User Requirement Specifications
Vial Filling and Stoppering Machine
Equipment ID: F-VFS 01

URS Annexure List

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

Table of Contents

nne pharmaplan	User Requirement Specifications			
	Equipment/System	Vial Filling and Stoppering Machine		
	Identification	F-VFS 01	**Document**	URS/F-VFS 01
	Effective Date	2013-06-06	**Revision**	04

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 Vaccine 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 and authorized by the appropriate Project Authority.

Prepared by		
Name/ Designation	**Signature**	**Date**
Mr. Nihit Singhal **Sr. Engineer – Projects (Biotech)** **NNE Pharmaplan India Ltd.**		

Checked by		
Name/ Designation	**Signature**	**Date**
Dr. Naveen Nagaraj **Sr. Project Manager - Head Biotech Division** **NNE Pharmaplan India Ltd.**		
Mr. Vikas Katial **GM –Head COC Vaccines** **NNE Pharmaplan India Ltd.**		

Approved by		
Name/ Designation	**Signature**	**Date**
Mr.Narendra Prasad **Director-Technical** **NNE Pharmaplan India Ltd.**		
Mr. Hartmut Schaz **Senior Technology Partner, Experts I** **NNE Pharmaplan, Germany**		
HLL Lifecare Limited		

Authorized by		
Name/ Designation	**Signature**	**Date**
Project Authority **Pasteur Institute of India**		

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.	In feed starwheel, turret/screw	For uniform spacing
3.	Filling Machine	Filling of product in vials
4.	Hopper with vibration unit	Used for feeding the rubber stoppers to the stoppering unit.
5.	Rubber Stoppering Machine	Rubber stopper placement
6.	Star wheel	This indexes the vial into and out of the pocket on the conveyor belt
7.	Outfeed starwheel/ turret / screw	Transfer from stoppering machine to sealing turntable

Machine should have all operation automatic with minimum manual intervention with specified ±1% accuracy up to 2ml fill volume and ±3% accuracy up to 10ml 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 take place automatically. All operation should take place in aseptic condition under laminar air-flow (class A zone) with **O-RABS (active)** and background of class B.

This equipment is a part of an integrated line.

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

- 4.1.11, 4.1.13, 4.1.17
- FDA Guidance for industry, GAMP- 21 Part CFR 11, ANSI/NSF 49-2008,
- 5.6

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 HLL before submitting the quotes.
X.	The makes requested are standard international makes. In case of any deviation, vendor to seek clarification from HLL before submitting the offers.
XI.	Refer document Installation Requirement Specification and Specific Instructions with URS; NPI_110831_IRS_PII_05
XII.	Refer Tender document with URS; NPI/110831/EQP/TD/05

Specifications	Remarks
3.0 Process Description	
3.0 Input & Charging method	
a) **Sterilized and Depyrogenated vials from depyrogenating tunnel**: The depyrogenated vials **(6R size according DIN ISO 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 conveyor and reach filling station. This operation should conform to GMP guidelines	
b) **Steam sterilized rubber stoppers (siliconized / non-siliconized) (according DIN ISO 8362-2 for liquid vials):** The rubber stopper will be sterilized in Autoclave cum bung processor, sterilize rubber stoppers shall be collected into pre-sterilized tyvek bag under LAF. From Tyvek bag stoppers will be charged within hopper manually under RABS with the help of glove arrangement. The machine shall be have the capability to operate with siliconized / non siliconized rubber stoppers. ***Format : 20mm Nominal Size***	
c) **Bulk Product Transfer Philosophy:** 500 L formulated bulk prepared in the Blending vessel will be transferred to filling line buffer vessel (10L) directly with the help of hard piping (316 L) ends in sterile group valve with triclover. The drop is to be connected with the pipe directly via Actuated diaphragm valve. The product will be then transferred from the buffer vessel to the manifold with the help of a recirculation pump which will be interconnected with the weighing scale of the buffer vessel. **Refer Annexure 2 Showing transfer philosophy from blending vessel to the buffer vessel of filling machine.**	
d) **Buffer Vessel:** The capacity of the buffer vessel to be 10L (WV) which will be placed on the manifold. This will be connected to the bulk vessel (Blending vessel) aseptically. The product will be recirculated between manifold and buffer vessel as the product has the tendency of sedimentation. **Note:** Vendor shall provide buffer vessel mounted on the Load cell (platform balance).This shall have interlock for the controlled flow and transfer of vaccine from Bulk Vessel to buffer Vessel. The valves V1, V2, V3 and V5 will be in the vendor scope. ***(Refer URS Annexure 2)***	
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 and capping.	
Note: for detailed technical requirement refer section 7.0	
3.1 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.	

Specifications	Remarks
d) Dosing of product liquid within vial of 6R with the help of rotary piston pump with a filling of 5.8 ml (5 ml + 15 % overages) with an minimum accuracy of ± 3%(This is up to 10ml fill volume and minimum accuracy of ± 1% up to 2ml fill volume) within a 3 sigma range. e)Transportation of filled vial to stoppering station. 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***	
3.2 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 to produce filled and stoppered vials at the rate of: 6R | 200 vials/ min ***Vendor shall consider ISO 6R vial.*** ***Efficiency: Overall line efficiency of the filling & stoppering machine shall be 99%.***	
4.2 Standard batch size	
A) Product A, Product B, Product C – 13 Million vials per annum • Vial size – 6R • Vial filled volume – 5.8 ml • Vial filling time – 9 hrs • Standard batch size should be 90,000 vials/ batch (6R).	
4.3 Change Over Time	
Not Applicable	
4.4 Other Productivity Requirement	
a) Hold-up volume should be less than the 1% of the 10L buffer vessel.	
b) Any single change part should be not more than 5 kg.	
5.0 Containment	
Vial filling and 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	

Specifications	Remarks
(number of vials/ minute)	
b) Stoppering height shall 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:	
a) Emergency stop activated	
b) Opening of the RABS door of filling unit & stoppering unit will 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, depyrogenation 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 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.	
C. Following Interlocks with alarm for procedural control	
d) No Vial no fill	
e) No vials no stoppering	
f) Jamming of the stoppers in the transport chute	
6.3 In – Process control	
a) Provision to be provided for continuous monitoring of particulate is required in 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	

Specifications	Remarks
equipment and in a direct meeting with vendor.	
b) Isokinetic sampling system ports for plate exposure and for particle count of Class A condition. Ports 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 - 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	Load cell
Pumps	To fill the product into the vials	Rotary 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

Specifications			Remarks
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.	

6.5 Batch data display and record printing (Specific to filling and Stoppering)

Basic / standard data acquisition system to be provided. 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 or 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 the 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. (HEPA not under the supplier scope)

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: bulk bottle, bags with sterilized filling arrangement, bags with sterilized stoppers) and outside the RABs.

Specifications	Remarks
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 be maintenance friendly e. g. pumps, motors, filters, etc.	
6.7.2 All open doors should be under LAF, so vendor shall provide the provision for 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 and 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 and stoppering machine is mandatory and would be part of User requirements.	
6.7.8 Product contact parts shall 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 class A and shall be designed for minimum friction	
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 egronomic glove port.	
6.7.14 **Transport Belt/ turret/ screw**	
a) Frictionless, continuous motion shall be provided and driven by programmable servo motor drive.	

Specifications	Remarks
6.7.15 **Filling Station**	
a) Buffer Vessel, manifold – Capacity of the vessel shall be 10 L – Level control using Load cell (platform with Asymmetric positioning slot for buffer vessel) 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. ***(Refer URS Annexure-3 for Technical specifications of buffer vessel)***	
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 sterilisation under LAF in to the filling machine. – 2 sets of nozzles shall be provided along with the filling machine.	
c) Rotary Piston Pump – 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	
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) Full stoppering of the vial shall take place.	
d) Vibrating hopper shall be provided.	
e) Hopper guiding rail shall be provided.	
f) 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).	
g) Pick and place system shall be provided or vendor shall provide alternate option.	
6.7.17 **Reject Station**	
a) Rejection station shall be provided to collect faulty vials. (i.e. empty vials, unstoppered vials).	
b) Vendor to provide proper rejection system.	

Specifications	Remarks
c) Rejection station shall have tray to collect the vials in front of the machine 90 degree to good vials collection.	

7.0 Constraints

6.7 Equipment location and available space

This equipment will be installed in the Formulation Block of **Revival of D.P.T Vaccine Manufacturing Facility, PII, and Coonoor.**

Equipment Location:

Floor: Ground floor-Formulation Block

Room No: **F1G055**

Room dimension : 44 m²

False ceiling height: 3000 mm

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

Physical condition of the rooms:

Filling and stoppering

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

6.8 Utility

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

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

8.0 Abbreviation

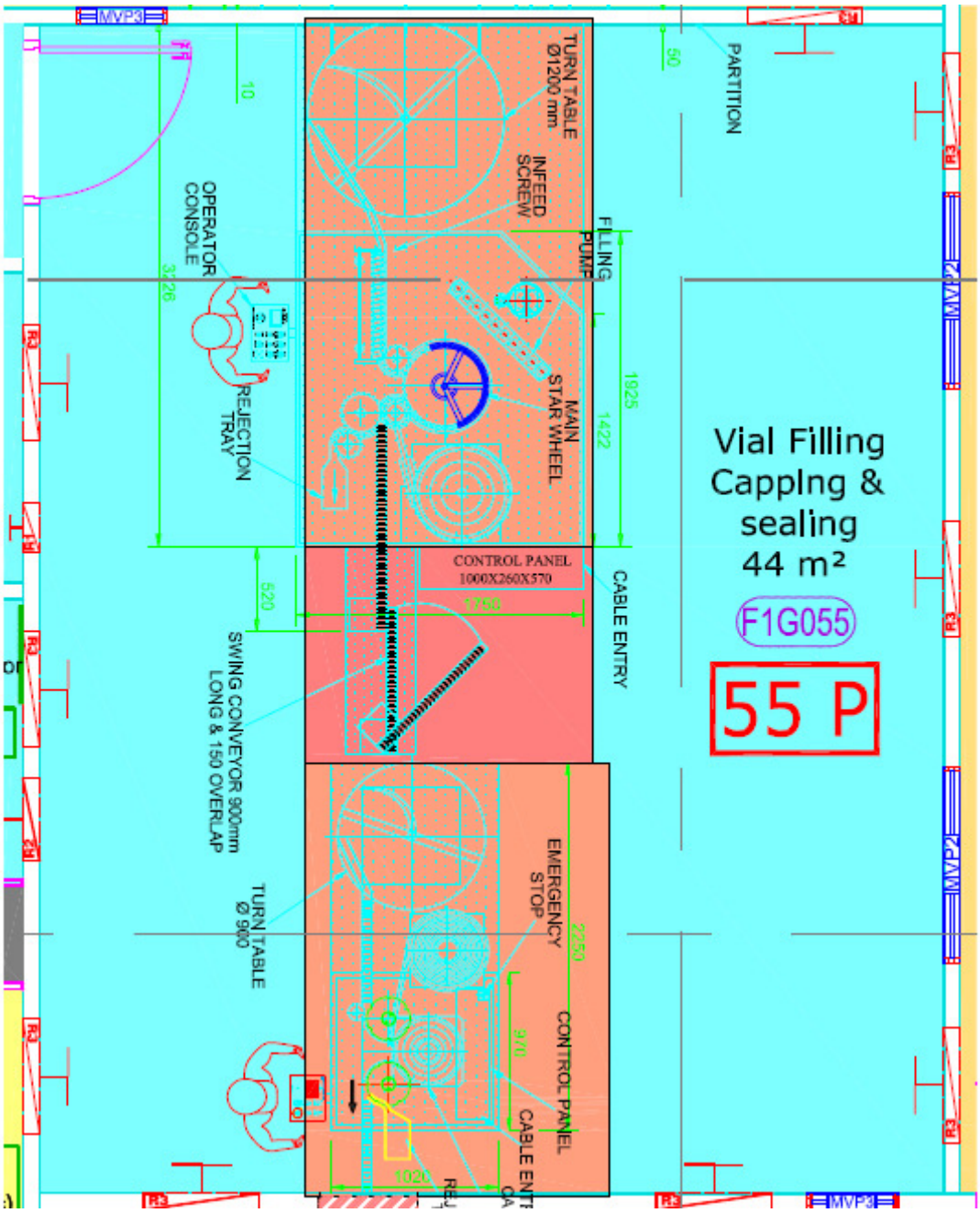
Abbrevation	Definition
FAT	Factory Acceptance Test
GA	General Arrangement
GMP	Good Manufacturing Practice
HMI	Human Machine Interface
ISO	International Standards Organization
LAF	Laminar Air Flow
MOC	Material Of Construction
NPI	NNE PHARMAPLAN INDIA LTD
O-RABS	Open- Restricted Access Barrier System
PLC	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
DEHS	Di Ethyl Hexyl Sebacat

Revision index

Revision	Date	Reason for Revision
00	2012-05-18	First Draft for Client's Review
01	2012-12-20	Format changed as per HLL requirement
02	2013-04-15	As per technical discussions had with HLL during BCGVL URS preparation
03	2013-04-25	As per BCGVL pre-bid meeting MOM dated on 12.04.2013
04	2013-06-06	As per discussion had with PIIC team on 2013-05-28

URS Annexure 1: LAYOUT POSITION

Room No: F1G055, Room Area: 44 m²



URS Annexure - 4

List of components and make for Vial Filling & Stoppering Machine

S.No	Description	Preferred List
1.	Load Cell	SARTORIUS / 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 / Honey well / Siemens
17.	HMI	Allen-Bradley / Siemens
18.	Optical sensor	Contrinex / Pepperl Fuchs

Note: Vendor shall follow the similar make for the entire instrument.