel, manifold, nozzles to be provided for cleaning and after sterilization under LAF in to the filling machine. – 2 sets of nozzles shall be provided along with the filling machine.	
c) Rotary Piston Pump – Sterilizable grade SS316 L – Individual rotary piston pump to every nozzle shall be provided. – Servo driven rotary piston pump to be provided and controlled by PLC – Suck back function to be provided to avoid dripping of the nozzle. – Size of the rotary piston pump shall be small and easy installation of tubings from glove port shall be achievable. (gloves used should be of sanitable grade)	
6.7.16 **Stoppering Machine**	
a) Loading of stoppers area shall be provided under integrated extended LAF of the machine at the back side of the filling machine.	
b) Chute shall be provided under RABS to load the stoppers.	
c) The equipment control system shall be suitable to adjust and maintain the rate of sealing (number of vials/ minute).	
d) Vibrating hopper shall be provided.	
e) Full stoppering of the vial shall take place.	
f) Hopper guiding rail shall be provided.	
g) Vendor to provide the diameter or the size of the chute to load the stoppers and number of stoppers which can be loaded in one go. (Minimum capacity should be 3000 bungs/load).	
h) Pick and place system shall be provided or vendor shall provide better option.	
i) Vacuum system shall be provided for full stoppering of the vials.	
6.7.17 **Reject Station**	
• Rejection station shall be provided to collect faulty vials. (i.e. empty vials, unstoppered vials).	
• Vendor to provide proper rejection system.	
• Rejection station shall have tray to collect the vials in front of the machine 90 degree to good vials collection.	

Specifications	Remarks
6.7.18 Software ladder logic shall be provided.	
6.7.19 Change parts to be provided for 2R and 6R size vials including nozzle.	

7.0 CONSTRAINTS

7.1 Equipment location and available space

This equipment will be installed in the **Bacterial vaccine Formulation Block** of **Integrated Vaccine Complex**, Chengalpattu

Equipment Location:
Floor: Ground Floor, Bacterial Vaccine Formulation Block
Room Size:81 m^2
False Ceiling:3000mm

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

Physical condition of the Filling Room (F2G044):

1. Room will be non-hazardous
2. Class: EU Class “B”
3. Differential Pressure: 65 Pa Absolute
4. Temperature maintained: 22°C ±2°C
5. Relative Humidity: <55%

7.2 Utility

a) Electricity: Single Phase (220 V) & 3 phase (420 - 440 V) (Report Requirement)

b) Compressed air 6-8 bar (Report Requirement)

Note: Vendor to provide Pressure reducing valves and Pressure gauges along with the equipment as per equipment utility requirements.

Vendor to provide the all utility consumptions in details for the equipment during pre-bid.

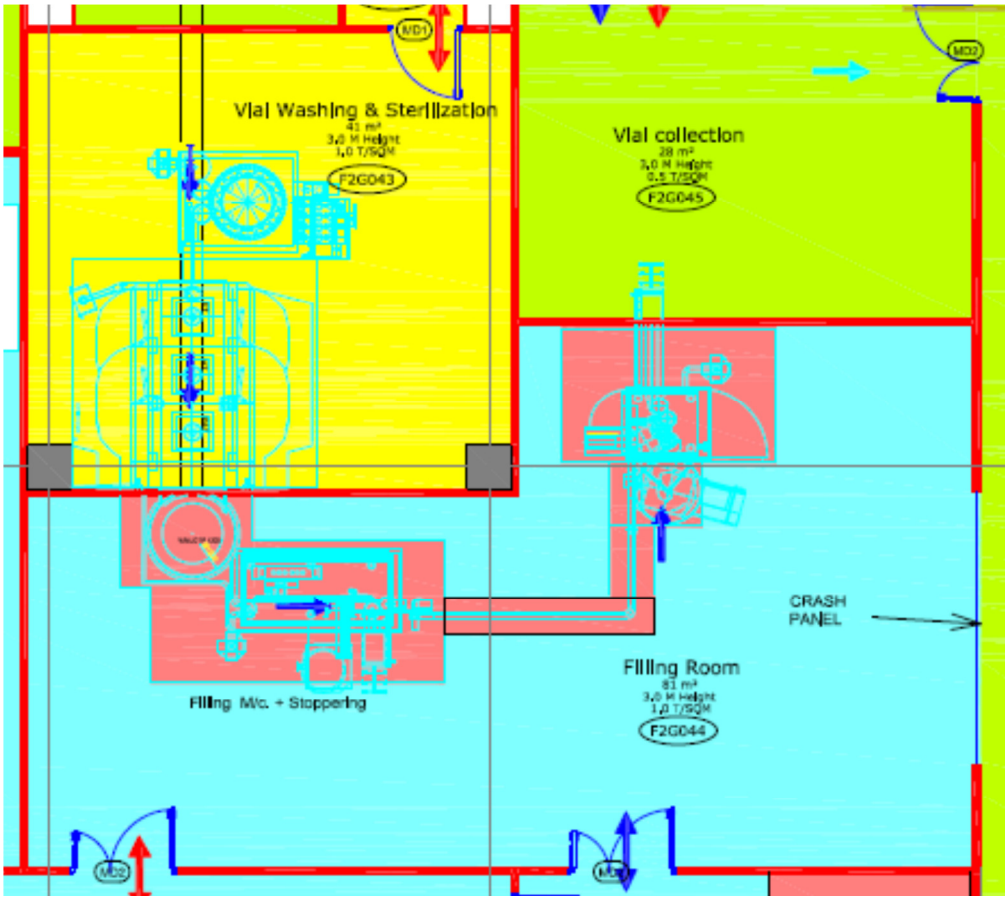
8.0 ABBREVIATION

Abbrevation	Definition
ANSI	American National Standards Institute
CE	European conformity
FAT	Factory Acceptance Test
FDA	Food and Drug Administration
GA	General Arrangement
GMP	Good Manufacturing Practice
HMI	Human Machine Interface
ISO	International Standards Organization
IRS	Installation requirement specifications
LAF	Laminar Air Flow
MOC	Material Of Construction
NPI	NNE PHARMAPLAN INDIA LTD
O-RABS	Open- Restricted Access Barrier System
PLC	Programmable Logic Controller
QA	Quality Assurance
Ra	Roughness Average
SAT	Site Acceptance Test
SOP	Standard Operating Procedure
SS	Stainless steel
VFS	Vial Filling and Stoppering Machine
WV	Working Volume

REVISION INDEX

Revision	Date	Reason for Revision
00	25-07-2012	First Draft for Client's Review
01	27-05-2013	As per comments given by HBL on 27-05-2013 by email.
02	07-11-2013	As per comments given by HBL on 28-10-2013 by email.
03	28-11-2013	Updated as per MOM dated 26-11-2013
04	10-12-2013	As per comments given by HBL on 07-12-2013 by email.

URS Annexure 1: LAYOUT POSITION
Room No:F2G044, Room Area:81 m²



URS Annexure - 2

List of components and make for Vial Filling & Stoppering Machine

S.No	Description	Preferred List
1.	Load cell	E&H / Mettler
2.	Vacuum Pump	Becker/Bosch
3.	Vacuum Gauge	Wika/E&H/Rosemount
4.	Pressure Transmitter	Rosemount / Dwyer / Wika
5.	Main Drive Gear Motor	Bonfiglioli / Siemens/ABB
6.	Frequency Inverter	Allen-Bradley/ Siemens
7.	Gear Box	Bonfiglioli/Bauer
8.	Proximity Switch	Contrinex/Rockwell/Omron/
9.	Proximity Sensor	Contrinex/Rockwell/Omron
10.	Peristatlic pump	Masterflex / Watson Marlow
11.	Pressure Gauge	Rosemount / Dwyer / Wika
12.	Solenoid Valve	Gemu / Burkert
13.	Air Connection	Festo / SMC / Sweglok
14.	Temperature Sensors (PT-100)	E & H / Negele / Rosemount
15.	Pressure sensors	E & H / Negele / Rosemount
16.	PLC	Allen-Bradley / Honeywel / Siemens
17.	HMI	Allen-Bradley / Siemens
18.	Optical sensor	Contrinex / Pepperl Fuchs

Note: - vendor shall follow the similar make for all the instrument.