User Requirement Specifications
Cell Disruption Mill

Block Code	Area	Identification #	Quantity(No.s)	Capacity (L)
B1	Multiple Bacterial Block (Hep – B)	B1-CDM 01	1	25 L

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1	Layout showing location of the Cell Disruption mill in the Multiple Bacterial Bulk Block
2	List of preferred MAKE of components

HLL BIOTECH LIMITED, CHENNAI

INTEGRATED VACCINES COMPLEX, CHENGALPATTU

nne pharmaplan	User Requirement Specifications				HBL HLL BIOTECH LIMITED
	Equipment/System	Cell Disruption Mill			
	Identification #	B1-CDM 01	Document No.	URS/CDM 01	
	Effective Date	26-11-2015	Revision#	02	

1.0 APPROVAL SIGNATURE

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 shall 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.

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2.0 EQUIPMENT DESCRIPTION

The Equipment described in this URS is "Cell Disruption Mill" used for cell disruption of Yeast cells to be used for production of recombinant Hepatitis B vaccine. The recombinant Hepatitis B vaccine is produced as an intracellular product during fermentation.
The Cell Disruption Mill is an agitator bead mill with horizontal grinding container for disruption and finest wet grinding in a completely enclosed system.

TABLE 1: General Specification

Sl.No	Description	Specification	Remarks
1	Model	Vendor to specify	
2	Type	Glass bead Mill – GMP model	
3	Number of passes	3 times	
5	Flow Rate	Minimum : 40 LPH Maximum : Vendor to specify	
6	Type of product Pump	Lobe Pump / Screw pump	
7	Working temperature	2 to 8 °C	
8	Disruption container operating volume	25 L	
9	Disruption Bead Size	0.5 mm	
10	No. of disks on shaft	Vendor to specify	
11	Maximum Working Pressure for grinding chamber	4 Bar	
12	Quantity	1 No.	

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
- FDA Guidance for industry- Documentation for sterilization Process Validation
- ANSI/NSF 49-2008
- ISO 14664
- ISO 8362
- 5.4 – Specifications – ((< 0.5µ Ra for filling line and < 0.8µ Ra for Lyophiliser) and external surface matte finish (< 1.2µ Ra)

Note:

1.	This Technical Specification is the basis for an inquiry to a vendor and therefore the basis for the vendor's proposal.
2.	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 any deviation a comment must be inserted or enclosed as a separate annexure by referring to the respective URS specification number.
3.	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.
4.	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.
5.	The final version of this document including the vendor's comments will become basis of a potential purchase order or contract.
6.	The Technical Specification serves to define a summary of all vendor's requirements concerning scope of delivery and services.
7.	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.
8.	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.
9.	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.
10.	The makes requested are standard international makes. In case of any deviation, vendor to seek clarification from HBL before submitting the offers.
11.	Refer document "Installation Requirement Specifications and Specific Instructions" with URS NPI_120310_EQP_IRS_S1_01
12.	Refer tender document NPI-120310-EQP-S1-TD-20

Specifications	Remarks
3.0 PROCESS DESCRIPTION	
3.1 Input & Charging method	
3.1.1 Input & Charging to the cell disruption mill will be done through vessel via external pump. (The feed pump contains adjustable feed flow meter with minimum flow rate of 0.8 L/min).	
3.1.2 Glass beads shall be added before the process using funnel.	
3.2 Brief Process Steps	
3.2.1 Yeast cells undergo disruption and the output is collected in to another vessel (600 L)	
3.2.2 The necessary energy for disruption and grinding is transmitted to the grinding beads via easily exchangeable agitator disks mounted on a shaft. The grinding beads should be retained in the mill via dynamic gap separator.	
3.2.3 The material to be milled has to be constantly fed in to the mill by a separate product pump.	
3.3 Output & Discharging method	
3.3.1 Output from the cell disruption mill shall be collected in vessel 600 L.	
4.0 PRODUCTIVITY REQUIREMENT	
4.1 Change Over Time	
Not Applicable	
4.2 Others(If any)	
Not Applicable	
5.0 CONTAINMENT	
Not Applicable	
6.0 GMP REQUIREMENTS	
6.1 Process control	
The equipment must operate and control the following process parameters.	
6.1.1 Motor shaft speed	
6.1.2 Product flow rate	
6.1.3 Product temperature	
6.1.4 Inlet pressure	
6.1.5 Fluid level in the rinsing tank	
6.2 Failure mode detection	
Equipment Should be capable to detect the following failure, notify the operator with alarm and shutdown the process:	

6.2.1	Motor shaft speed out of range	
6.2.2	Product outlet temperature out of range	
6.2.3	Inlet flow rate out of range	

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:

Type of control	Purpose	Instrumentation
Pressure	To indicate, monitor and record the inlet pressure.	Pressure transmitter
Pressure	To monitor and control the shaft seal circuit pressure.	Pressure Indicator controller
Pressure	To indicate the seal rinsing liquid pressure.	Pressure Gauge
Temperature	To monitor, control and record the product outlet temperature	Temperature sensor with transmitter
Level	To monitor and control the level of the seal rinsing liquid	Capacitive Proximity Switch
Flow rate	To control the inlet flow rate into the system	Mass flow meter
Speed	To monitor and control agitator speed	Variable frequency drive with indicator

6.5 Batch data display and record printing

6.5.1 Equipment shall be operated through HMI and shall be possible to control through PLC

6.5.2 Batch data printing should include these parameters, but not limited to these,

- Time, date, Temperature, pressure, flow rate
- Operator name and space for signing

6.5.3 Control panel (HMI) with the following (not limited to these)

- Provision for manual operation, Emergency stop Button
- Provision for data acquisition and batch data print in non-editable format.

6.5.4 Equipment shall have provision to connect the equipment with Ethernet.

6.6	**GMP requirements (Others)**	
6.6.1	All product contact parts (inner chamber, shaft, disks, spacers) shall be made from SS 316 L with Ra of ≤ 0.6 µm and SS304 for external components with Ra of ≤ 1.2 µm and gap separator shall be made of tungsten carbide or equivalent material	
6.6.2	Make of the O-rings shall be FDA approved material	
6.6.3	All nozzle connection shall be sanitary type and special attention shall be given in shape and dimension of the nozzle and connection to realize efficient cleaning and steaming process. All nozzle connection should comply with dead leg requirement	
6.6.4	All nozzles shall be flushed to the wall on closure.	
6.6.5	Steam traps shall be provided where ever required at the system.	
6.6.6	Isolation valves should be provided wherever necessary.	
6.6.7	All gaskets should be made up of food grade/Silicone/EPDM	
6.6.8	Cell disruption mill should meet ASME standards, ASME section VIII,DIV.1,ASME BPE 2012,bio-procecessing equipment, GAMP 5, a risk based approach to compliant ,US FDA 21 CFR part 11 for electronic records and electronic signatures, GAMP for validation of automation system, IEC 60529 standards for protection of panel enclosure.	
6.7	**Specific requirements**	
6.7.1	The equipment should be suitable for microbial disruption.	
6.7.2	Equipment shall be provided with funnel to load the beads.	
6.7.3	Equipment should be designed for settable operating parameters.	
6.7.4	The motor shaft should be sealed with double mechanical seal.	
6.7.5	Equipment shall be supplied with exchangeable inner cylinder and removing device for the same.	
6.7.6	Non return valve shall be considered for product inlet line.	
6.7.7	Grinding container shall be provided with spiral jacket for maximum heat exchange efficiency.	
6.7.8	Vendor to provide the size of the TC ended connections for the following: • To connect with the cooling system • Product inlet and outlet • Cooling water inlet and outlet for main motor • Drain outlet • CIP inlet • Steam inlet	
6.7.9	Double mechanical seal shall be provided for the shaft with coolant arrangement.	
6.7.10	The equipment shall be steam sanitizable	
6.7.11	The equipment should have grinding beads separation system by means gap separator	

6.7.12	The equipment should be Ideal for continuous and batch operation with constant efficiency and achievement of the narrowest particle size range	
6.7.13	Equipment should have provision for rinsing and pressurising of the shaft seal by means of separately driven, stainless steel pump.	
6.7.14	It should have rinsing liquid reservoir and separate leakage container.	
6.7.15	In general the equipment has to be designed in a way to get easy and quick access to all necessary maintenance points.	
6.7.16	Operating pressure shall be adjustable with manual control valve	
6.7.17	The equipment should be designed for minimum dead zones / stagnant zones	
6.7.18	The equipment should be fully drainable and CIPable.	
6.7.19	Screen shall be provided in the drain line to prevent the flow of beads into drain line.	
6.7.20	Following interlocks shall be provided for the equipment • Cylinder open ----- Equipment not start • Front cover open ----- Equipment not start • High pressure in the chamber ----- Equipment stop • Temperature of the product out of range ----- Machine stop • Motor / Pump overload ---- Machine stop	
6.7.21	Nozzles, adaptors, instrument shall comply with ASME BPE 2012 compliant.	
6.7.22	Product Pump specifications • 1 Ph / 3 Ph, • IP 55 • PTC probes for the integrated frequency converter	
6.7.23	Motor Starter Cabinet shall be provided with following specification (for separate installation beside the equipment) • Housing of SS304 • IP 55 • Main switch • Star-delta contactor for mill motor • Contactor for pump motor • Contactor for rinsing pump motor • Relays with control circuits for safety and control instruments, • Transformer 400/230 V for control voltage • Current transformer for ammeter • Time-counter • Pre fuses	
6.7.24	Control panel shall have 3 ON/OFF push buttons, pilot lamps, EMERGENCY switch and ammeter	
6.7.25	Total motor drive assembly with SS304 cover with TEFC eff 1.	
6.7.26	Product pump must be in-line sterilisable.	

6.7.27 **Design Parameters:**

6.7.27.1	Capacity Range	: Vendor to specify
6.7.27.2	Shell design Pressure-	: Vendor to specify
6.7.27.3	Shell design Temperature-	: Vendor to specify
6.7.27.4	Jacket working Pressure-	: Vendor to specify
6.7.27.5	Jacket working Temperature	: 140°C
6.7.27.6	Jacket design Pressure-	: Vendor to specify
6.7.27.7	Jacket design temperature-	: Vendor to specify
6.7.27.8	Wall thickness of grinding cylinder	: Vendor to specify

6.7.28 The equipment shall be easily accessible for cleaning the product non-contact part at maintenance side of the equipment.

6.7.29 Cleaning:

- External surfaces and possible open vents should be resistant to at least 70% IPA
- WFI, buffer, solution shall be used to rinse and sanitise the system.

7.0 CONSTRAINTS

7.1 Equipment location and available space

This equipment will be installed in the **Multiple Bacterial Bulk Block** of IVC Vaccines manufacturing facility at HLL BIOTECH LIMITED, Chengalpattu. Location details are as follows:

Floor: Ground floor Multiple Bacterial Bulk Block
Section : Hepatitis-B (Hep-B)
Room No. : B1G010
Room dimension : 4282 X 4045 mm
False ceiling height: 3000 mm

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

7.2 Available Utility

7.2.1	Cooling Water @ 28-30°C,3 bar	_____ (Report requirement)
7.2.2	Chilled Water @ 7-12 °C and 3 bar	_____ (Report requirement)
7.2.3	Electricity : 1 phase /3 Phase	_____ (Report requirement)

8.0 ABBREVIATION

Abbreviation	Definition
cGMP	current Good Manufacturing Practices
CIP	Clean In Place
EPDM	Ethylene propylene diene monomer (M-class) rubber
FAT	Factory Acceptance Test
GMP	Good Manufacturing Practices

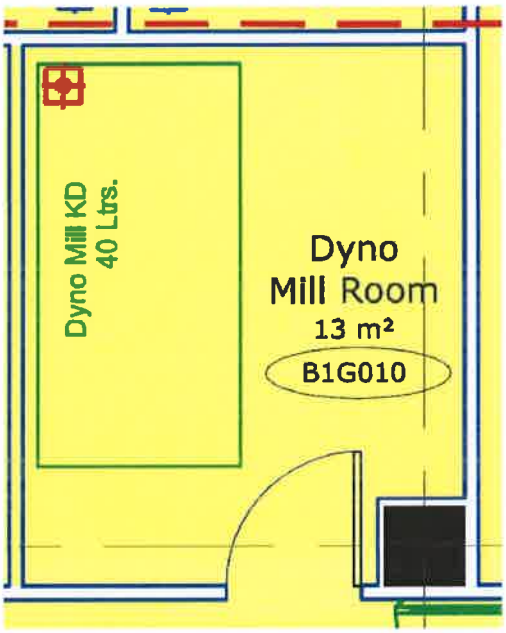
HBL	HLL Biotech Limited
HMI	Human machine interface
IRS	Installation Requirement Specification
LPM	Litre per minute
NA	Not Applicable
NPI	NNE Pharmaplan India Ltd
PRV	Pressure Reducing Valve
SAT	Sight Acceptance Test
SIP	Sterilization In Place
TBD	To be discussed
TC	Tri-clover Clamp
TEFC	Totally Enclosed and Fan cooled
URS	User Requirement Specification

9.0 REVISION INDEX

Revision	Date	Reason for Revision
00	15-09-2015	New document
01	09-10-2015	Revised as per the comments given by HBL dated 29-09-2015
02	19-11-2015	Revised as per the comments given by HBL dated 28-10-2015

URS Annexure 1: Layout showing location of the Dyno mill in the Multiple Bacterial Bulk Block

Dyno Mill room (B1G010)



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/E&H/Anderson-negele
4	Temperature sensor	Negele/ Radix/E&H/Yocogawa
5	Pressure transmitter	Wika /Dwyer/Siemens
6	IPC	Allen Bradley/ Siemens
7	Flow sensor	E&H/ Burkert
B	MECHANICAL	
8	Pressure gauges	Wika/waree/Denver/Negele
9	Pressure regulator	Festo/SMC
10	Diaphragm valve(Manual)	Gemu / ITT
11	Ball valve(Manual)	Modentic/Saunders/Alfa laval
12	Safety relief valve jacket	Herose/SS Spirax /Amtech valves
13	Steam trap	Steriflow/Spirax
C	PNEUMATIC	
14	Diaphragm valve(Automatic)	Gemu / ITT/SED/Saunders/Burkert
15	Angle seat valve(Automatic)	Gemu / ITT/Saunders/Burkert