User Requirement Specifications Isolator for Compression Machine Equipment ID: S-CMI01

Revision index

Revision	Date	Reason for revision
00	25/06/2014	First Draft

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1.0 Approval signatures

This document is prepared by validation team of HLL for the "Oral formulation facility" of HLL Lifecare Limited under the authority of the Project Manager. Hence, this document before being effective shall be authorized by Head QA.

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2.0 Overview

2.1 Project introduction

HLL Lifecare Limited, Formerly Hindustan Latex Limited (HLL) is a public sector undertaking under the Ministry of Health and Family Welfare. It was incorporated in 1966 with the primary goal of producing quality condoms for the National Family Planning Program. HLL continues to be a leader in manufacturing condoms and contraceptives in India. HLL had since diversified into the manufacturing of other healthcare products such as Blood Bags, Surgical Sutures etc.

HLL in its quest to become a comprehensive healthcare player proposes to set-up new plants for manufacture of hormonal solid dosage form facility at Kanagala, near Belgaum, Karnataka.

2.2 Project Standard

The facilities, upon completion, shall be in compliance with the Indian FDA (Schedule M), WHO, USFDA, MHRA and EUGMP and also the HLL's internal quality standards.

2.3 Equipment description

Since potent medicinal product being manufactured in the facility, the negative pressure containment isolator will be used in manufacturing process to protect the personnel and environment from product contamination .A containment level of OEB 4 is required.

Air Handling Unit

The Air Handling unit of the isolator to provide the airflow and pressure necessary to keep the isolator environment within the specified requirement as follows: -

a) Inlet and outlet air is HEPA filtered to 99.997% efficiency.
b) Inlet standard pre filters with single HEPA over cap safe change cartridge filters.
c) Outlet filters with Double HEPA safe change cartridge filters. The 5 Micron pre filter fixed before exhaust HEPA.

Controls and Instrumentation

The Isolator with a dedicated Control and Instrumentation system to control air handling and to provide indication and alarms.

Equipment performance is indicated by the air leakage rate as per ISO 10648-3. The system shall be designed such that emission of powder to the surroundings shall be minimized in worst-case condition.

2.4 Refrence standard/guideline for equipment

The equipment should comply with the following guidelines / standards:

ISO

- ISO 14644 – 1 (For Cleanliness Class)
- ISO 14644 – 3 (For HEPA integrity testing)
- ISO 10648 – 3 (For leakage rate)

Note: - 1) This URS has been prepared based on our in-house knowledge & understanding for this equipment. It is possible that certain points might have been overlooked. As a vendor we expect you to go through the

document in depth and give your suggestions separately as an option. However, the base offer shall be as per the URS. All suggestions and deviations shall be highlighted and summarized separately

2) Vendor shall provide response as "Yes" or "No" against each specification for the compliance of their offered equipment in the remarks column.

Specifications	Remarks
3.0 Process Description	
3.1 Input & Charging method	
3.1.1 In all below stated equipments, the IBC provided with 6 inch passive split butter fly valve shall be lifted and lubricated granules shall be transferred to a continuous liner bag in a contained manner.	❑ Yes ❑ no
3.1.2 Liner bag with 6 inch active split butter fly valve and active trolley for docking is in vendor scope of supply.	❑ Yes ❑ no
3.1.3 This liner will be taken inside through pass box and granules shall be transferred to the compression machine hopper in a contained manner.	❑ Yes ❑ no
3.2 Brief Process Steps	
3.2.1 Operating through the glove ports of the isolator (Flexible canopy).	❑ Yes ❑ no
3.2.2 Metal detector + deduster combo should be in rigid isolator under negative pressure with common exhaust of main canopy having double HEPA in exhaust.	❑ Yes ❑ no
3.2.3 Safe change arrangement should be provided for HEPA filters	❑ Yes ❑ no
3.3 Output & Discharging method	
3.3.1 During operation, the product is collected in IBC through high containment valve interfaced with Isolator. Once the IBC filled upto desired level the high containment valve is closed manually and taken out of the isolator. 3.3.2 All waste collected through a port (approximate size of 200 mm), equipped with a e.g plastic sleeve device which allows the sleeve to be drawn and heat sealed, containing the waste and maintaining containment within the isolator.	❑ Yes ❑ no
4.0 Productivity Requirement	
4.1 Desired/ suggested capacity	
Vendor shall propose the dimension of Isolator for the following equipments and should ensure operation suitability: • Isolator for Compression Machine-1 • Dedusting & Metal detection equipment) Note: GA drawing of equipments along with room layout is attached as Annexure-1. **Please note that above sizes are approximate and likely to be changed during detail engineering phase. Actual sizes and equipment general**	❑ Yes ❑ no

Specifications	Remarks
arrangement drawing of all above equipments shall be submitted after site visit. The drawing will be subjected to the approval by HLL.	
4.2 Standard batch size	
Not Applicable	❑ Yes ❑ no
4.3 Change Over Time (if applicable)	
Not Applicable	NA
4.4 Cleaning	
4.4.1 Applicable arrangement for CIP & WIP should be provided. This shall be accomplished through a spray ball or spray gun. The isolator shall be capable of being manually cleaned to validate clean standards with residue below tolerable levels.	❑ Yes ❑ no
4.4.2 Isolator shall be suitable for cleaning cycle, decontamination followed by rinsing with purified water. Wash water shall runs to the catch pot detachable type to the floor of the Isolator. Visual level indicator on the catch pot to displays its occupancy level shall be provided.	❑ Yes ❑ no
4.5 Other Poductivity Requirement	
Not Applicable	NA
5.0 **Safety requirement**	
5.1 General	
In the event of malfunction or loss of utilities, the isolator must contain all necessary protection devices to ensure that the equipment and the product remain in a safe condition.	❑ Yes ❑ no
5.1. 1 Emergency stop function on accessible area.	❑ Yes ❑ no
5.1. 2 Noise level below 75 db at a distance of 1 m from the equipment.	❑ Yes ❑ no
5.1. 3 All electrical wiring should conform to current electricity rules & act.	❑ Yes ❑ no
5.1. 4 All the motors must have suitable double earthing.	❑ Yes ❑ no
5.1. 5 Total earthing to the HLL grid is in the scope of supply.	❑ Yes ❑ no
5.2 Power failure and recovery	
5.2.1 On power failure equipment shall come to rest, to protect operator, equipment itself and the product.	❑ Yes ❑ no
5.2.2 Power restart must not be automatic and human intervention must be required.	❑ Yes ❑ no

Specifications	Remarks
5.3 Containment	
The material handling and transfer in isolator shall be carried out through continuous and sealable, plastic tubes or split valves or RTP so that the powder does not leak into the personnel-working environment.	❑ Yes ❑ no
6.0 **GMP requirements**	
6.1 Process control	
The isolator should essentially have the necessary provision for adjustment / control of the following critical process parameters:	❑ Yes ❑ no
The following parameters of environment shall be controlled by the isolator	
a) Differential pressure – (Negative to room), NLT 40 Pa.	❑ Yes ❑ no
b) Providing a minimum of 25 air changes per hour at normal running conditions in all chambers.	❑ Yes ❑ no
6.2 Failure mode detection	
Equipment shall be capable to detect the following failure, notify the operator with alarm	
a) Leak in the isolator.	❑ Yes ❑ no
b) Emergency stop	❑ Yes ❑ no
c) Containment breach.	❑ Yes ❑ no
d) Differential pressure between room and isolator out of limit	❑ Yes ❑ no
e) Differential pressure across HEPA filters out of limit.	❑ Yes ❑ no
6.3 In –Process control	
Not Applicable	NA
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	
Alarms	Monitor and control of the working of isolator	Display with Hooter	❑ Yes ❑ no
Differential pressure	Monitor and control the pressure difference between a) Room & Isolator	Magnehelic gauge of Range: 0-100 Pa Accuracy: 2% Least count: 2 Pa	❑ Yes ❑ no
	b) Across exhaust HEPA filter		❑ Yes ❑ no

Specifications		Remarks
6.5	**Cleaning requirement**	
6.5.1	Applicable arrangement for CIP & WIP should be provided, accomplished by spray ball or spray gun.	❑ Yes ❑ no
6.5.2	All bolts, nuts on the exterior part of equipment will be with cap head or cap nut.	❑ Yes ❑ no
6.5.3	Isolator shall be provided with cleaning water connection and drain connection with drain pot.	❑ Yes ❑ no
6.5.4	Slope towards drain must be ensured	❑ Yes ❑ no
6.5.5	Wash water is drained into the catch pot.	❑ Yes ❑ no
6.5.6	Design of equipment should enhance cleaning feasibility by providing minimum sharp corners, minimum crevices & smooth finished welds joints and proper slopping.	❑ Yes ❑ no
6.5.7	Parts, which are required for cleaning out of place, should be provided with quick fixing arrangement.	❑ Yes ❑ no
6.5.8	Inflating sealing gaskets can also be considered.	❑ Yes ❑ no
6.5.9	All gaskets provided to avoid leakage should be amenable for easy removal & re- fixing.	❑ Yes ❑ no
6.6	**Qualification requirement**	
6.6.1	Equipment shall be qualified for design phase (DQ), installation phase (IQ), Operational phase (OQ) and the performance phase (PQ).	❑ Yes ❑ no
6.6.2	Vendor shall support client in execution of all the qualification phases.	❑ Yes ❑ no
6.7	**Material of construction**	
6.7.1	All metallic internal surfaces should be constructed of 316L grade stainless steel or better with internal mirror finish < 0.8 µm Ra and external surface finish < 1.2 µm Ra matt finish.	❑ Yes ❑ no
6.7.2	All metallic external surfaces should be constructed of 304 grade stainless steel or better with external surface finish < 1.2 µm Ra matt finish.	❑ Yes ❑ no
6.7.3	Gaskets, seals and O-rings should be constructed of FDA approved Food grade polymeric materials only.	❑ Yes ❑ no
6.7.4	All welds should be ground finished to < 1.2 µm Ra and properly passivated.	❑ Yes ❑ no
6.7.5	Windows shall be made up of suitable compatible transparent material, which can with stand vibration during equipment operation.	❑ Yes ❑ no
6.7.6	Hand gloves should be made of suitable compatible material, which should be inert to the product. Preferably Hypalon.	❑ Yes ❑ no
6.7.7	Construction of equipment should have minimum sharp corners, minimum crevices & smooth finished welds joints.	❑ Yes ❑ no

Specifications	Remarks
6.7.8 Aluminum and PVC should not be used in any material of construction (Due to incompatibility with the product)	❑ Yes ❑ no
6.8 Use of lubricants	
6.8.1 Any lubricant, if used must be food grade and non-toxic.	❑ Yes ❑ no
6.9 21 CFR Part 11 compliance	
Not applicable	NA
6.10 Data integrity	
Not applicable	NA
6.11 Batch data display and record printing	
Not applicable.	NA
6.12 Desired documents	
Following documents, but not limited to these, are expected from the vendor as part of the supply package as hard copy (02 Nos.) and electronic editable versions in **English** language:	
6.12.1 Vendor shall supply the document package in phases throughout the life cycle of the project as follows:	❑ Yes ❑ no
6.12.2 Phase 1: Preordering of the equipment	
6.12.2.1 Filled in URS	❑ Yes ❑ no
6.12.2.2 Equipment layout drawing fitted in the room layout block	❑ Yes ❑ no
6.12.2.3 Detail technical offer that support the compliance of the URS	❑ Yes ❑ no
6.12.3 Phase 2: Post ordering and prefabrication stage of the equipment	
6.12.3.1 Functional design specification and technical specification, that should contain the following:	❑ Yes ❑ no
• Equipment descriptions and its function	❑ Yes ❑ no
• Equipment operation steps	❑ Yes ❑ no
• List of failure indications	❑ Yes ❑ no
• List of interlocks	❑ Yes ❑ no
• List of input/outputs and its functions	❑ Yes ❑ no
• Critical list of major component, devices and instruments with their specific functions, specifications data sheet	❑ Yes ❑ no

Specifications	Remarks
• List of article contact surface and its MOC	❑ Yes ❑ no
• Schematic/GA diagram of the equipment.	❑ Yes ❑ no
Based on the above documents, equipment design shall be evaluated and approved by the user for the fabrication	
6.12.4 Phase 3: Fabrication stage of the equipment	
6.12.4.1 Vendor shall provide the FAT protocol at least 1 month in advance of the date of FAT, for the approval by the user.	❑ Yes ❑ no
6.12.5 Phase 4: Delivery of the equipment	
Vendor shall provide the following documents in the delivery package in minimum 2 sets. The delivery package shall reach the site of user atleast 15 days before the delivery equipments for the engineering check of the documents.	❑ Yes ❑ no
6.12.5.1 Operation and maintenance manuals, preventive maintenance schedule for equipment major component as well as the operating system	❑ Yes ❑ no
6.12.5.2 Operation and maintenance manuals for the bought out items.	❑ Yes ❑ no
6.12.5.3 Installation instructions/ guideline for equipment	❑ Yes ❑ no
6.12.5.4 Final as-built drawing for equipment.	❑ Yes ❑ no
6.12.5.5 Detailed drawing (plan and minimum one elevation) marking clearly all the necessary dimensions and locations of utilities along with requirement of utilities on the drawing along with the offer.	❑ Yes ❑ no
6.12.5.6 Other drawings (electrical, instrumentation etc.)	❑ Yes ❑ no
6.12.5.7 Software ladder logic/ operation and controls flow charts	❑ Yes ❑ no
6.12.5.8 Spare and/ or change parts list with ordering information	❑ Yes ❑ no
6.12.5.9 MOC certificates for all direct/ indirect product contact surfaces.	❑ Yes ❑ no
6.12.5.10 Weld verification reports of pipelines and chamber	❑ Yes ❑ no
6.12.5.11 Instrument calibration certificates with respect to the traceable national reference standard instrument and their calibration procedure.	❑ Yes ❑ no
6.12.5.12 Recommended SOP's for operation, cleaning and maintenance of each equipment (optional)	❑ Yes ❑ no
6.12.5.13 Guaranty/ warranty certificates for each equipment and major bought-out items, such as PLC, printer, recorders, etc.	❑ Yes ❑ no
6.12.5.14 Tagging of the components	❑ Yes ❑ no
6.12.5.15 IQ and OQ protocols	❑ Yes ❑ no
6.12.5.16 Control System input / output verification data and report (Optional)	❑ Yes ❑ no
6.12.5.17 Types of Lubricant and Lubrication instructions. Food grade certificate	❑ Yes ❑ no

Specifications	Remarks
6.13 Training	
6.13.1 Training for operators has to be included in the offer.	❑ Yes ❑ no
6.13.2 Training for technical staff has to be included in the offer	❑ Yes ❑ no
6.14 Specific GMP requirement (others)	
6.14.1 Vendor to give code numbers for each component. And also provide special tools for maintenance.	❑ Yes ❑ no
7.0 **Technical requirement**	
7.1 Basic technical requirement	
7.1.1 The layout must be taken into account when determining the layouts of the units.	❑ Yes ❑ no
7.1.2 The manufacture has to give the clear details on the total weight and the capacity of the equipment.	❑ Yes ❑ no
7.1.3 The heat given off by the unit must be stated.	❑ Yes ❑ no
7.1.4 Vendor shall provide special tools for maintenance of the equipment	❑ Yes ❑ no
7.1.5 Cables, top (industrial plug), air tubes, etc required from the point (Single utility point) to equipment are in scope of vendor	❑ Yes ❑ no
7.2 Critical points for qualification criteria: **Following points should be fulfilled for qualification failing which quotations are liable for rejection.**	
Scope of supply: In addition to all other points mentioned in URS following items are also in the scope of supply.	
7.2.1 Flexible canopy for compression machine 20 stn. (DB tooling)	❑ Yes ❑ no
7.2.2 Rigid isolator of Elevating de-duster + Metal detector (Combo)	❑ Yes ❑ no
7.2.3 Active table for docking of liner to IBC bin & 100 pieces of liner bag	❑ Yes ❑ no
7.2.4 Operation suitability should be ensured (space, working platform, positions of gloves etc.)	❑ Yes ❑ no
7.2.5 Split butterfly valve should be compatible with existing set of SBV (Make M/s Bectochem)	❑ Yes ❑ no
7.2.6 If SBV is not compatible with existing set, optional quote should be submitted to make it compatible.	❑ Yes ❑ no
7.2.7 At the time of supply, gloves/canopy should have minimum 80-90% shelf life.	❑ Yes ❑ no
7.3 Specific requirements	
7.3.1 The isolator has to be equipped with gloves which are ergometrically positioned to reach all points for normal operation, decontamination, cleaning and trouble shooting.	❑ Yes ❑ no

Specifications		Remarks
7.3.2	For all the parts of the system a clear separation between the critical areas (Clean operation) areas and the covered and sealed technical area must be realized.	❑ Yes ❑ no
7.3.3	Various cleaning cycles shall be possible like alkali, purified water.	❑ Yes ❑ no
7.3.4	Inbuilt air handling unit shall be designed for minimum 25 air changes per hour.	❑ Yes ❑ no
7.3.5	Testing ports for measurement of non-viable particulate count.	❑ Yes ❑ no
7.3.6	Testing ports for integrity test of HEPA filters (aerosol in and 100% monitoring)	❑ Yes ❑ no
7.3.7	HEPA filter cutouts should be provided with removable cover to protect filter during cleaning of isolator	❑ Yes ❑ no
7.3.8	Isolator width should be minimized so that maximum wall portion should be reachable by hand gloves	❑ Yes ❑ no
7.3.9	Provision for glove integrity testing.	❑ Yes ❑ no
7.3.10	The isolator shall be fitted with a drain with proper slope (3%) and valve.	❑ Yes ❑ no
7.3.11	The exact positions as well as the amount of gloves are to be identified in a mock up/Ergo test.	❑ Yes ❑ no
7.3.12	Isolator has to be controlled by PLC based control panel (make Allen Bradley or Siemens).	❑ Yes ❑ no
7.3.13	Provision of drain collection tank (Catch pot with proper slope and drain.	❑ Yes ❑ no
7.3.14	For all the parts of the system a clear separation between the critical (clean operation) areas and the covered and sealed technical area must be realized.	❑ Yes ❑ no
7.3.15	All isolator claddings have to be designed in a way for easy removal for routine maintenance purposes without using any tools.	❑ Yes ❑ no
7.3.16	Provision for nozzle connections for utilities.	❑ Yes ❑ no
7.3.17	Supply & Exhaust airline shall be provided with filters with 'push-push'/ safechange design to allow the changing of the filters without exposure of the filter to the operator or the environment.	❑ Yes ❑ no
7.3.18	Approved make of: • Blower / fan: Kruger • Energy efficient Motor (With class EFF-1): Siemens /Hindustan/CG • VFD: Allen Bradley,Delta • Magnehelic pressure gauge: Dwyer • Sensor: Pepprl +Fucsh, Omron,Honeywell. • Cable: Finolex, Havells or other subjected to approval by HLL Should be used.	❑ Yes ❑ no
7.4	**Utility Requirements**	
7.4.1	Electricity: _____ (Report Requirement)	❑ Yes ❑ no
7.4.2	Compressed air pressure _____(Report Requirement)	❑ Yes ❑ no

Specifications	Remarks
8.0 Good Engineering Practices Requirements	
8.0.1 Equipment must be fabricated following all Good Engineering Practices. The vendor's Quality System must follow applicable national or international standards.	❑ Yes ❑ no
8.0.2 The vendor shall provide a quality and project plan as part of their proposal.	❑ Yes ❑ no
8.0.3 The vendor shall provide a project manager for the project to provide a single communication point with the user	❑ Yes ❑ no
8.0.4 Vendor must generate all applicable documents during all phases of equipment fabrication i.e. design, fabrication, testing and shipment as per applicable standards.	❑ Yes ❑ no
8.0.5 All sensors, controllers, PLC, transmitters, indicators and any other controller or indicators to read, print or control any of the parameter, will have to be calibrated, traceable to National or international standards. Original calibration certificate along with traceability to be submitted by vendor in their IQ file.	❑ Yes ❑ no
8.0.6 All material of construction should have test certificate	❑ Yes ❑ no
8.0.7 When the preventative maintenance requirements recommended by Vendor are followed, the machine shall have no more than one unscheduled repair per year.	❑ Yes ❑ no
8.1 Inspection and testing	
8.1.1 System shall be inspected and tested (FAT) at the Vendor's site in the presence of user's representative before delivery.	❑ Yes ❑ no
9.0 Constraints	
9.1 Equipment location and available space	
This equipment will be installed in the area as follows. **Floor: Ground Floor Plant: Hormonal Formulation Block.**	❑ Yes ❑ no
9.2 Timelines	
9.2.1 Response to URS: Within 1 weeks of receipt of URS	❑ Yes ❑ no
9.2.2 Quotation Submission: Within 1 weeks of receipt of URS	❑ Yes ❑ no
9.2.3 Submission of detail functional design specification (FDS) and schematic drawings: 2 weeks after order finalization	❑ Yes ❑ no
9.2.4 Submission of FAT/SAT Specification-: before 1 weeks of FAT	❑ Yes ❑ no
9.2.5 Submission of Installation Qualification (IQ) and Operational Qualification (OQ) protocols -: 1 months before delivery	❑ Yes ❑ no

Specifications		Remarks
9.2.6	Mechanical and electrical drawings-: 2 weeks before delivery.	❑ Yes ❑ no
9.2.7	Submission of control system details and control system verification protocol: 2 weeks before FAT.	❑ Yes ❑ no
9.2.8	Equipment Delivery: Maximum 8 weeks from the approval of specification and drawing	❑ Yes ❑ no

We have read and understood the above Specifications and agree to abide by the same.

Place: **Signature of the Bidder**

Date: **Name, Seal and Address of the Bidder**

10.0 Abbreviation

Terms	Abbrevation
API	Active pharmaceutical ingredient
CD	Compact Disc
CFR	Code of Federal Regulation
Db	Decibel
DQ	Design Qualification
EU	Endotoxin Unit
EU-GMP	European –Good Manufacturing Practice
FAT	Factory Acceptance Test
GAMP	Good Automated Manufacturing Practices
GMP	Good Manufacturing Practices
HEPA	High efficiency particulate air
HDPE	High Density Poly Ethylene
HLL	HLL Lifecare Limited
HMI	Human Machine Interface
HTM	Health Technical Memoranda
Hz	Hertz
IPA	Isopropyl Alcohol
IQ	Installation Qualification
ISO	International Standards Organization
LED	Light Emitting Diode
MOC	Material Of Construction
OQ	Operational Qualification
NPI	NNE Pharmaplan India Limited
PID	Proportional Integral Derivative
PLC	Programmable Logic Controller
PQ	Performance Qualification
PVC	PolyVinylChloride
RTD	Resistance Temperature Device
RTP	Rapid Transfer Port
SAT	Site Acceptance Test
SOP	Standard Operating Procedures
SS	Stainless Steel
UPS	Uniterrupted Power Supply
US FDA	United State Food and Drugs Administration
WHO	World Health Organisation
WIP	Wash In Place