User Requirement Specifications

Dry Heat Sterilizer

Block Code	Area	Identification #	Qty (Nos)	Chamber Size W x H x D in mm
B1	Multiple Bacterial Bulk block-Hep B	B1-DHS-01	01	1200 x 1200 x 1200
B1	Multiple Bacterial Bulk block-Hib	B1-DHS-02	01	1200 x 1200 x 1200
F4	BCG Bulk and Formulation block	F4-DHS-01	01	600 x 600 x 600

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1	Layouts showing location of the Dry Heat Sterilizers (DHS)
2	List of Preferred Make for Components
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1.0 APPROVAL SIGNATURES

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

NNE Pharmaplan			
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2.0 EQUIPMENT DESCRIPTION

DHS will be used at integrated vaccines complex at Chengalpattu for sterilization and depyrogenation of glassware and other components.

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

S. No.	Description	Purpose
1	Main Chamber	To keep the items for Drying, sterilisation and Depyrogenation
2	Doors on both loading and unloading side.	To close the chamber for operation and to have classification between loading and unloading side.
3	Chamber carriage	To keep the items for Depyrogenation / sterilization
4	Air inlet filter module with pre filter and HEPA filter.	To filter the air and to supply the filtered air to the circulation HEPA filter. Filtered air supply into the chamber and recirculation to maintain aseptic condition inside the chamber
5	Air exhaust Module with damper	To exhaust the air from the chamber to the atmosphere through HEPA filter
6	Exhaust HEPA filters-Heat resistant	To avoid the contamination of chamber from outside environment
7	Heat resistant HEPA filter	To sustain the higher Depyrogenation temperature
8	Main circulation HEPA filters	To supply the filtered air inside the chamber to create class-100 (Grade-A)
9	Main blower	To circulate of the HEPA filtered air inside the chamber
10	Heating module	To achieve the set temperature of drying, sterilisation and Depyrogenation
11	Bio shield	To isolate the sterile and non-sterile area
12	Material Of Construction	Main Chamber – SS 316L Loading & unloading Trolley - SS 304 Carriage with wheels – SS 316 L

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

- 4.1.11, 4.1.13, 4.1.17
- **Sec 5.1 Table 2**
  - Sl.NO 5 CE Conformity,
  - Sl.NO 7 ANSI/NSF 49-2008,
  - Sl.NO 9 ISO 8362

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. In case of a 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. These 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 Should be considered as "NO" and b. If there is no reply / comments against the complete URS by the vendor then it Should 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-15

	Specifications	Remarks
3.0	**PROCESS DESCRIPTION**	
3.1	**Input and charging method**	
3.1.1	The Dry heat steriliser should be provided with carriage with removable and adjustable type shelves for more flexibility. Suitable provision for inserting additional shelves, if required for loading the articles should be provided.	
3.1.2	The loading trolley should be provided for easy loading of the carriage with articles inside the chamber.	
3.1.3	A pair of railing should be provided inside the chamber for smooth and easy loading of the carriage inside the chamber. The railing should be of removable type to facilitate cleaning.	
3.1.4	Articles such as SS items, glass bottles and other articles for Depyrogenation/Sterilization should be loaded on to the carriage and the carriage is loaded inside the chamber on the railing provided.	
3.2	**Brief Process Steps**	
3.2.1	The Dry Heat sterilizer Should perform the following process steps ➢ Loading ➢ Moisture removal ➢ Heat up ➢ Sterilisation/Depyrogenation Hold Period ➢ Cooling ➢ Unloading	
3.2.2	Loading of the articles manually in to the carriage and loading of carriage in to the DHS chamber ***Note: Loading level Should be defined by the vendor***	
3.2.3	Drying at 100 -110 °C for Moisture removal.	
3.2.4	Heating up with exhaust damper in closed condition till temperature reaches sterilization/depyrogenation set point.	
3.2.5	Holding up for a set period at sterilization/Depyrogenation temperature (250 - 300 °C)	
3.2.6	Cooling the articles to ambient temperature with HEPA filtered air from cooling zone/ unloading area.	

Specifications	Remarks
3.3 Output & Discharging method	
3.3.1 Unloading of the carriage onto unloading trolley with the depyrogenated items from the chamber at the unloading side under the LAF.	
3.3.2 Unloading of the depyrogenated items from the carriage in sterile side. ***Note: Unloading level Should be defined by the vendor***	
4.0 PRODUCTIVITY REQUIREMENT	
4.1 Desired/ suggested capacity	
Dry Heat Sterilizer (DHS) **Internal chamber size:** **B1-DHS 01 and B1-DHS 02:** 1200mm x 1200mm x 1200mm (Width x Height x Depth) **F4-DHS-01:** 600mm x 600mm x 600mm (Width x Height x Depth)	
4.2 Standard batch size	
Not applicable	
4.3 Change over Time (if applicable)	
Not applicable	
4.4 Other Productivity Requirement	
4.4.1 The equipment Should be able to run for 24 hours/batch based on process requirement	
4.4.2 Sterilisation / Depyrogenation cycle including cooling and unloading should be completed within 4 Hours.	
5.0 CONTAINMENT	
Not applicable	
6.0 GMP REQUIREMENTS	
6.1 Process control	
The dry heat sterilizer should essentially have the necessary provision for adjustment / control of the following critical process parameters:	
6.1.1 Multipoint temperature probe (minimum 6 no's) for measuring chamber temperature, the range should be ambient to 300°C.	

Specifications	Remarks
6.1.2 Moisture removal temperature.	
6.1.3 Moisture removal time.	
6.1.4 Heat up time (not more than 45 min)	
6.1.5 Depyrogenation temperature. (255 ± 5 °C)	
6.1.6 Depyrogenation time (45 to 120 min)	
6.1.7 The control of hold temperature should be as per the following concept: ***Thyristor*** based temperature control required for depyrogenation hold time. While designing the heater bank the voltage bank to be considered as 415±20 V.	
6.1.8 Sterilization overshoot temperature not more than 275 °C	
6.1.9 Sterilization end temperature.	
6.1.10 Sterilization reset temperature.	
6.1.11 Process end temperature.	
6.1.12 Total cycle should not exceed more than 5 hours including cooling set point of 55 to 60°C	
6.1.13 Door opening temperature (55 °C).	
6.1.14 Over pressure in chamber during depyrogenation cycle (Not more than 15 pa).	
6.1.15 The depyrogenation cycle should be controlled based on the slowest heating or lowest temperature indicating probe.	
6.1.16 Chamber Probe Temperature uniformity from probe to probe should not vary more than ±5 °C during hold period.	
6.1.17 The temperature band for each probe should be within "Set temperature ± 5 °C" during hold period.	
6.1.18 Individual Probe temperature variation should be within ± 5 °C during hold period.	
6.1.19 Manual Operation must be possible apart from PLC based operation.	
6.1.20 Positive pressure maintained in chamber to be specified by vendor.	
6.1.21 The heaters should be easily removable for servicing and checking.	
6.1.22 Empty chamber heat distribution to be conducted.	
6.1.23 Sterilization efficiency of 6 log reduction.	
6.1.24 Equipment should pass the ISO-5 & cGMP and Velocities and circulation pattern of air should be achieved up to the sterilization zone.	
6.1.25 After Process End, the Pressure Module and Exhaust Module continue to run until the equipment is reset (using Process End acknowledgement through HMI) to prevent pressure build up and facilitate partial cooling of the load.	
6.1.26 Equipment should provide airflow of 0.6 to 0.8 m/s ± 20%.	
6.1.27 The DHS must meet specifications for total particulates for a Class 100 area, less than or equal to 100 for less than 0.5 micron per ft^3 or less than or equal to 3,500 for less than 0.5 micron per m^3 and 0 for 5 micron per m^3.	

Specifications	Remarks
6.2 Failure mode detection	
6.2.1 Equipment Should be capable to detect the following failure, notify the operator with alarm and shutdown the process:	
6.2.1.1 Low compressed air pressure. (used for pneumatic operation)	
6.2.1.2 Temperature below low limit of depyrogenation temperature	
6.2.1.3 Temperature beyond the safe limit of chamber temperature	
6.2.1.4 Differential pressure of the chamber below low limit	
6.2.1.5 Loss of UPS power	
6.2.1.6 Activation of emergency stop switch	
6.2.1.7 Fresh air motor over load	
6.2.2 Following condition need only notification to operator for procedural control:	
6.2.2.1 Low/high differential pressure across HEPA filter of supply, circulation and exhaust	
6.2.2.2 Malfunctioning of heater / blower	
6.2.2.3 Overshoot temperature reached	
6.2.2.4 End of cycle	
6.2.2.5 Power failure	
6.2.2.6 Door opening after the end of cycle	
6.2.2.7 Motor trips	
6.2.2.8 Pressure module motor trips	
6.2.2.9 Exhaust module motor trips	
6.2.2.10 Too long time for heat up	
6.2.2.11 Too long time for cooling	
6.2.2.12 Heater supply off	
6.2.2.13 Door pre-condition fail	
6.2.2.14 Compressed air pressure low	
6.2.2.15 Chamber pressure greater than set value	
6.2.2.16 Door pre-open fails	
6.2.2.17 Vacuum pump trips	
6.2.2.18 Too long time for post vacuum	
6.2.2.19 Vacuum leak test failed	
6.2.2.20 Emergency stop activated	
6.2.3 After uncontrolled shut down during active cycle, equipment should follow the following process, when it is restarted by operator:	
6.2.3.1 Should skip all proceeding steps	

Specifications	Remarks
6.2.3.2 Reach to "end" sequence but do not allow the sterile side door to open and display & print CYCLE FAILURE.	
6.2.4 Following Interlocks to be provided	
6.2.4.1 The door should not open during sterilization process.	
6.2.4.2 The process will not start unless both the doors are locked.	
6.2.4.3 Both doors will not open simultaneously.	
6.2.4.4 Only sterile side door Should open after completion of cycle	
6.2.4.5 After the command from unloading completion by the operator in the sterile side, the door from loading side can be opened.	
6.2.4.6 Heaters interlocked with circulation fan motor.	
6.2.4.7 The door should not open with a high pressure inside the chamber (More than 5 Pascal approx.).	
6.2.4.8 The door should not open with a high chamber temperature inside. (More than 60 °C approx.)	
6.2.4.9 Blind temperature controller to be provided to switch off the circuit in case the temperature overshoots.	
6.3 In –Process control	
Not applicable	
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 at multipoint	Chamber temperature monitoring, controlling, displaying and recording	Temperature probe with transmitter and indicator
Temperature	To control temperature in manual mode.	Temperature Indicator cum Controller
Temperature	To switch off the circuit/machine when temperature overshoots.	Blind temperature Controller
Time	Cycle time monitoring, controlling, displaying and recording	Timer

Specifications			Remarks
Differential pressure	Differential pressure, across supply air HEPA, Exhaust HEPA filter and recirculation HEPA filter displaying.	Magnehelic Gauges	
Differential pressure	Chamber differential Pressure with respect to room for monitoring, displaying and recording	Magnehelic Gauge & Pressure transmitter with indicator	
Air pressure	Controlling and alarm	Air pressure switch	
Strip chart recorder	Recording and display of temperature and time	Data logger with digital display (DDMMYYYY/ HRS:MIN:SEC)	

6.5 Batch data display and record printing

Batch report should be in the mode of Dot matrix online printing and strip chart recording. HMI should be able to store minimum of 1 cycle & provision for connecting with PC to be provided.

HMI size should not be less than 5.5 inches and it should be colour display with graphics

6.5.1 The HMI display Should include the following important parameters not limited to these

- Process parameters (Batch No:, Equipment ID)
- Alarm event
- Event log
- Process value display
- F_H value

6.5.2 The Printer Should include the following important parameters not limited to these:

- Process parameters
- Start time and End time (cycle)
- Batch No, Equipment ID
- Name of company: HLL Biotech Limited
- Name of the operator
- Alarm event
- Event log
- Process value
- F_H value

Specifications	Remarks
6.6 GMP requirements (Others)	
6.6.1 **Validation port:** a. The validation ports with tri-clamp connections and with special leak tight ferrules for insertion of 16 flexible temperature sensor (Vendor to provide the Thermocouple entry gland using finger plate assembly for all sterilizers) b. There must be one sanitary port complete with sanitary blank, for validation thermocouples. The port Should be located on one side of chamber in an easily accessible location (Size: 2" OD) c. The sanitary port Should have validation connections for thermocouples (Size: 2" OD)	
6.6.2 Data logging frequency should be min. 180 readings/ hold cycle and other than holding time 10sec.	
6.6.3 Suitable port (DOP Port) for charging and measuring the aerosol challenge at upstream of each HEPA filter (supply air, exhaust air and circulation HEPA filter). There should have location for scanning the downstream by photometer for HEPA integrity testing.	
6.6.4 The equipment should have operator comfortable accessibility for cleaning/disinfection.	
6.7 Specific requirements	
6.7.1 Hinged type doors construction.	
6.7.2 Audio-Visual LED for door open/ close on both loading and unloading side.	
6.7.3 Exhaust blower capacity should be designed to blow out an exhaust air up to 15 m distance from the equipment exhaust point of DHS. Ducting for exhaust air from the exhaust blower outlet to the outside atmosphere will not be in the vendor scope. The downstream connections of the supply and exhaust air HEPA filters with the duct should be easily removable (preferably without nuts/bolts) for periodic HEPA filter replacement.	
6.7.4 The carriage should be provided with removable and adjustable shelves for more flexibility and suitable provision for inserting additional shelves, if required.	
6.7.5 Depyrogenation cycle restarting from zero time if the temperature at any point of time goes beyond the defined temperature control band (255 ± 5 °C).	
6.7.6 Automatic F_H value calculation for each temperature monitoring port.	
6.7.7 HEPA filtered air from cooling zone / sterile area should be considered for cooling of the equipment.	
6.7.8 Fully automatic PLC based operation with option for manual operation.	

Specifications	Remarks
6.7.9 UPS provision to be provided for control panel [for instruments & PLC].	
6.7.10 Computer system specification i.e. Hardware design specification (HDS) and software design specification (SDS)	
6.7.11 Software ladder logic/ operation and controls flow charts	
6.7.12 **Performance criteria** a) The Depyrogenation cycle is valid if the Endotoxin test confirms the > 3 log reduction in Endotoxin in the depyrogenated samples. It must be conducted during FAT and SAT. b) 6 log reduction of microbial count.	
6.7.13 All utility points will be provided nearer to the equipment. Hooking up of the equipment to the nearest utility points will be in the vendor's scope.	
6.7.14 Equipment should be flushed with wall on both loading and unloading side with bio seal.	
6.7.15 Emergency stop switch should be provided on both loading and unloading side.	
6.7.16 Push button switches system should be provided.	
6.7.17 SS supporting stand should be provided to facilitate the cleaning below the equipment.	
6.7.18 Vendor to perform empty chamber validation during SAT and also necessary validation to be performed pertaining to DHS	

7.0 CONSTRAINTS

7.1 Equipment location and available space

This equipment will be installed in the **Multiple Bacterial Bulk block and BCG bulk & Formulation block** of **Integrated Vaccines Complex, at Chengalpattu**

Floor: All equipment's will be installed in Ground floor

Block name	Equipment ID	Loading side room no.	Unloading side room no.
Multiple Bacterial Bulk block-Hep B	B1-DHS-01	B1G022	B1G045
Multiple Bacterial Bulk block-Hib	B1-DHS-02	B1G120	B1G137
BCG Bulk and Formulation block	F4-DHS-01	F4G034	F4G035

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

Specifications	Remarks
7.2 Available Utility	
a) Electricity: Single Phase (220 V) & 3 phase (420 - 440 V) (Report Requirement) b) Compressed air@6 bar(g) _____(Report Requirement) **Note: Vendor to provide FRL, Pressure reducing valves and Pressure gauges along with the equipment as per equipment utility requirements.**	

8.0 ABBREVIATION

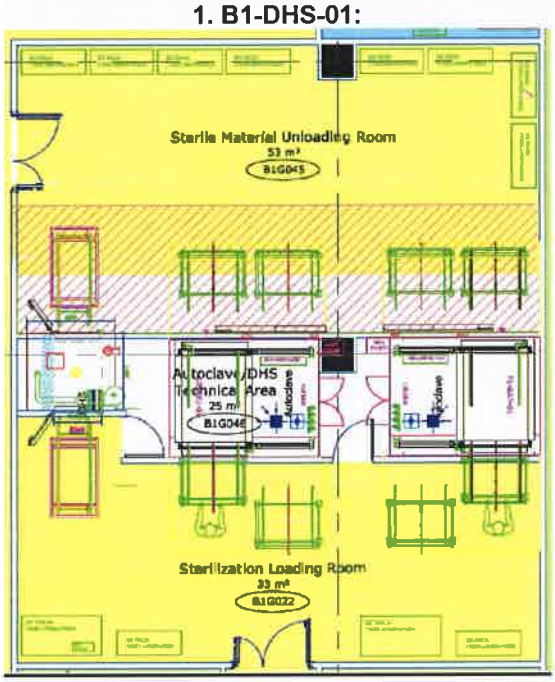
Abbreviation	Definition
DHS	Dry Heat Sterilizer
DOP	Di-octyl-phthalate
EUGMP	European Union Good Manufacturing Practices
FAT	Factory Acceptance Test
GMP	Good Manufacturing Practices
HBL	HLL Biotech Limited
HEPA	High Efficiency Particulate Air
IRS	Installation Requirement Specifications
ISO	International Standards Organization
LAF	Laminar Air Flow
NPI	NNE Pharmaplan India Ltd
PLC	Programmable logic controller
PLC	Programmable Logic Controller
SAT	Site Acceptance Test
SS	Stainless Steel
UPS	Un-interrupted Power Supply
URS	User Requirement Specifications

9.0 REVISION INDEX

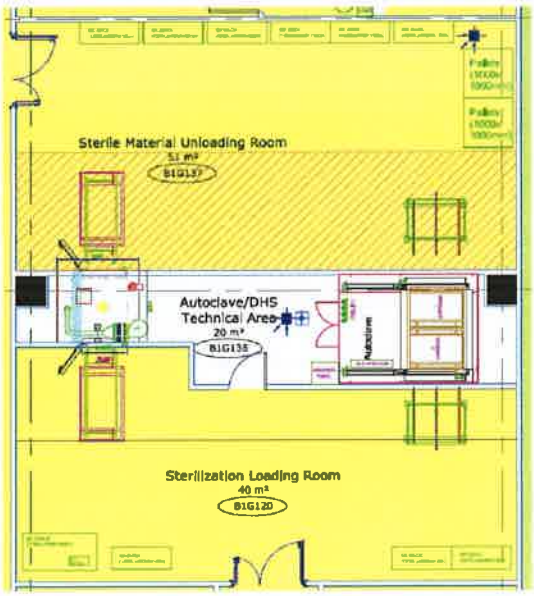
Revision	Date	Reason for Revision
00	25-08-2015	First draft for client's review
01	06-10-2015	Updated as per comments given by HBL dated 24-09-2015

URS Annexure 1: Layout showing location of the

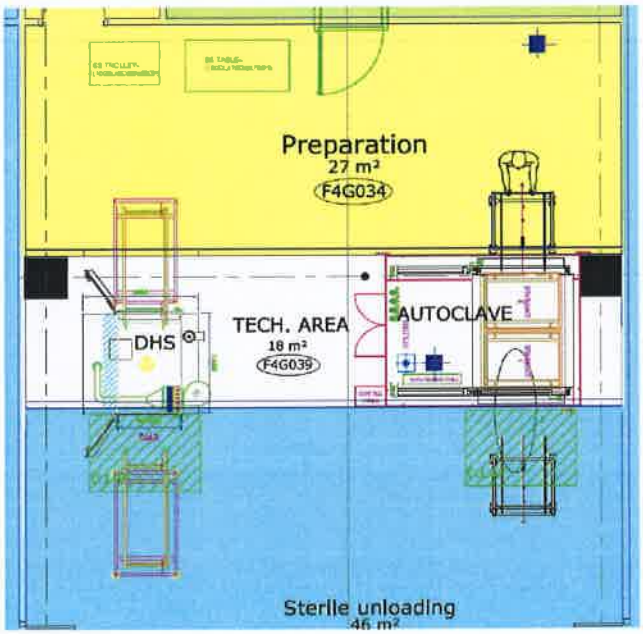
1. B1-DHS-01:



2. B1-DHS-02:



3. F4-DHS-01:


Preparation
27 m²
F4G034
TECH. AREA
18 m²
F4G039
DHS
AUTOCLAVE
Sterile unloading
46 m²

URS Annexure 2: List of Preferred Make of components

SL.NO	DESCRIPTION	MAKE
A	**INSTRUMENTATION**	
1	PLC	Allen Bradley/ Siemens
2	Operator Interface/HMI	Allen Bradley/ Siemens
3	Temperature transmitter	Radix/ Yokogawa/ Emerson
4	Pressure transmitter	Dwyer/Sensocon/ Wika
5	Temperature indicator controller	Radix/ Wika/ Waaree instruments
6	Blind Temperature controller	Radix/ Nutronics/ Micronix Instruments
7	Printer	Epson/ HP/ Canon
8	DC source	Shavision/ Yokogawa/ Emerson
B	**MECHANICAL**	
9	Magnehelic gauges	Dwyer/Sensocon/ Waaree Instruments
10	Pre filter	Airtech/Fine airsys/ Millipore
11	Room temperature HEPA filter	Airtech/Fine airsys/ Dyna filters
12	Pressure switch	Orion/ Wika/ Emerson
13	High Temperature HEPA filter	TROX/Pharma tech/Dyna filters
C	**PNEUMATIC**	
14	Pneumatic door cylinder	Janatics/Rotex/ Parker
15	Solenoid valves for door cylinder	Janatics/ Festo/ Parker
16	Filter Regulator Lubricator	Janatics/ Festo/ Ingersoll
D	**ELECTRICAL**	
17	Limit switches	Bohmen/ Siemens/ Emerson
18	Heater	Common wealth / Magma / Vijayalakshmi
19	Electrical motor	Kirloskar/Crompton greaves Ltd./ABB
20	Switch gear and Relays	Siemens/ L&T/ Schneider
21	Miniature circuit breaker	Siemens/ Havells/ Legrand
22	Rotary switch	L&T/ Siemens/ Schneider
23	Indication lamps	Technik / Mimic/ Schneider

URS Annexure 3: List of critical items to be supplied along with the package

SL.NO	DESCRIPTION	No. Of quantity
1	Door gasket	2 No.s each
2	Heating element	1 set each
3	Door locking cylinders	1 set each
4	Flasher cum buzzer	1 set each
5	3 C/O Relay with base	2 Nos
6	O/L Relay 5 to 8 AMP 2 to 3.2 AMP 1.6 to 2.5 AMP	 1 No 1 No 1 No
7	Coil for Solenoid valves for doors	1 set each
8	Rotary switch	3 No.s
9	Push buttons	2 Nos
10	Indication bulb sets	3 Nos
11	Heat resistant HEPA filters	1 set each