VACCINE PRODUCTION CHAIN

100L /300L VIRUS VACCINE BIOREACTOR + 300L STAINLESS STEEL FERMENTER + 300L STORAGE TANK

100L-300L virus vaccine bioreactor

300L stainless steel fermenter (meet GMP standard)

300L Storage tank

300L Virus Vaccine bioreactor

Parameters:

1. System Composition:

System composition	Performance and technical indicators
Bioreactor Vessel	Total volume: 300L, working volume: 90-210L Tank structure: external surface polishing, internal no blind angle; tank material is 316L stainless steel material, clip material is stainless steel 304. Internal tank large visual angle liquid level observation sight glasses, 12V automatic delay Philips safety sight lamp; Two 25mm side holes can connect pH, DO and other sensors, with temperature, pH, DO Tank: design pressure 0.3 Mpa Clip: design pressure is 0.3 Mpa, use the optimization diversion design, improve the exchange efficiency and tank temperature uniformity. Aspect Ratio (Height: Diameter ratio): about 2:1.5 Surface treatment: internal and external polishing, internal electrolytic polishing, precision: 0.2-0.4um. Sterilization method: full automatic sterilization of tank, full automatic control program Sterilization adopts the sterilization method of steam into the clip, temperature control uses electric heater when culture, don't need long-term supply of steam Cooling system with exhaust (organic matter and water of tank will not be lost with the gas exhaust) diaphragm valve control the exhaust not to be infected, specially designed exhaust pipe without the accumulated liquid and bacterium. Using special low shear mixer (turbine) when suspension cell culture.
Mixing system	Top stirring, double mechanical seal, including condensed water seal tank, 0.2um asepsis steam filter, air pressure protection pipe and valve group, sterilizing pipeline and diaphragm valve group, steam trap group Including 2 gear blades, low shear mixing blades, can be used in the spherical carrier or suspension cell culture Shaft seal sealing standard: shaft seal tank liquid level declines less than 2mm within 10 days, pressure protection shall not see any air bubbles, when tank pressure protection, the shaft seal tank liquid pressure doesn’t increase within 24 hours Speed control: 300L:20-200 r/min , resolution 1 rpm, control precision ±1rpm
Sterilizing filter	Filtering precision is 0.02 um. Four-way gas through the filter into the cultivation tank, add check valve in the pipe

Sterilize method	Sterilization in place, auto control
Clean method	Clean in place, auto control in program. 300L fermenter have 2 spray balls
Temperature automatic control system	Water through the water inlet valve, electric heating, water cooling, circulating pump circulation, with over temperature protection function, good heat exchange efficiency; intelligent PID control not only ensures the quickness of temperature control, but also realized the energy saving. Fermentation temperature control range, temperature control: display range 0-150℃, resolution 0.1℃, control precision ±0.1℃, the precision and stability of the temperature has a decisive influence on the result of the fermentation.
Flow test and pressure test system	Variable area flow meter manually controls the inlet flow. Pressure transmitter automatically display the tank pressure, pressure control range: 0-0.3 Mpa, pressure gauge display.
PH control	Variable area flow meter and electromagnetic valve automatic control CO_2 flow, control PH, PH control: display range 2-12, resolution pH 0.01, control precision ±0.01 PH
N2 by pass system	Electromagnetic valve and variable area flow meter automatic control nitrogen mix with air
Inlet O_2 by pass	Electromagnetic valve and variable area mass flow meter control the flow rate of O_2 and air to adjust the DO
Inlet CO_2 by pass	Electromagnetic valve and variable area mass flow meter control the flow rate of CO_2
Liquid level control	Control accuracy: ±4mm
DO on-line inspection	Linkage control through oxygen, etc. DO control: display range 0-200%, resolution 0.1%, control precision ±2%
Antifoam control	Tested by foam sensor and added anti foamer by peristaltic pump/ pneumatic diaphragm valve. Electrode detection, peristaltic pump automatically and manually add antifoam agent.
Filling material control	With the perfect filling material system, filling material can be measured, automatic control the filling liquid, convenient dis-assembly, 300L with peristaltic pump and filing liquid bottle
Air inlet system	Auto control by mass flow meter, with two kinds of deep ventilation and surface ventilation mode, ventilation system: micro bubble ventilation system, air inlet filter, exhaust filter (need to be equipped with electric heating set), exhaust condenser, top blowing device
Sensor	DO sensor: Mettle/Hamilton electrode; PH sensor: Mettle/Hamilton electrode Temperature sensor: imported PT100 electrode;
Weighting system	Have Mettler weight system 0-300KG

Inspect glass	Have inspect glass, with light
Exhaust	Exhaust bacteria filter function, proportional regulating valve
Harvest valve	At the bottom, automatic
Tank lid lift	Have lid lift system
System equipped with the diaphragm valve	Burkert or Gemu imported valve
BLBIO-S biological process controller	Temperature, pH, stirring speed, multi-channel filling, DO, air flow, oxygen, dissolved oxygen
	Configuration: Siemens PLC and industrial control computer Color touch screen operation interface, PLC controller PH transmitter, DO transmitter, temperature transmitter, liquid level transmitter Servo motor controller and mixing control program Four channel gas mixing device and controller Peristaltic pump automatic control program Special animal cell culture automatic control software, automatic control temperature, pH, DO, stirring speed, loading and unloading, four-way gas inlet ratio Graph display control parameter curve Tank cap lifting device controller Tank automatic sterilization control program Water over temperature automatic protection device of circulating water pipe Automatically save the process parameters when U disk connects the USB plug Configuration software: SIEMENS S7 + FORCE CONTORL, SIEMENS S series PLC controller and data collection and control module e most advanced domestic technology control system, with the standard 10 inch LCD touch screen as the display interface, can use the keyboard and mouse operation at the same time, simple and clear interface, easy to operate. PH, DO electrode can be easily calibrated by software. Data collection and control software package: data A/D or D/A conversion, data collection and display, each control loop PID operation and setting, value control, sequential control
Computer system	Control parameter data collection and storage Graph display real-time control parameter curve Graph display history control parameter curve Internet remote monitoring function Software can connect multiple fermenters Remote telephone alarm function: when alarm signal, make alarm call by

	dialing the alarm telephone Mobile remote monitoring: realize the Internet real-time collecting the related data of multiple fermenters through mobile phones

2. Main Components

No.	Name	Description	Brand	Source
1	Tank	Main body material use 316L+304 clamp	Bailun	China
2	Mechanical sealing	Double mechanical sealing	Bergman	Germany
3	Stirring motor	SEW	SEW	Germany
4	Speed regulator	Fuji	Fuji	Japan
5	Site control system	Germany's Siemens S7-200 series PLC control system + 10 inch touch screen +control circuit board+ electrical box and various appliances, including cabinets, control core, signal acquisition, transmitter, power drive and various type of actuator	Bailun	China
6	Flow meter	200L/min	Chengfeng	China
7	Air intake precise filter	5 inch, 0.2μm	Sartorius	Germany
8	Exhaust gas precise filter	5 inch, 0.2μm	Sartorius	Germany
9	Halitus filter	Sartorius φ25	Sartorius	Germany
10	Peristaltic pump		Spriax	UK
11	Pneumatic diaphragm valve		Burkert/Gemu	Germany
12	PH Electrode	Originally imported from Switzerland 120	Mettler/Hamilton	Switzerland
13	PH Electrode	Originally imported from Switzerland 3M	Mettler/Hamilton	Switzerland
14	DO Electrode	Originally imported from Switzerland 120	Mettler/Hamilton	Switzerland
15	DO Cable	Originally imported from Switzerland 3M	Mettler/Hamilton	Switzerland
16	Temperature Electrode	PT100	Burkert	Germany
17	Bearing	SKF	FKF	Sweden

18	Piping	316L Stainless steel		China
19	Other parts	Feeding bottles, silicone tube, piping, pipe racks, various types of valves, Pressure parameter, bearing, sealing, tools, etc.	Imported from Europe	Europe
20	Pressure sensor	-0.1—0.3Mpa，sanitation	BD	Germany
21	Control valve	Pneumatic angle seat valve for drainage control	Burkert/Gemu	Germany
22	Control valve	Pneumatic angle seat valve for isolation control	Burkert/Gemu	Germany
23	Control valve	Pneumatic angle seat valve for cooling control	Burkert/Gemu	Germany
24	Control valve	Pneumatic angle seat valve for sterilization control	Burkert/Gemu	Germany
25	Pneumatic diaphragm valve	For gas control, etc.	Burkert/Gemu	Germany
26	Exhaust control valve	ON/OFF	Burkert/Gemu	Germany
27	Pilot valve	Control pneumatic valves	Burkert/Gemu	Germany
28	Diaphragm valve	Feeding system sterilization	Burkert/Gemu	Germany
29	Manual diaphragm valve	For sampling systems	Burkert/Gemu	Germany
30	Pneumatic diaphragm valve	For air intake and exhaust system	Burkert/Gemu	Germany
31	Hydrophobic valve	Release condensate water for sterilization, share with system	Spirax	UK
32	Industrial control computer	Advantech	Advantech	Taiwan
33	Circulation pump	Grundfos	Grundfos	Denmark

300L Stainless steel Reactor

Parameters:

System composition	Quantity	Performance and technology index
Reactor	1	Total volume 300L, Working volume:30%-70% Tank structure: main material is 316L stainless steel and there is no dead corner inside the tank; equipped with fermentation tank special sampling, feeding valve; big view liquid level observation glass, 12 V safety sight light, temperature, connection, PH electrode Tank: designed pressure 0.35Mpa Diameter height ratio:1:1 Surface treatment: inner polishing precision: 0.6um, External polishing precision: 0.6um. Stirring shaft: employs adjustable 2 grades stirring shaft, 1ST and 2nd are P-4 impeller. With exhaust gas release condensation and filter system
Sterilization filter	1	Can steam sterilization
Temperature control system	1	Electric heating and water-cooling, circulation pump loop temperature control. Temperature manual control range: cooling water temperature +5 to 65° C; precision: ± 0.1° C

PH control system	1	2.00-12.00±0.05pH, manual control by adding acid and base, pH sensor (Hamilton/Mettler, Switzerland)
Valves and pipelines for system	1	Any metal parts and pipelines in contact with material are 316L stainless steel.

Technical hardware requirements:

- Total capacity: 300L.
- Temperature steam sterilization capacity - up to + 143C;
- Bottom serializable drain valve (membrane valve), a device without dead zones;
- Pressure clean steam sterilization - up to 3 bar;
- Material AISI 316 L;
- Pharmaceutical performance of the equipment (for the preparation of culture medium);
- All connections with fasteners in standard TC (tri-clover)
- Pressure gauge sanitary performance
- Hand-washing equipment through the top window;
- Gaskets and O-rings: Silicone (with spare sets);
- Spare ports on top of the pressure vessel in the standard TS with plugs and clamps.

Main Components of Mixture Tank 300L

No.	Name	Description	Brand	Country or Area
1	Tank	Main body material use 316L	Bailun	China
2	Stirring motor	(750W, 400VAC,60Hz,)	XiDa	China
3	Speed regulator	Fuji	Fuji	Japan
4	Halitus filter	φ25	Dominica	HK
5	Temperature Electrode	PT100	Burkert	Germany
6	Bearing	SKF	FKF	Sweden
7	Piping		316L Stainless steel	China
8	Magnetic agitation	Bailun		China
9	PH electrode	Hamilton/Mettler	Hamilton/Mettler	Switzerland

300L					
NO.	Product name	Spec	Qty	Unit	Origin
1	Tank	300L	1	set	Shanghai
	Configuration Table				
2	Magnetic stirrer	0.55KW	1	piece	Shanghai
3	Frequency converter	0.55KW	1	piece	Fuji
4	Cleaning Ball	1”	1	piece	Shanghai
5	Sight lamp/ Sight glass	DN40	1	piece	Shanghai
6	Long side sight glass		1	piece	Shanghai
7	Diaphragm pressure gauge	0.60Mpa	1	piece	Shanghai
8	Aseptic sampling valve	N6, Single hole after sampling it can be sterilized, yes	1	piece	Shanghai
9	Static pressure liquid level sensor	ST100	1	piece	NEXON
10	Temperature sensor	PT100	1	piece	NEXON
	PH sensor		1	piece	Hamilton
11	Manual tank bottom diaphragm valve	DN40	1	piece	Shanghai
12	Control cabinet （ Stainless steel box, inverter and other electrical accessories on the inside）		1	piece	Shanghai

300L Stainless steel Storage Tank

Storage tank

Parameters

System composition	Performance and technology index
Tank	Total volume 300L The main material of the fermenter is made by 316L stainless steel and jacket 304L stainless steel. Tank with wheel for mobile Tank structure: main material is 316L stainless steel and there is no dead corner inside the tank; equipped with fermentation tank special sampling, feeding valve; big view liquid level observation glass, 12 V safety sight light, temperature, connection Tank: designed pressure 0.35Mpa Diameter height ratio:1:1 Surface treatment: inner polishing precision: 0.6um, External polishing precision :0.6um. Stirring shaft: employs adjustable 2 grades stirring shaft, 1ST and 2nd are P-4 impeller. With exhaust gas release condensation and filter system
Sterilization	Can steam sterilization
Temperature control system	Electric heating and water cooling, circulation pump loop temperature control. Temperature manual control range: cooling water temperature +5 to 65 ° C; precision: ± 0.1 ° C
Valves and pipelines for system	Any metal parts and pipelines in contact with material are 316L stainless steel.

Material and brand of key components

No.	Name	Description	Brand	Country or Area
1	Tank	Main body material use 316L and 304	Bailun	China
2	Stirring motor		XiDa	China
3	Speed regulator	Fuji	Fuji	Japan
4	Halitus filter	φ25	Dominica	HK China
5	Temperature electrode	PT100	Burkert	Germany
6	Bearing	SKF	FKF	Sweden

7	Piping		316L Stainless steel	China
8	Magnetic agitation	Bailun		China

300L			
NO.	**Product name**	**Spec**	**Origin**
1	Tank	300L	Shanghai
	Configuration Table		
2	Magnetic stirrer		Shanghai
3	Frequency converter		Fuji
4	Cleaning Ball	1”	Shanghai
5	Sight lamp/ Sight glass	DN40	Shanghai
6	Long side sight glass		Shanghai
7	Pressure gauge	0.60Mpa	Shanghai
8	Aseptic sampling valve	N6, Single hole after sampling it can be sterilized, yes	Shanghai
9	Temperature sensor	PT100	NEXON
10	Manual tank bottom diaphragm valve	DN40	Shanghai
11	Control cabinet （Stainless steel box, inverter and other electrical accessories on the inside）		Shanghai

SINGLE-LAYER TANK WITH MICROPOROUS MEMBRANE FILTER SS316L

PRODUCT SPECIFICATIONS

Product	Single-Layer Tank Filter	Capacity	100L	
Categorisation	Non-Code	Quantity	1 Set	
Design Code	ASME BPE/ GB/T150-2011 Pressure Vessels			
Technical Parameters			**Brand**	**QTY.**

	Material	Internal Lining：SS316L	Other Materials: SS304	KEAN	1 Set
	Structure	Vertical installation, can be designed to move or legs according to customer requirements support			
	Roughness	A smooth, bright internal finish by mechanical polishing (Ra≤0.4um). Mirror finish top and bottom heads, matt finish tank body			
	Microporous membrane filter	Single-Layer Tank With Microporous Membrane Filter SS316L		KEAN/Millipore	1 Set

Working Principle: filter is used to prevent the solid particles from media mixed into the follow-up pipeline facilities. The large solid particles or impurities will remaining in it after the media is put into proper filter core, as it can reach the request. When surrounding pressure of the filter exceeds demand, or change new filter core, and re-install it.

Filters can be matched by different cores according to usage requirements. There are three types of cores (metal mesh, perforated plate and wedge wire) The filtering capabilities are as follows.

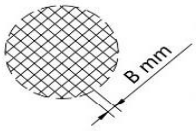

Angle-type Strainer


Straight Strainer


卫生级微孔过滤器
Sanitary Micro-Filter


Y 型过滤器
Y-type Strainer

Metal Mesh

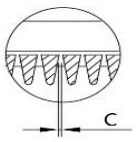


目数 Mesh	B(mm)	有效面积 Useful surface(%)
30	0,55	48
40	0,40	46
60	0,30	52,6
80	0,20	42
100	0,15	36,2
165	0,10	45,4

Perforated Plate

A 孔径	有效面积 Useful surface(%)
0.5	15
1	28
1.5	33
2	30
3	33
5	46

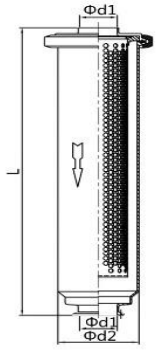
Wedge Wire



目数 Mesh	C(mm)	有效面积 Useful surface(%)
30	0,55	48
40	0,40	46
60	0,30	52,6
80	0,20	42
100	0,15	36,2
165	0,10	45,4

SANITARY STRAINER FILTER

ST–V1086



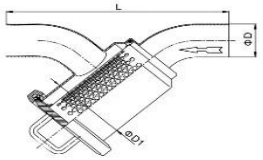
Welded Straight Strainer DIN

DN	D	d2	L
25 32	28 34	70	386
40 50	40 52	70	472
65 80	70 85	114.3 129.0	648
100	104	139.7	798

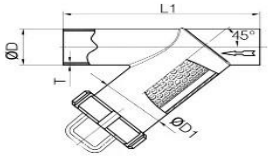
INCH

Size	D	d2	L
1" 1–1/2"	25 38	70	377 462
2" 2–1/2"	51 63	70 114.3	637
3" 4"	76 102	114.3 139.7	784

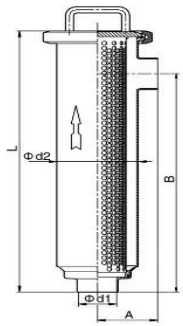
ST–V1087



ST–V1088



ST–V1089



Welded angle–type Strainer DIN

DN	D	d2	A	B	L
25 32	28 34	70	75	250	306
40 50	40 52	70	75	250 300	306 406
65 80	70 85	114.3 129.0	100 110	380 420	503 561
100	104	139.7	125	500	660

INCH

Size	D	d2	A	B	L
1" 1–1/2"	25 38	70	75	250	306
2" 2–1/2"	51 63	70 114.3	75 100	300 380	406 503
3" 4"	76 102	114.3 139.7	100 125	420 500	561 660

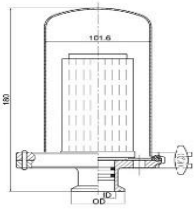
过滤器
Welded Y–type Strainer DIN

DN	D	D1	L	L1
25 32	28 34	76.2	235 240	125 140
40 50	40 52	101.6	260 280	165 195
65 80	70 85	114.3	320 375	330 280
100	104	154	400	340

INCH

Size	D	D1	L	L1
1" 1–1/2"	25 28	76,2 101,6	213 242	123 144
2" 2–1/2"	51 63	114,3	300 348	195 210
3" 4"	76 102	154	378 468	240 340

REBREATHER



ST–V1090

Size	ID	OD
1"	22	50.5
1 1/4"	29	50.5
1.5"	35	50.5
2"	48	64

DISC CENTRIFUGES DHC300

For Pharmacitical Industrial Processing

Disc StackCentrifuges

Disk stack centrifuges are high-speed centrifuges for the mechanical separation and clarification of mixtures comprising solids and liquids. These machines can be used in a wide range of applications. Due to their special design, disk stack centrifuges work at a higher rotation speed than other centrifuges such as decanters. As a result, the centrifugal acceleration (g-force) generated by a disk stack centrifuge is significantly more powerful than in decanter centrifuges. Moreover, the disks included provide a large

clarifying area. Thus, it is possible to separate ultra fine solid particles from a liquid and to separate liquid mixtures in an efficient way

Power drive adopts the friction clutch, Transfer power by the fluid, start reliably, prevent overland. The bearings used the machine are SKF grade in Sweden., guarantee working precision of the machine.

The separator adopts the PLC automatic control system, can carry out automatic de-slugging, ability of fitness is stronger, automatic degree is high. Easy to adjust, worker labor strength is opposite to ease, the solids content ratio in the mixture fluid is widely.

Separation theorem

The mixture fluid to be processed are fed to the bowl from feeding pipe ,under the effects of centrifugal force, the solids which has heavier density collects on the bowl wall .it include jams and impurities ,collected in sediment holding space .After a while ,the separated soilds are ejected from the bowl at controlling of PLC .the intervals at which de-slugging have to take place depend on the quality of the mixture fluid .De-slugging include automatic de-slugging ,total de-slugging ,partial de-slugging ,Normally customer don't need total de-slugging ,put up partial de-slugging under the condition of effects of automatic de-slugging are bad .the interval between two partial de-slugging is up to two minutes ,and electric current is normal .then re-establish the automatic de-slugging interval .The lighter products (lower density) flow along the inner side of the discs into the passage in the upper distributor ,the lighter product is discharged from the machine by the centrifugal pump .Thus the mixture fluid is separated well ,the centrifuge adopts self de-slugging and centripetal pump .Thus the machine can work continuously for a long time ,attain good separation effects in long run.

Disk Centrifuge Parameters:

Model	DHC300
Bowl speed (rpm)	7300
Capacity (L/H)	50-500
Outline size (L*W*H)	1050×850×1200
Weight (kg)	580
Inlet pressure (Mpa)	0.05
Outlet pressure(Mpa)	0.1
Disc stack thickness (mm)	0.6
Noise (dB(A))	90
Vibration at nominal speed (mm/s)	4.5
Solid recovery (%)	80-95
Motor power (KW)	4
Voltage (v)	400V
Frequency (HZ)	50 3 Phase
Protection grade	IP-55
Control box	PLC control Panel (Siemens brand)

FREEZE DRYER

Model: Lyopro-2-CIP-SIP

1. MAIN FEATURES

LYOMAC LYOPRO series Freeze Dryers, have been engineered and are manufactured to comply with the stringent requirements of the Pharmaceutical and cosmetic industry and rich experiences achieved in different application of industrial.
Plant manufacturing and commissioning references has established at worldwide customers.
The highest levels of process versatility, efficiency and operational safety are guaranteed by a careful engineering and best material choice.
The automatic process control accomplished by a PLC together with the LYOMAC SCADA Software & touchscreen interface, allows a total and easy management of the various process phases; the various plant's sections are clearly visualized on dedicated graphical pages reporting the physical parameters and additional process data necessary for a correct process development and control including the alarms visualization. The automatic filing of the various process data, parameters and alarms, allows an easy reporting while the desired issues can be printed.

LYOMAC PRO series freeze dryers are equipped with all the necessary tools for being validated including “Installation and Operational Qualification Protocols” – IQ/OQ - as well as the Factory Acceptance Test documents to be verified during the plant testing in our workshop. The plant engineering phases and manufacturing, have been developed in

accordance with the National and European Safety Regulations as per CE. Particularly meaningful is the installation of a special safety locking system at the freeze dryer main door to insure the plant safety during the SIP(Sterilization in Place).

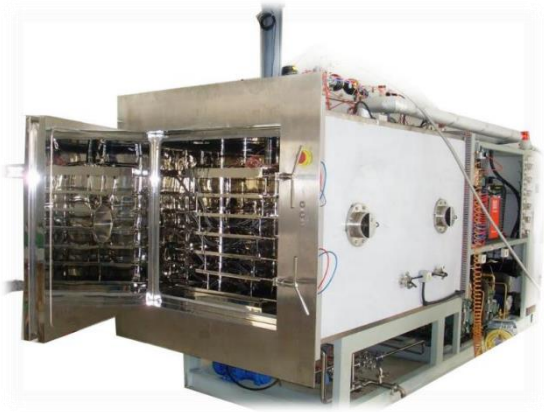
LYOMAC PRO series Freeze Dryers, can be equipped with the following systems:

- SIP: to pressure sterilizing the chamber and condenser Inner surfaces by means of saturated steam;
- CIP: to cleaning the loading shelves and internal chamber;
- Stoppering system: to move the freeze dryer shelves for an easy loading of the product to be freeze dried and to unload the final product.
- **Loading trays:** Specially made with mirror polished trays to load sterile product, material with stainless steel 316L, high grade equal to medical use. Set of trolley also included for easily move the trays.

2. TECHNICAL CHARACTERISTICS FOR CONSTRUCTION

LYOMAC PRO series Freeze Dryers are mounted on a duly painted carbon steel skid for an easy deployment of the Factory Acceptance Test at LYOMAC workshop and a well as a smooth and fast installation and start up at Customer site.(SAT)

The refrigeration groups including the compressors and the additional equipment are mounted on a painted carbon steel structure (skid).



LYOMAC Freeze Dryers include the supply of a stainless steel front panel mechanically polished Ra<0,6, which allowing the opening of the freeze dryer door into the sterile room, while the ancillary equipment is located into the technical area.

All the surfaces in contact with the product are in stainless steel AISI 316L, engineered, manufactured according the cGMP - Good Manufacturing Practices.

In the following paragraphs are reported more details of the various characteristics of the LYOMAC PRO Freeze Dryers, and in the enclosed “TECHNICAL SPECIFICATION” table the detailed technical characteristics of the plant offered.

2.1 MACHINE FABRICATION DETAILS

2.1.1 FREEZE DRYER CHAMBER

- The freeze dryer chamber can be either of a cylindrical or rectangular section as indicated in the annexe “Technical Specification” table
- Made in stainless steel AISI 316L, engineered and manufactured for high

vacuum and pressure process conditions (for SIP version), for the sterilization of the chamber and condenser internal parts and components

- Process and validation connections, including the chamber / condenser one,
realized in suitable diameter
- Air line filter equipped. Including N2 and clean air.
- Two illuminated sight glasses (depending on the PRO model and dimensions) is
Needed, both equipped in chamber and condenser
- Internal surfaces mechanically polished at Ra < 0,4
- Front panel in stainless steel AISI 304L mechanically polished Ra<0,7 applied on
the door sterile chamber site for connecting sanitary panel
-All surface of Chamber, which actually located at machine room, all surface coated with AISI304, with Ra<0.6.

2.1.2 CHAMBER DOOR

- The freeze dryer door can be either of circular or rectangular shape according to the chamber shape (see enclosed “Technical Specification” table)
- Made in stainless steel AISI 316L, engineered and manufactured for high vacuum and pressure process conditions (for SIP version)
- Internal surfaces mechanically polished at Ra < 0,4
- Supported by a duly dimensioned hinge
- Sealing gasket in suitable material Installed In the related cave realized on the peripheral chamber ring
- View sight glasses (depending on the PRO model and dimensions)
- External panel in stainless steel AISI 304 Plate Ra <0,7 mechanically polished
-Locking system specifically designed for high vacuum process conditions, manual handle or pneumatic pistons
- Locking system specifically designed for high vacuum and pressure process conditions (for SIP versions), including a series of pneumatic safety pistons installed all along the peripheral ring border out of the sterile chamber including an automatic safety locking system.

2.1.3 LOADING SHELVES

- One series of loading shelves (please refer to the Technical Data Table)
- One set of hollow shelves for thermal oil.
- Manufactured in stainless steel AISI 316 L
- Supplied AISI flexible hose, with an internal chicane for diathermic oil flow allowing the highest heat
transfer efficiency

- <1mm/m planarity
- Surfaces mechanically polished at Ra < 0,4 all the sides mirror polished.
- AISI 316L stainless steel" profiles for the ideal loading shelves positioning

2.1.4 CONDENSER

A special care has been devoted by LYOMAC Engineering Department in designing the condenser, based upon the actual experiences from different production and process. The peculiar design of the internal exchange coils as well as their installation peculiarities inside the condenser shell, guarantee in all the various sections the most regular and optimal pressure drop in the refrigerating circulation, achieving the ideal and uniform temperature profile distribution all along the circuit, driving to an optimal ice coating formation distribution all along the coils.

Main features of the LYOMAC PRO condenser are:
- Circular section(or square section as per "TECHNICAL SPECIFICATION" table)
- Made in stainless steel AISI 304 or AISI316L as per "TECHNICAL SPECIFICATION" table,
- Designed for high vacuum / pressure process conditions (for SIP versions), for the condenser inner parts steam sterilization
- Condensation coils made in stainless steel AISI 304L, on which are condensate,
under shape of ice, the process vapors
- Internal surfaces mechanically polished at Ra < 0,7
- Sight glass with light for easy inspect
- Cone shaped filter placed on the condenser drain to avoid ice blocks formation
- Duly dimensioned process and validation connections
- Automatic butterfly valve or hydraulic mushroom shape valve (as per "TECHNICAL SPECIFICATION" table)to isolate the Freeze Dryer Chamber from the condenser, made in stainless steel AISI 316 mirror finished, EPDM/silicone sealing gasket.

2.1.5 REFRIGERATION SYSTEM

The refrigeration group (low consumption; high efficiency model) is supported on
a skid and is composed of :
- At direct expansion of refrigerating gas R 404 A in the condenser
- Shelves cooling circuit by cooling low viscosity of

silicone oil.
- Primary two stage semi-hermetic refrigerating group.
- Thermostatic valves, interception valves and connections.

NOTE :

- The cooling is obtained by water coming from the cooling tower/chiller(customer's charge; LYOMAC will indicate the characteristics of the water on the Technical Data)
- We provide to recovery the heat coming from compressor's exhaust gas to heat the diathermic fluid in order to reduce the power consumption
- LYOMAC guarantee sufficient redundancy in terms of cooling capacity in such a way to avoid loss of product

2.1.6 THERMAL FLUID CONTROL SYSTEM

The thermal system is finalized to provide the loading shelves with the exact heat required by the process, by promoting the recirculation of the diathermic oil realized by a dedicated centrifugal pump in a circuit Inside the loading shelves. The diathermic oil ideal temperature is realized by means to dedicated heat exchangers.
The whole system has been engineered and manufactured to guarantee the ideal heat distribution and uniformity on loading shelves surface.
And the heating and the cooling systems are managed by an automatic control to allow the diathermic fluid to reach a temperature comprised between -55°C and 80°C (as per "TECHNICAL SPECIFICATION" table) to get an ideal temperature control during the heating phase, according to the pre-set curve parameters.

The system includes the following components:
- High efficiency plate type heat exchanger made in stainless steel AISI 304, primary circuit dedicate to the refrigeration fluid circulation
- Dual motor pump for diathermic fluid recirculation
- AISI 304L expansion buffering tank including level control
- AISI 304L interconnection piping and valves

2.1.7 VACUUM PUMPING SYSTEM

The system includes the following main components:
- oil sealed vacuum pump, dual stage (as per "TECHNICAL SPECIFICATION" table)
-Gas Ballast
- Anti-suction valve avoid valve to avoid oil carry over

during pump's shutdown phase
- Roots type vacuum pump equipped with pressure regulation valve
- Pirani vacuum measuring device
The vacuum group is installed on a carbon steel skid duly painted, condenser
Interception valve to avoid oil carry over during pump's shut down phase
Operated valve, piping made in stainless steel AISI 304L and at the chamber and at the condenser, with vibration buffering joint, instrumentation to allow a correct freeze drying process.
- Calibrated pressure control - The plant allows the control and automatic
Regulation of the vacuum Into the chamber during the freeze drying process, by
air or inert gas purging.

2.1.8 THERMAL INSULATION

The ideal process thermal efficiency is achieved by applying a thermal insulation to the following main plat's components:
- freeze dryer chamber
- condenser
- piping, heat exchangers and equipment where necessary
The insulation materials, duly chosen according to the application peculiarities, are protected by applying aluminum diaphragm, water and fire proof.

2.1.9 PROCESS AUTOMATION SYSTEM

"LYOMAC" SCADA System

The LYOMAC PRO series Freeze Dryers, are equipped with two sections, the
control cabinet where the process control system is installed,another is remote control industrial use computer. Electrical cabinet installed on the Freeze Dryer supporting structure already connected to the plant components; however, if differently required by the customer lay out and/or by space availability. In this case the electrical wiring, signal wiring as well as the pneumatic piping will be prepared in advance of the required length to allow an easy and fast installation at Customer side.

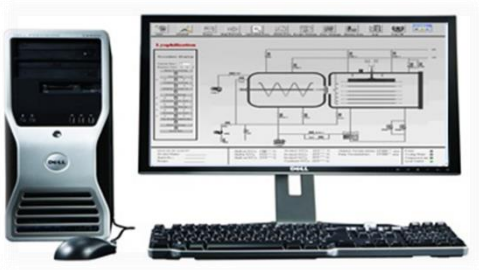
- Fabric of electrical cabinet

It is made in carbon steel plate, duly painted, engineered to include all the process
and safety electrical devices, motors protection thermal switches, sequences
auxiliary relais, locks, interlocks, switches, lamps, power

metering instruments,
lamps, volts, wiring and connections; the electrical board is manufactured according to IP55 classification, including auxiliary circuits 24/220/380 Volts and the internal lighting.
Water splitting sealed doors.
Manufactured in accordance with the CEI, CENELEC present regulations.

- SCADA systems

The automation system is realized by means of a PLC (Process Logic Control) supervised by a SCDA package (OMEON,SIEMENS or equivalent) on a PC including a colour Touchscreen for an easy access about production process on machine operation site.
The SCADA graphic software and process control has been developed to allow the visualization, selection, modification and printing of all the process configuration parameters in particular:



- Freeze Drying process recipes
- SIP process parameters setting
- CIP process parameters setting
- Management of Freeze Drying batches and cycles
- Continuous process data acquisition and storage
- Real time parameters trends
- Process data graphic trends storage
- Graphic pages with plant main sections synoptic
- Alarms visualization and storage
- Maintenance programme steps visualization

The software controls in automatic the condenser defrosting cycle and the SIP (Sterilization in Place) cycles and CIP(Cleaning in place) cycles (when included in the scope of supply).
The system allows a periodic data back up on another server or conservable media.
The access to various system interfacing levels, is protected by pass words.
On the PC monitor will be shown the following process parameters:

- Steam pressure
- Freeze dryer chamber pressure
- Freeze dryer chamber vacuum level
- Condenser pressure level
- Condenser vacuum level
- Heating fluid inlet/outlet to shelves temperature
- Product loaded on shelves temperature
- Chamber/steam drain temperature
- All valves,motors,signals on/off status data
- Cycle running time / setting time

……

Data output, allow the printing of the following data related to a single production batch:

- Cycle identification and description, by curve or tables
- Activated alarms
- Reset alarms
- Operator data
- Log in / Log out record

The Process Logic Control Programed, allows a careful vacuum level control into the chamber during the freeze drying process, according to the product's temperature.
The PLC system equipped with an UPS to avoid the loss of the stored information in case of power blackout (for more than 30 minutes)
If required by the Customer, a chart recorder can be installed on board of the Process Control Panel,Refer to “Techniccal specification”table.

- OPERATOR PANEL INTERFACE

At one side of the Freeze Dryer door (sterile room side) an operator panel is installed allowing the control of the basic operations (e.g Shelves moving upwards/downwards, door opening/closing, chamber light on/off, main emergency switch) requiring to be accomplished by the operator.

2.2 PROCESS FLUIDS

Included in the scope of supply, are the following fluids:
- Low viscosity of silicone oil;
- Refrigeration gas
- lubricating oil for refrigeration system;
- Vacuum pump oil.
- Hydraulic lubricant, If applicable.

2.3 DOCUMENTATION

The supply will include the following documentation:
- Plant lay out including plant dimensions and distances (within 5 days from order definition)
- P&ID (Process and Instrumentation Diagram)
- Electrical wiring schemes
- Pneumatic and hydraulic schemes
- Qualification certificate
- Factory test certificate
- Installation manual
- Operation manual
- Maintenance manual
- Trouble shooting
- Electrical and mechanical equipment list
- Process control system Hardware material list

- Reference manual for all main components installed.
- Instruments calibration certificates
- Materials certificates
- Spare parts list
- Set of IQ, OQ, PQ, protocols

2.4 UTILITY SUPPLY

According to layout drawing, customer need connect to bellow utilityes, which has different connection ports size:

-Power
-Compressed and Instrument air
- Service chilled water
- Steam
-Cleaning water/WFI
- Nitrogen
- Clean air
- Drains
-Hot water(If applicable for Non-sterilization machine for defrosting of condenser)

Note:

The LYOMAC installed one UPS only support power for

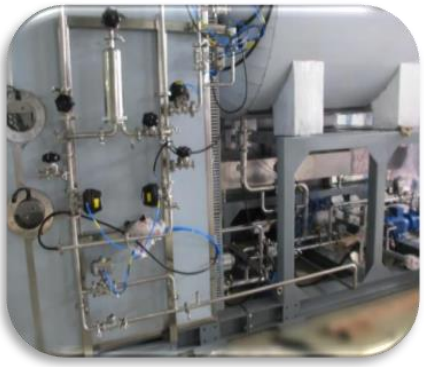
- PLC running
- Main control parts running;
- Touchscreen operation
- All signal and sensors data input to PLC.

Customer need prepare stable power for:

- Main power supply for all motors
-Power for computer

2.5 PLANT TEST

The Freeze Dryer will undergo to a two batch production duration test further to the completion
of the installation.



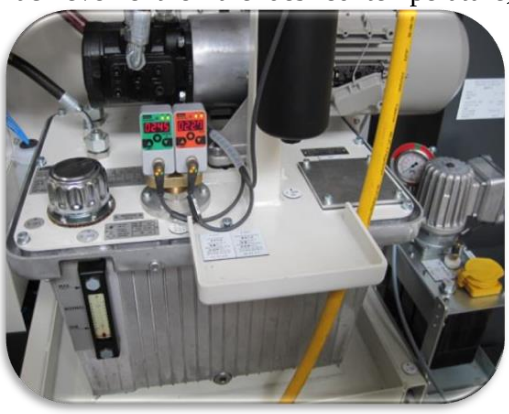
3. OPTIONALS

LYOMAC PRO series Freeze Dryers can be equipped with the following optional
equipment, on Customers' request depending on single installation requirements.

3.1 STERILIZATION - S I P –

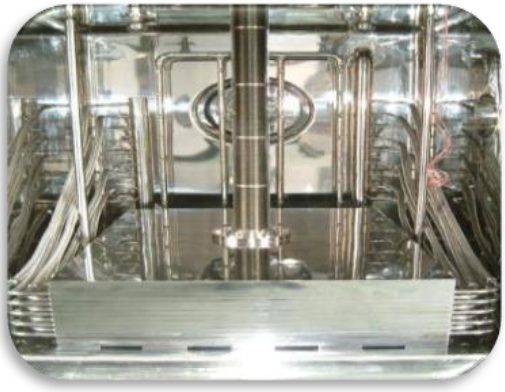
In case the **SIP** is foreseen, the Freeze Dryer chamber and condenser are engineered and manufactured to be exercised under pressure and tested in accordance to the GB150-1998 or PED regulation(refer to"TECHNICAL SPECIFIATION "table) norms to a design pressure of 2 barg.
To get an efficient sterilization of the chamber and condenser internal surfaces, a saturated steam sterilization at 2 barg is considered corresponding to a temperature of 130°C.
The chamber door is duly equipped with a series of Pneumatic actuated pistons,Installed on the freeze dryer body out of the sterile room which allow a perfect and safe sealing during the saturated steam pressure process. The sealing gasket's profile and material have been engineered according to process conditions.

The SIP system includes:
- Liquid ring vacuum pump, operating also during the drying phase further to the freeze drying process ;
- Electrical board and process control cabinet review to allow a correct automatic control of the sterilization process, allowing a chamber and condenser pressure and temperature regulation.
- The cycle parameters can be modified by interfacing at the process control touchscreen and SCADA system.
- The SIP duration, is pre set and starts at the achievement of the desired temperature, controlled at the discharge points.



Furthermore:
Chamber cooling system to reduce the temperature at the end of the SIP cycle, realized by circulation of tap water all along the chamber external walls. This system allows a faster decrease of the chamber temperature for a prompt starting of coming further Freeze Drying cycle.

3.2 CLEANING SYSTEM - C I P –



The system foresees the Freeze Dryer chamber and condenser inner surfaces cleaning by means of stainless steel AISI 316L spraying nozzles both fixed and rotary type, duly installed on stainless steel manifolds. The spraying nozzles allow the WFI (Water For Injection, to be provided by Customer) high pressure spraying on the of the

chamber and condenser inner surfaces allowing their ideal cleaning.
- Electrical board and process control cabinet review to allow the automatic CIP Cycle by easily input all parameters flexibly.
A further improvement of the CIP cycle, can be achieved by the "Shelves Lifting System".

3.3 STOPPERING

The device allows the lifting of the chamber loading shelves at the end of the freeze drying cycle, for the closure of the vials in vacuum or inpresence of inert gas.
The device drives the translation of the shelves towards the bottom, supported by proper lateral rails and later the lifting towards the top of each plate.
This application involves the following integration to the freeze dryer chamber:
- Shelves reaction and push frame stainless steel AISI 316 L.
- Flexible hose connections between manifolds and shelves.
- Dynamic cylinder with vacuum/pressure seal and necessary safety devices.
The piston of cylinder is made in stainless steel AISI 304 ,installed on the chamber upper plate, duly dimensioned, in stainless steel AISI316L and equipped with a flexible bellow avoiding any accidental hydraulic oil leaks during the running phases, in order to prevent any contamination of the chamber inner part.
- Hydraulic unit complete of pressure regulation valve and all the necessary Interconnections fittings.
- Electrical board and Process Control Cabinet implementation to allow a correct Freeze dryer operation.

Stoppering system can be automatically running as pre set parameters on below cycles of :
- Stoppering after freeze drying cycle finished;
- CIP cycle for auto moving upwards/downwards while nozles spraying

Stoppering pressure and moving speed is relatable for meeting different requirement of different vial and rubber cap closure.

3.4 Pizza door-

Pizza door is mounted on front of chamber, with moving up and downwards for loading/unloading operation.
Moving operation either driven by hydraulic or server motor.
Set of protection devices including safety grating devices to avoid any potential mis-operation.
Shelves are moving up through pizza door under constant height.
Set of bridge can be provided by seller to easily support material moving in/out of shelves.
More details in specification list.

3.5 Semi-Autoloading system

Semi-Auto loader is build for pushing trays from conveyor to freeze dryer through pizza door All operation by touchscreen. And protected by Rabs /laminar flow.
Unloading will be required manually after vial rubber cap sealed. And need push to conveyor manually for capping.

4. COMMERCIAL PART

Price include:

Pharmaceutical Freeze Dryer Mod. LYOMAC LYOPRO-2-CIP-SIP

- CIP&SIP systems are included
- Pizza door and auto loading system not included
- Hydraulic stoppering system for vial rubber cap closure enclosed is not included in offer.
- One set of tray included
- Use of know-how, engineering documents and supplies as per paragraph 2-3 and enclosed 'Technical specification'

ENCLOSURES:

5.1 TECHNICAL SPECIFICATION TABLE

Technical Specification

Main data		
1.	Model	LYOPRO-2.0
2.	Drying capacity(if load with trays)	Max ice capacity with 50 liters
3.	Power supply	380VAC/50Hz，3phase, 25KW
4.	Control system	PLC+HMI+PC with Auto, Manual control mode.
5.	Cooling water consumption	≥12m^3/h (T≤28℃/P=0.15~0.2Mpa)
6.	Compressed air consumption	≥20L/Min（P=0.6~1.0Mpa）
7.	Water for washing	≥60L/Min（T=80℃/P≥P=0.15~0.2Mpa）
8.	Steam for SIP	60Kg/batch, P=0.2~0.3Mpa
9.	Steam for de-icing	30Kg/batch, P=0.2~0.3Mpa
10.	Install dimension	3700×1500×2800mm（Approx.）(Final design need follow sketch)

11.	Weight	4,500kg（Approx.）
12.	Shelf installation	Build and fixed in vacuum chamber
13.	Layout arrange style	● Cubical chamber and Cubical condenser isolated by mushroom valve ● Integrity frame design. ● Another remote control pc
Performance Data		
1	Shelf cooling rate	≤60min (from 20℃ to -40℃, empty load)
2	Shelf temperature scope	80℃~-50℃
3	Shelf heating rate	≥1℃/Min
4	Shelf ultimate temperature	-55℃
5	Condenser cooling rate	≤30min (from 20℃ to -40℃, empty load)
6	Condenser ultimate temperature	-75℃
7	Chamber ultimate vacuum	≤3 Pa
8	Chamber evacuate rate	≤30min (from 1 Atm to 10Pa, empty load)
9	Chamber leakage performance	≤3×10^{-2} mbar•lit/sec
Chamber ,condenser, Shelf		
1	Chamber shape	Cubical type
2	Chamber roughness	Internal: Ra≤0.4 μm (0.4Micron) External: Ra≤0.6 μm (0.6Micron), grinded and without sharp edge
3	Chamber material	Internal material with AISI316L External cover material with AISI304
4	Chamber insulation	Aluminum silicate and polyisocyanurate foam
5	Chamber bottom slope	1% (For complete drain residual water)
6	Chamber validation port	One port with ISO40 connection
7	Condenser shape	Cubical type
8	Condenser roughness	Internal: Ra≤0.5 μm (0.5Micron) External: Ra≤0.6 μm (0.6Micron), grinded and without sharp edge
9	Condenser material	Internal material with AISI316L External cover material with AISI304
10	Condenser insulation	Aluminum silicate and polyisocyanurate foam
11	Condenser coil	Electrical Polished Serpent form design Material: AISI316L
12	Condenser temperature sensor	Type: PT100

		Temperature of coil in condenser
13	Chamber door material	Internal material with AISI316L
		External cover material with AISI304
14	Chamber door roughness	Internal: Ra≤0.4 μm (0.4Micron)
		External: Ra≤0.6 μm (0.6Micron), grinded and without sharp edge
15	Chamber door insulation	Aluminum silicate and polyisocyanurate foam
16	Chamber door open direction	View face to door: from right to left
		Open angle: ≥110°
17	Chamber door flange	Square flange is available for connecting sandwiched panel.
		Material:AISI304
		Clean room side surface polish: Ra≤0.4 μm (0.4Micron)
18	Chamer&condenser design standard	GB150, China Steel Pressure Vessel Regulate
		Design pressure: 0.25 Mpa (Absolute pressure)
		Design temperature: 130℃
19	Chamer&condenser Jacket(Excluded)	Water cooling jacket designed for facilitating cooling after SIP
20	Chamber-condenser isolation valve	Mushroom shape valve with hydraulic cylinder driven ,Maintenance free design-no change parts
		Size: DN250
		Material: AISI316L
21	Chamber and condenser internal corners	Coving shape, smoothly and polished
22	View port	One DN150 in center of chamber door
		One DN150 in side of chamber with lamp
		One DN150 in side of condenser with lamp
23	Shelf stack	Single size: 900*600*20 (L*W*T)
		Totally 4 useful shelves with extra one for radiation
		Total useful shelf area: 2.7 m^2
		Inter-shelf distance: 90mm
24	Shelf operate	Fixed in chamber
25	Shelf temperature uniformity	≤±1℃ (Balance state)
26	Shelf surface flatness	≤±0.5mm/m
27	Shelf surface roughness	Ra≤0.4 μm (0.4Micron)

28	Shelf material	AISI316L
29	Shelf temperature sensor	Type: PT100
		Four sensors (One for each shelf)
		One sensor for Silicone oil inlet(double sensor with one for standby)
		One sensor for Silicone oil outlet
30	Shelf hose	Material: AISI316L
		Connection: welding
Refrigeration system		
1	Compressor	Brand: Germany Bitzer Two stage semi-sealing piston reciprocating type.
		Power: 12HP/compressor
		Quantity : One
2	Sub-cooling exchanger	Bitzer,Germany, Built with compressor
3	Expansion valve	Danfoss,Denmark
4	Solenoid valve	Danfoss,Denmark
5	Pipeline sight glass	Danfoss,Denmark
6	Water condenser	Tube&shell type.
7	Liquid and air filter	Emerson,USA
8	Pressure controller	Danfoss,Denmark,Denmark
9	Pressure meter	Refco, Switerland
10	Vibration absorber	Packless, USA
11	Oil Separator	Emerson, USA
12	Refrigerant	R404A (CFC free, environment friendly), Honeywell,USA
Vacuum system		
1	Vacuum pump	Ulvac, Japan brand
		Quantity : One
		Evacuate rate: 40M^3/H
2	Butterfly valve(pump isolate)	Gemu, Germany
		Size:DN50
3	Vacuum sensor	Edwards, Pirani type. UK
		Quantity : two
4	Vacuum pump anti- suck valve	Siegvac solenoid valve
		Size: KF40
5	Chamber Venting Filter	Stainless steel 316L shell,
		Type:0.22μm
Circulation system		
1	Circulation pump	Grundfos, Denmark UPS40-120F
		Quantity: One
		Motor Power: 0.46Kw/Motor

2	Thermal media	Silicone oil, 5cst
3	Heat exchanger	Alfa Laval
		Quantity: One
4	Temperature over heating temperature controller	Danfoss,Denmark
5	Lack pressure controller	Danfoss,Denmark
6	Circulation pipelines material	AISI304
7	Electrical Heater	4KW
8	Heating control	PID control system ● Over heat- protection ● Less pressure protection
Hydraulic and Pneumatic system		
1	Hydraulic motor	Siemens
	Hydraulic solenoid valve unit	YUKEN, Japan,
2	Hydraulic oil container	15L
3	Bellow	Material with AISI316L
4	Stoppering design pressure on shelf surface	0~0.1Mpa/cm^2 (Pressure adjustable)
5	Pneumatic air source unit	Mindman, Taiwan
6	Pneumatic Solenoid valve	Mindman, Taiwan
CIP,SIP and De-icing system		
1	Chamber door lock system	Automatically pneumatic latch assist by manual handle
2	Chamber door gasket	T shape made with silicone rubber material
3	Liquid ring pump	Brand: SIHI , German ， LEMC50
4	Water and steam inlet Pipeline material	AISI316L
		Orbit welding
5	Steam and WFI inlet valve	Diaphragm type, Yuanan
6	Steam and WFI outlet valve	Actreg, Ball type. Italy
7	Shelf cleaning nozzle	Wide-angle type, material AISI316L
8	Chamber cleaning sprayer	Rotary type, material: AISI316L
9	Temperature sensor	Type: PT100
		One for Chamber drain point at lowest temperature point
		One for Condenser drain point at lowest temperature point
10	Steam trap valve	Miyawaki, Japan
11	Pressure sensor	JUMO /WIKA,Germany
12	Seal gasket	Silicone rubber material of sanitary grade
Control system		
1	PLC+HMI	Omron, Japan
2	Touch screen	Omron, Japan
3	Monitor PC	Dell (LCD monitor)

4	Low voltage components	Schneider, France
5	Electrical cabinet	Dull polished in all surface.
6	PC program	LYOPRO-5.0 Net Scada system based on conception of FDA 21CFR
		Electronic signature, Electronic record
		Auto, annual and emergency mode available.
		History data table and curve recorded
		Privilege level and password setting function
		Alarm displayed and link to PLC input and output for protection.
7	Safety measures	Control system power failure protection
		Vacuum failure alarm and protection
		Shelf and condenser cooling alarm and protection
		Shelf heating alarm and protection
		Heater failed alarm and protection
		All motors overload alarm and protection
		Shelf anti-drop protection
		Insulation on hot surface
		Warning labels on potential risk surface
Documentation		
1	Layout drawing	Supplied with English language
2	PID drawing	Supplied with English language
3	Electrical drawing	Supplied with English language
4	Operation manual	Supplied with English language
5	Maintenance manual	Supplied with English language
6	FAT protocol	Supplied with English language
7	SAT protocol	Supplied with English language
8	Components List	Supplied with English language
9	Material certificate	Supplied with original version with translated for reference
10	Components certificate and manual	Supplied with original version with translated for reference
11	Pressure vessel design certificate	Supplied with original version with translated for reference
12	IQ,OQ,PQ	Supplied with English language

ENCLOSURES:

5.2 SPARE PARTS LIST

SPARE PARTS LIST

Spare Parts list			
1	Refrigerant system	Expansion vale	1 No.
		Solenoid valve	1 No.
		Solenoid valve coil	1 No.
		Liquid filter core	1 No.
		Pressure meter	1 No.
		Refrigerant oil	5L
2	Vacuum system	Vacuum Pump oil	4L
		KF gasket	1 No
3	Circulation system	Silicone oil	10L
		Pipe Flange gasket	1 No.
4	Hydraulic and Pneumatic system	Hydraulic oil	5L
		Pneumatic tube	10m
		Pneumatic connector	3unit
		Hydraulic flange gasket	1 No
5	CIP and SIP system	Clamp	3 No.
		Pipe clamp connector	3 unit
		Clamp gasket	10 Unit
		Gasket for Chamber door	1 No.
6	Chamber and condenser	View port flange gasket	1 No.
7	Control system	Chamber door sensor	1 No.
		PT100 sensor	1 No.
8	Tools	Refrigerant charge tool	1 No.
		Refrigerant pipe flaring and cutting tool	1 set
		Ratchet tool for refrigerant check valve	1 Set