User Requirement Specifications
Vial Washing Machine
With
Depyrogenating Tunnel
Equipment ID: FG-VWD 01

Revision index

Revision	Date	Reason for revision
00	09.12.2011	First Draft for Client's Review
01	05.04.2012	NP expert and Client's inputs incorporated.
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07	2013.04.08	As per HLL's inputs dated 2013.04.05 by email

URS Annexure List

URS Annex No.	Detail
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2	List of components and make

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1.0 Approval Signature

This document is prepared by the Validation and GMP compliance team of "NNE Pharmaplan India for the project "Revival of BCG Vaccine Laboratory" (**Project number:-110729**) of BCG Vaccine Laboratory, Guindy, Chennai 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.

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2.0 Equipment description

The vial washing machine and the depyrogenating tunnel shall be made in combination with proper synchronization to each other. The vial washing machine shall have a speed of 200 vials/min. This equipment is a part of an integrated line.

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

S. No.	Description	Purpose
Vial Washing Machine		
1	In feed turntable	Feeding the vials to the turntable with tray. The vials will be unscrambled and singled to the washing station.
2	Transport system	Transporting the pre washed vials to the washing unit.
3	Recirculation unit	Recirculating the WFI drained from final rinse of vials to be used for initial rising of vials
4	Washing Cycle	Washing the vials with WFI/PW.
5	Vapor Exhaust unit	Vapor Exhaust from the washing unit.
6	Out feed	Feeding the vials into the Tunnel
Depyrogenating tunnel		
1	Conveyor	Vials to be transported through appropriate transport system.
2	Drying zone with HEPA	For drying the washed vials with HEPA filtered air
3	Depyrogenating zone with HEPA	For depyrogenating the vials with circulation of HEPA filtered air (hot air)
4	Cooling /stabilization zone with HEPA	For cooling the vials with circulation of HEPA filtered air to bring the temperature to ambient

Machine shall have all operation in automatic mode. All the regulatory requirements shall be followed. The loading of the vials to the infeed bay shall be done by conveyor. The vial shall be transferred to the washing unit in a group by the transport system. The vials in the washing unit shall be washed from the inside as well as from outside. The washing cycle shall include washing with recirculated WFI, fresh purified water & WFI with intermediate sterile compressed air drying. The equipment shall reduce contaminations and particle amount. It shall also reduce the amount of endotoxins by the use of WFI for a last rinse. A combination of at least six washing and drying cycle shall take place in the washing zone. The washed vials shall be transferred to the tunnel by the conveyor system.

The Tunnel shall be designed to produce the depyrogenating condition by achieving a temperature in the range of 250-350^{0}C.The process shall be capable of doing a 6 log reduction for viable germs and ≥ 3 log for endotoxins.
The temperature of vial at the outlet of cooling zone should be 23ºC (±2ºC). The system shall maintain a uniform temperature inside the tunnel. The wire mesh conveyor shall transport the vials from the in feed to the filling area through the drying, depyrogenating and cooling zone.

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 become necessary the item must be clearly stated.
IV.	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.
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_110729_IRS_BCG_01
XII.	Refer Tender document with URS; NPI/110729/EQP/TD/08

Specifications	Remarks
3.0 Process Description	
3.1 Input & Charging method	
3.1.1 Vial Washing Machine	
The rotary washing machines shall be capable to accommodate multiple cleaning station in total): • Station 1: Recirculated WFI 1 x interior / 1 x exterior • Station 2: Compressed air 1 x interior • Station 3: Fresh water (PW) 1 x interior • Station 4: Compressed air 1 x interior • Station 5: Fresh water (WFI) 1 x interior • Station 6: Compressed air 2 x interior / 1 x exterior	
a) Unwashed vials: Vials shall be loaded through tray onto the turntable (unscramble), and the vials will be singled to the washing stations.	
b) Re-circulated WFI: Re-circulated WFI is used in the initial rinsing of vials (internal and external). The vial washing machine shall have all arrangement for recirculation of water. The recirculated water shall pass through a pre-filter 5-micron filter. The vendor shall inform the exact arrangement of recirculation system in its technical offer. Purified water to be considered as make up of the tank.	
c) Filtered Compressed air: Filtered (0.22 micron) compressed air shall be used to blow out water from the vial between different washing steps. Compressed air shall also be used for removing water from the washed vials after final rinse to make it dry. *Filter housing with staubli connection (suitable for connection with integrity test apparatus) shall be vendor scope.*	
d) Purified Water: Purified water is used for intermediate washing step. The vial washing machine shall be suitable to collect purified water directly from the room supply valve of purified water distribution loop and it will passed to the machine through sterile filter of 0.22 micron. *Filter housing with staubli connection (suitable for connection with integrity test apparatus) shall be vendor scope.*	
e) Fresh WFI: WFI shall be used as washing media in the vial washing machine. The vial washing machine shall be suitable to collect WFI directly from the room supply valve of WFI distribution loop and it will be passed to the machine. WFI shall be used for final rinse of vials. The interface location of connecting WFI line to the washing machine will be in the scope of the vendor. *Filter housing with staubli connection (suitable for connection with integrity test apparatus) shall be vendor scope..*	
f) Transport System: Appropriate system for holding of vials to provided during transportation of vials to the washing station in upside down position for easy cleaning and after washing the vials will be re-inverted to their original position and transferred it to the depyrogenation tunnel.	

g) Exhaust Module: The Machine shall have exhaust module to extract water vapour generated during washing cycle from the washing machine / room. The module shall consist of: Filter flange and flap to connect the blower which shall be in the technical area. *The SS duct with drain, suction motor, and filter will be in user scope.*	

3.1.2 Depyrogenating Tunnel

Performance requirements:

- No decoloration of the vial
- No breakage of vial
- ≥ 3 log reduction in endotoxin to be achieved.
- No change in the vial property.

a) Washed vials from the washing machine: The washed vials shall be transported automatically to the infeed zone of the tunnel by a conveyor from washing machine.	
b) Air: The room air shall be sucked, supplied and re-circulated by the air handling unit of the tunnel. Final filtration is done by H 13 HEPA filter for hot zone and H 14 HEPA filter for drying and cooling zone respectively. The air shall be delivered as unidirectional airflow from the laminar flow unit of the equipment. Vendor shall inform the quantity of air intake from room.	
c) Infeed Zone: Glass Vials enters the tunnel belt and is spread to the width of the tunnel belt.	
i. **Temperature:** Limited amount of heated air from the heat zone passes into the infeed zone to rise the temperature of the glass vials, prior to their entry in to the heat zone. Heat zone should have suitable temperature monitoring, recording and display system in place.	
ii. **Air Flow:** The glass is subjected to unidirectional air flow consistent across the width of the zone. Air velocity is maintained +/-20% of the average airflow, and is delivered from the HEPA air filter at a rate of 0.7 m/sec. Fresh air is provided to the inlet of the HEPA filter. Air is not re-circulated (once through). A differential pressure device with display and alarming capabilities will monitor the differential pressure between the internal zone and the outside room pressure. Exhaust air exits the Infeed Zone through a duct to the outside of the washer and sterilisation room.	
iii. Heat Zone: The glass is transferred into the heat zone where the temperature is controlled to a level capable of providing the required thermal activation factor (FH). The FH provides the necessary temperature and time to ensure the required 6 log reduction for viable germs and ≥ 3 log for endotoxins.	
iv. **Temperature:** The temperature within the heat zone must be adjustable in 5°C increments from ambient to a maximum of 350°C. The temperature uniformity / distribution measured above the conveyor in the empty tunnel should be within the range of +/- 5°C of the average, as measured in line across the belt. The temperature uniformity / distribution measured inside of the vial should be within the range of +/- 5°C for tubing glass, as measured in line across the belt. A suitable temperature monitoring, recording and display system in place.	
v. **Air Flow:** The glass is subjected to laminar air flow consistent across the width of the zone. Air velocity is maintained to +/-20% of the average airflow, and is re-circulated	

through the HEPA air filter at a rate of 0.7 meters/sec. Fresh air is provided to the inlet side of the HEPA filter. There is no exhaust in the heat zone. Fresh air is used to make-up air that is lost to the adjacent zones through the gates. A differential pressure device with display and alarming capabilities will monitor the differential pressure between the internal zone and the washer/tunnel room pressure.

d) Cool Down Zone: The glass is transferred to the cool down zone where the glass is cooled down gradually to near ambient temperatures to prevent cracking of the glass, or damage to the outfeed guides due to high temperatures.

i. **Temperature Control:** The temperature of the glass must be cooled down to a maximum of 23±2°C at the exit of the tunnel. Cooling of the vials is accomplished using fresh HEPA filtered air. A suitable temperature monitoring, recording and display system in place.

ii. **Air Flow**: The glass is subjected to unidirectional air flow consistent across the width of the zone. Air velocity is maintained to +/-20% of the average airflow and passes through the HEPA air filter at a rate of 0.7meters/sec. Fresh air is provided to the inlet side of the HEPA filter through a roughing filter. Air is not recirculated, but exhausted out through a vent located at the top of the tunnel. A differential pressure device with display, recording and alarming capabilities will monitor the differential pressure between the internal zone and the outside room pressure.

3.2 Brief Process Steps

Exact cleaning sequence is to be proposed by the vendor. However following rules are to be complied.

a) The Vials shall be loaded on the turntable through tray/ magazine.
b) Initial washing of the Vials shall be with Re-circulated WFI for **internal and external surfaces**.
c) Drying of washed Vials after washing with filtered compressed air for **internal surfaces**.
d) Further washing of the Vials with purified water for **internal surfaces**.
e) Drying of washed Vials after washing with filtered compressed air for **internal surfaces**.
f) Spraying with fresh WFI for **internal surfaces**.
g) Final drying of blow-dry with compressed air for **internal and external surfaces**.
h) Transportation of vial to depyrogenation tunnel.

The tunnel shall follow the process as below:

a) Transportation of dried vials to depyrogenation zone
b) Transportation of depyrogenated vials to cooling zone
c) Progressive cooling of hot vials to ambient by cold HEPA filtered air (unidirectional air flow)
d) Transportation of depyrogenated vials through conveyor to the turntable of filling machine placed in filling room.

3.3 Output & Discharging method

The depyrogenated vials are transferred from the cooling zone to the filling machine

turn table by the conveyor movement.

4.0 Productivity Requirement

4.1 Desired/ suggested capacity and Efficiency

Capacity:

The washing machine shall be suitable to produce washed and sterilized vials at the rate of 200 Vials per minute, based on the vial size of 2 R **(as per DIN: ISO 8362-1 standard)**

Efficiency:

- Washing machine and Depyrogenation : 95%

4.2 Standard batch size

Standard batch size should be 40,000 vials/ batch (@2R.

4.3 Change Over Time (if applicable)

Not applicable

4.4 Other Productivity Requirement

4.4.1 Vendor to give information on change over time from one product to another product with the suitable output.

4.4.2 The equipment shall be able to run for 24 hours.

5.0 Containment

Not Applicable

6.0 GMP requirements

6.1 Process control

6.1.1 Washing Machine

Equipment to have suitable control system to verify and control the process.

6.1.2 Depyrogenating Tunnel

Equipment to have suitable control system to verify and control the process.

6.2 Failure mode detection and Alarms

6.2.1 Washing Machine

A. Equipment shall be provided with Audio visual alarms and the equipment must restart with manual intervention.

a) Main drive motor overload, Turntable motor overload, Pump Overload

b) In feed/ out feed empty

c) In feed jamming and Maximum out feed condition reached at the inlet of tunnel	
d) Toppled vials, machine should stop with alarm	
e) Emergency stop activated	
f) Safety covering of washing machine open	
g) Malfunctioning of vapour exhaust system / Vapour exhaust blower overload	
B. Interlock	
a) Washing machine stop - WATER STOP.	
b) Water injection start - when nozzle enters in the vials.	
c) Pressure of clean utilities - high & low	
6.2.2 Depyrogenation Tunnel	
A. Equipment shall be capable to detect the following failure, notify the operator with alarm and shutdown the process:	
a) Emergency stop activated	
b) In feed empty	
c) In feed/ out feed jamming	
d) Motor Overload	
e) Depyrogenation tunnel belt stops	
f) Maximum out feed reached in the in feed turntable of filling machine	
g) Positive differential pressure at drying zone with respect to depyrogenating zone i.e. the differential air pressure in the Depyrogenating zone must always be higher with respect to Drying zone, lower as compared to cooling zone, and the external room environment.	
B. Interlock for depyrogenation tunnel	
a. Pressure differentials of pre-hot zone, sterilization zone, cooling zone out of set limit – Machine shall interlock	
b. Temperature of pre-hot zone, sterilization zone, cooling zone out of set limit – Machine shall interlock	
6.3 In –Process control	
6.3.1 Sampling valve for washing media (PW, WFI) and compressed air to be provided at relevant location.	
6.3.2 In case re-circulated water, suitable sampling provision is required.	

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	Failure Mode Detection	Alarm
Vial Washing Machine				
Infeed/ Outfeed sensor	Vial counting	Sensor	NA	-
Temperature	For monitoring, indicating the temperature of WFI supply	Temperature probe with transmitter, and indicator	Low or High	Yes
Level	For monitoring, indicating and controlling the level of WFI in re-circulating tank.	Level sensor, indicator with controller	Low or High	Yes
Pressure	For all clean utility inputs	Feedback for the machine to hold	Low or high	Yes
Depyrogenating Tunnel				
Temperature	To monitor, control and record the temperature of drying zone	Temperature Transmitter	Low or High	Yes
Temperature	To monitor, control and record the temperature of depyrogenation zone (beginning)	Temperature Transmitter	Low or High	Yes
Temperature	To monitor, control and record the temperature of depyrogenation zone (end)	Temperature Transmitter	Low or High	Yes

Temperature	To monitor, control and record the temperature of cooling zone	Temperature Transmitter	Low or High	Yes
Air velocity	To measure air velocity of the tunnel laminar flow in all zones	Anemometer connected to PLC	-	Yes
Speed	To determine the conveyor speed	VFD	Low or High	Yes
Differential pressure	To monitor, control and record the differential pressure across HEPA filter	Pressure transducer (indicator)	-	-
Differential pressure with respect to adjoining room	To monitor and record the pressure cascade from filling room to washing and sterilisation room between each zone.	Pressure transducer	-	-

6.5 Batch data display and record printing

Refer Installation Requirement

6.6 GMP requirements (Others)

6.6.1 All parts of the machine exposed clean room area (Class D/C/B) must be resistant to standard disinfectants or vendor shall provide the name of specific disinfectants.

6.6.2 The machine has to be designed in such way, that air turbulence is minimized.

6.6.3 All sensoric, controls, PLC, HMI, all LAF, Differential cascades, ventilators, exhaust fans shall have provision to connect to the UPS supply.

6.6.4 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 another for main power supply.

6.6.5 The complete cabling from the electrical cabinets to the single machines and to the further equipment is in the scope of delivery including cable supports and trays

6.6.6 The complete cabling from the electrical cabinets to the single machines and to the further equipment is in the scope of delivery including cable supports and trays..

6.6.7 Vendor shall demonstrate 6 log reduction for viable germs and ≥ 3 log for endotoxins.

6.6.8 Vial washing

a) Manual hood lifting system shall be provided.	
b) Machine should not have any hold up water in the machine. Slopes should be designed for complete draining of any hold-up water.	
c) Machine should have manual intervention to start-up the cycle for flushing of hold water at intermediate washing steps if machine is stopped for sufficiently long interval.	
d) The water collection tub shall be completely drainable with drain valve for draining the water. The sloping inside the tub shall be towards the drain point	
e) When vial washing machine stops the machine shall have suitable outputs to close the WFI and purified water user points valves to avoid dead lags.	
6.6.9 Depyrogenating tunnel	
a) All LAFs should have UPS supply.	
b) The tunnel shall be provided with a minimum 6 point strip chart recorder for continuous graph of temperature of all zone and differential pressures between different zones and adjoining rooms	
c) All HEPA filters should have provision for DOP testing.	
d) The connections of DEHS test in the side cladding of the tunnel have to be Tri-clover connections.	
e) The tunnel will have a night mode that will allow an energy-efficient mode of operation to hold temperature and sterility of the tunnel between batches. It has to be possible to reduce the temperature at night and at weekend with a programmable clock or manually. When temperature is below 100°C the fan of the heating zone is turned off.	
6.7 Specific requirements	
6.7.1 Operating height: must be 900 mm ± 30 mm (to be finally decided during mock-up test of filling machine). The height of the machine has to be adjustable by means of adjustable legs.	
6.7.2 Size of the opening of the tunnel (outfeed) at the filling room shall be provided.	
6.7.3 Physical separation between washing area and out feed area is required, to avoid glass splinters from spreading into open area.	
6.7.4 In feed turntable shall be designed to provide 3 minutes buffer to the machine speed.	
6.7.5 All setting shall be user adjustable and through the control panel whichever is possible.	
6.7.6 All supply fans should be provided with variable frequency drives.	
6.7.7 The complete machine and its components have to be designed and constructed to avoid stagnation of water (slope of atleast 1%)	
6.7.8 Cable between the single machines/units and the control cabinets inside the clean rooms are within the scope of delivery.	

6.7.9 Control panel for the vial washing/tunnel shall be in the vial washing/Tunnel room.

7.0 Constraints

7.1 Equipment location and available space

This equipment will be installed in the Fill-Formulation Area of Revival of BCG Vaccine Laboratory at BCGVL, Guindy, Chennai.

Equipment Location:

Floor: Ground floor

Plant: Revival of BCG Vaccine Laboratory

Room dimension: 9400 mm x 5690mm + 2000 mm x 2145mm

Room No. FG020

False ceiling height: 3000 mm

The equipment location is indicated in the relevant block of the layout enclosed as **URS Annex-1.** The equipment must be positioned as per the generic layout provided below.

Physical condition of the rooms:

Washing and Sterilisation Room:

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

7.2 Utility

Vial Washing & Depyrogenation machine

a) Electricity: Single (220 V) & 3 phase (420 - 440 V) (Report Requirement)
b) Compressed air 6-8 bar (Report Requirement)
c) WFI @ 3-5 bar at 80 deg C (Report Requirement)
d) Purified water @ 3-5 bar (Report Requirement)

In the scope of the client, the supply will include the WFI, Purified water and compressed air (with pressure relief valve).

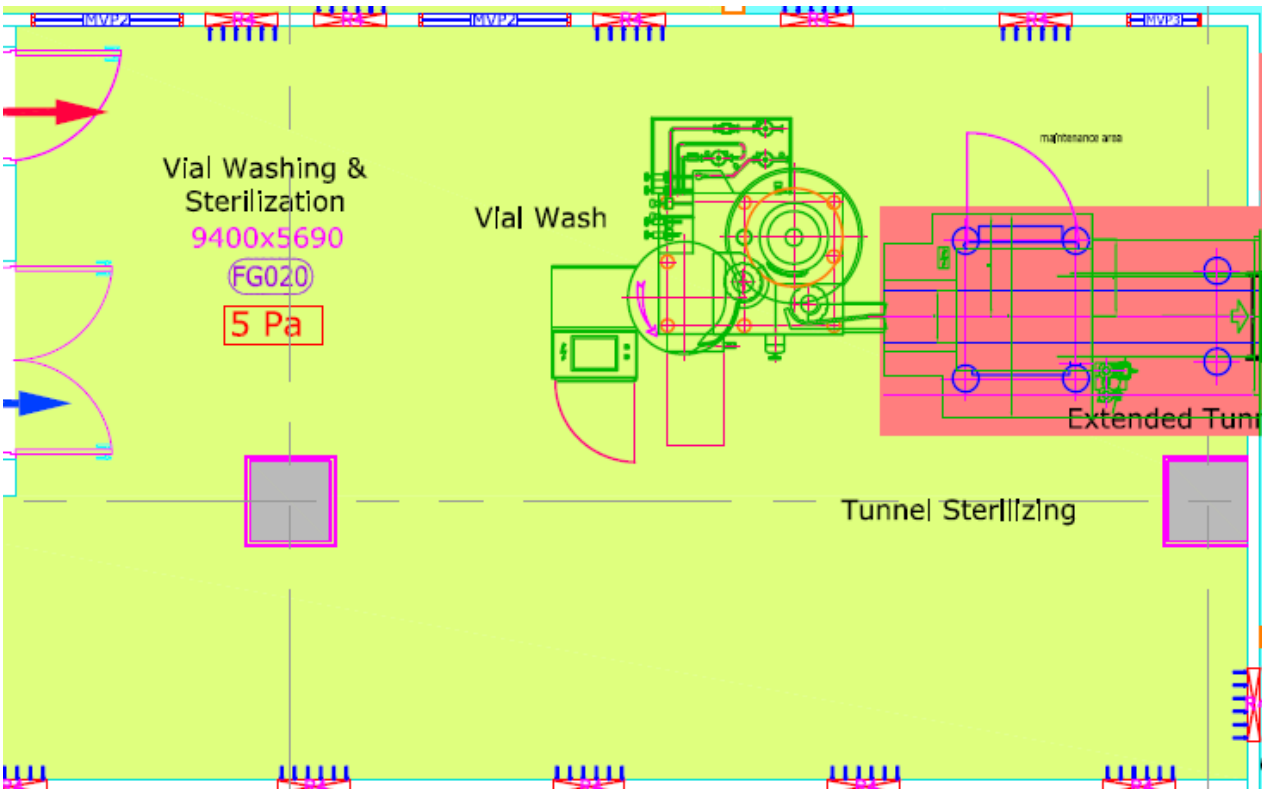
8.0 Abbreviation

Abbreviation	Definition
DQ	Design Qualification
DEHS	Di-Ethyl-Hexyl-Sebacat
GA	General Arrangement
HEPA	High Efficiency Particulate Air
HMI	Human Machine Interphase
MOC	Material Of Construction
NA	Not applicable
PLC	Programmable Logic Controller
PW	Purified Water
QA	Quality Assurance
Ra	Roughness average
RPM	Revolutions Per Minute
SS	Stainless steel
UPS	Uninterrupted Power Supply
VFD	Variable Freqency Drive
VWD	Vial washing machine with Depyrogenating Tunnel
WFI	Water For Injection

URS Annexure 1: LAYOUT POSITION

Room No: FG020

Room Name: Vial Washing & Sterilization



Annexure - 2

List of components and make for Vial Washing & Depyrogenating Tunnel

S.No	Description	Preferred List
1.	Mobile guide position transmitter	Pepperl Fuchs / Novotechnik
2.	Pressure transmitter	Bourdon Haenni / Dwyer / Wika / Testo
3.	Main Drive Gear Motor	Bonfiglioli/Seimens
4.	Frequency Inverter	Allen-Bradley/Mitsubishi/Siemens
5.	Gear Box	Bonfiglioli/Bauer
6.	Proximity Switch	Contrinex/Rockwell/Omron
7.	Proximity Sensor	Contrinex/Rockwell/Omron
8.	Pressure Transmitter	Rosemount / Dwyer / Wika
9.	Recirculatory Water Pump	Grundfos/Alfa Laval
10.	Peristatlic pump	Masterflex / Watson Marlow
11.	Pressure Gauge	Rosemount / Dwyer / Wika
12.	Solenoid Valve	Gemu / Burkert
13.	Filters & Filer Housing	Pall/Millipore/Sartorius
14.	Air Connection	Festo / SMC/Sweglok
15.	Temperature Sensors (PT-100)	E & H / Negele/Rosemount
16.	Pressure sensors	E & H / Negele/Rosemount
17.	PLC	Allen-Bradley/Mitsubishi/Siemens
18.	HMI	Allen-Bradley/Mitsubishi/Siemens
19.	Inlet shutter position sensor	Novotechnik / Pepperl Fuchs
20.	Transmitter for inlet gate position	Novotechnik / Pepperl Fuchs