

AUSTAR

AUSTAR

Customized GMP Freeze-Drying Solutions



Fill-finish

Contents

AUSTAR is a technology-based pharmaceutical engineering solution provider with deep understanding of pharmaceutical industry regulations and processes. Integrating global high-quality resources and being committed to helping clients improve pharmaceutical process and operational effectiveness. Through boosting global drug safety and efficacy to protect and promote human health.

As a leading solution provider for pharmaceutical industry, AUSTAR can provide clients with the most cost-effective and customized GMP freeze-drying solutions which are widely applied in Laboratory, pilot-scale and commercial production.

Our freeze dryer technology is originated from Europe, continuous technical innovation with resources integration is our power.

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AUSTAR Freeze-Drying Overview

Milestones

- > AUSTAR works in partnership with clients to develop the most appropriate freeze-drying solution, offering reliable and trouble-free process technology based on more than 30 years of experiences working with the pharmaceutical and biotech industries across variety of pharmaceutical applications.
- > Since 1991, AUSTAR has been devoting to promoting freeze- drying solution in pharmaceutical and biotech industries, and has successfully served customized products and services for over 60 pharmaceutical enterprises and R&D institutions.
- > As the first company to introduce European advanced large-scale freeze dryer and freeze-drying technology to China clients for API application, AUSTAR made outstanding contributions for the development of intermediates such as 6APA, 7ADCA and 7ACA, and its downstream cephalosporin antibiotics and ferment antibiotics.
- > In 1999, AUSTAR cooperated with STERIS GmbH (LEYBOLD origin), which used to be the global known manufacturer for freeze dryer and automatic loading & unloading system. The freeze dryer is widely used in European, American and Asian pharmaceutical enterprises and well appraised by customers.
- > AUSTAR freeze dryer business division was founded in Nanjing in 2014. The design team consists of international leading designers and domestic experienced designers from freeze-drying industry. In October of 2015, AUSTAR successfully launched the first freeze-drying line in the industry, and more than 100 Chinese customers participated in this launch event.

Integrated Solution

AUSTAR has the capabilities of design, fabrication, qualification and validation. AUSTAR freeze dryer can be integrated with other systems manufactured by AUSTAR including LAF, RABS, Isolator and Automatic loading & unloading systems, etc.

Integrating various core technologies, AUSTAR is constantly developing customized freeze-drying solution to address emerging challenges in pharmaceutical freeze-drying technology.



LYOCORE GMP Production Freeze Dryer

Product Description



From 3D design to as built

AUSTAR devotes itself to providing intelligent freeze dryer with purpose of product protection. As the key equipment for production of sterile preparation, AUSTAR freeze dryer is designed and constructed according to European technical standard. All systems are completely tested at factory under real working conditions. The industrial production freeze dryer provided by AUSTAR can be used to freeze-dry drug product in vials or trays, which complies with the cGMP guidelines and the FDA recommendations, and fulfils the most stringent requirements of the pharmaceutical and biotechnological industries.

AUSTAR freeze dryer products cover the range of 2-40 m².

Features and Advantages

cGMP Compliance

- The bottom surfaces of drying chamber are designed with bi-directional slope to facilitate drainage
- Fixed nozzles and auxiliary rotary spray ball are used to ensure maximum coverage for cleaning
- Construction of chamber makes all edges and rounded corners easy to clean
- All flanges and fittings are sanitary type
- Bottom multi solid supporting is better compliance with cGMP

High Efficiency and High Performance

- Vacuum/refrigeration/heating/water capture and other index are designed/ tested in compliance with European standards
- Electronic expansion valve is adopted to enhance the stability and controllability of shelf and cold trap temperature
- The design of condensing coil and channel of mushroom valve can increase water capture efficiency

Product Safety Guarantee

- The design by AUSTAR is based on the concept of product protection
- Unique control system of high quality product components can reduce the risk of product con-termination
- All critical systems adopt redundant design

Equipment Safety and Stability

- The freeze dryer is equipped with automatic door – locking to ensure the safety
- Strict helium leak test of vacuum system and refrigeration system to assure the complete tightness with no leaking
- The freeze dryer is built with best quality materials and components to avoid the risk of product contamination
- The comprehensive operation protection and automatic control system guarantees repetitive and reliable processing

Convenient Maintenance

- Both of maintenance door and slot door are equipped with the same type of sealing rings, which is simple and easy for maintenance
- All sensors are connected with sanitary type Tri-Clamp, which is easy for disassembly

LYOCORE Series

Equipment Basic Configuration

Configuration	Rectangular chambers with separate ice condenser, all models mounted on an open frame, monoblack skid or customized skid Containing all components. Control equipment located in a separate cabinet
Chamber	Mirror finish AISI 316L Roughness of 0.4 um Ra for product contact parts. Equipped with safety valve, validation flange, drain, illuminated sight glass, instrumentation nozzles. Insulated with vapour barrier and with brush finish metal cover cladding
Chamber door	Mirror finish AISI 316L Roughness of 0.4 um Ra for product contact parts hinged door with silicon seal, sight glass, insulated with vapour barrier and clad with brushed finish 304L stainless steel cover
Shelves	C type shelves manufactured in AISI 316L Roughness 0.4 um Ra with mirror finish
Ice condenser	Horizontal configurations, coiled pipe refrigerated by direct expansion of refrigerant/diathermic fluid recirculation/LiquidNitrogen rated for approximately 20kg/m2 load. Equipped with safety valve, thermophores, drains, illuminated sightglass, instrumentation nozzles, defrost manifold. Insulated with vapour barrier and clad with brushed finish metal
Main valve	AISI 316L Mirror Finish mushroom type with silicon seal, hydraulically actuated
Refrigeration system	2 stage reciprocating semi-hermetic/screw compressors. Separate circuits with control and safety instrumen-tation. Sufficient capacity to provide shelf cooling to-55°C and condenser cooling to-75°C. HFC refrigerants with electronic expansion valves
Electronic expansion valves	Greater precision in the control of the refrigeration system is provided by electronic expansion valves com-pared with mechanical equivalents
Vacuum system	Pump down to 0.1mbar within 30 minutes provided by oil sealed rotary pumps (plus roots blower on some models) fitted with Isolation valves and mist filters
Leak tightness	Overall system pressure rise test less than 0.01mabr/s
Vacuum measurement	Capacitance manometers MKS type gauge
Vacuum control	Automatic control using proportional needle valve
Control system	Manual, semi-automatic and automatic operation. PLC controlled with PC based Graphical user interface with printer and recorder. Slave LYOCORE range control system based on customer request PLC/HMI, DCS
PLC	Siemens S7-1500
Heat Exchange	Silicon oil circulating medium with hermetic/magnetic drive pump/sand expansion tank; plate exchangers cooled by direct Refrigerant expansion; multi-element electrical heating. Shelf temperature control ±1°C
Process valves	AISI316 Stainless steel product contact surfaces. Diaphragm, butterfly and all type valves with pneumatic actuation
Sanitary valves	Butterfly and ball valves exposed directly to the product are substituted by sanitary diaphragm valves (except for drain and vacuum valves). This option is included if SIP is selected
Temperature sensors	RTD product temperature measurement; heat exchange medium; individual condenser circuits
Electrical standards	NNEC, EN60204-1, JIS alternates
Safety standards	CE
Vendor internal testing	Execution of internal test protocols
Standard documentation package	Standard documentation package: Instruction and maintenance manuals, as built drawings (layout, P&IDs, electri-cal and Pneumatic diagrams, etc.), material and instrumentation calibration certificates. FAT, SAT, IQ and OQ

Option and Accessories

SIP	Vessels built by AISI316L stainless steel to comply with design codes to enable sterilization of chamber and condenser with steam at up to 126°C. Includes all controls and instrumentation required for the process. Water ring pump for post-sterilization drying is included. Sterilization at up to130°C is available, on request
Pressure vessel codes	ASME; PED and GB150 alternatives
Vent filter	A-Hydrophobic sterile filter housing, piping and valves to filter gas vented into chamber for vacuum break and control; B-as A configured for manual in-situ integrity test; C-as A with two housing in series; D-as C configured for manual in-situ integrity test
Auto FIT-WIThin	The optional vent filter configurations B and D may be further enhanced with an embedded test protocol providing results of the filter element integrity test within LYOCORE'SCADA and batch report
Cooling jacket	For accelerating the cooldown of a chamber after SIP by flowing cooling water/ diathermic fluids through an external jacket
CIP	Fixed and rotary nozzles mounted on manifolds to enable water to be sprayed at pressure onto internal surfaces of the chamber and condenser. AISI316L material
CIP recirculation	System comprising a clean pump with instrumentation and controls to increase efficiency by recirculating water used during the CIP process
Slot door	A Gull wing type slot door enables loading onto the shelves whilst minimizing exposure of the chamber to the environment. Useful when loading onto chilled shelves or interfacing with an assisted loading system. Slot doors can be supplied fitted to a main chamber door or within a chamber wall. A fixed bridge plate is included with the slot door to assist with loading and unloading of trays
Loading trays	AISI316L stainless steel trays and/ or fences for products in bulk and containers. Various sizes available
Hydraulic shelf movement	Hydraulically actuated system employing a stainless steel piston for moving the shelves, to utilize the easy loading of larger machines with vials or bulk trays
Hydraulic stoppering	Hydraulically actuated system employing a stainless steel piston for moving the shelves to enable vials to be sealed within the chamber.machines with vials or bulk trays
Stoppering bellows	AISI316L bellows shroud for the hydraulic shelf movement piston to further reduce the possibility of extraneous contamination.Includes controls and instrumentation for testing the bellows' integrity
Main valve bellows	AISI316L bellows shroud for the actuating rod of the main value to further reduce the possibility of extraneous contamination.Includes controls and instrumentation for testing the bellows' integrity
Variable shelf interdistance	Shelves can be latched to provide double shelf interdistance or variable shelf interdistance to accommodate large product containers
Variable frequency driver	VFD system allows better control of refrigeration screw compressors optimizing shelf set point temperature control and shelvesuniformity. Smoother compressors start up minimizing mechanical wear. Considerable energy saving during freeze drying cycle
Additional compressor	It can be supplied to improve the redundancy to the cooling system
Screw compressors	Substitution of 2-stage, semi-hermetic, screw compressors for the standard reciprocating models. Compared with reciprocating types, screw compressors provide greater efficiency and reliability whilst requiring less maintenance and generating lower noise
Compressor variable speed drives	The compressor's speed can vary between 30Hz and 60Hz. Soft starting and stoppering reduces, and operation at low speed extends maintenance periods. Controlling the compressor speed reduces electrical power consumption as well as system noise
Fluid circulation condenser	Instead of the standard coil direct expansion of refrigerant, condenser cooling can be performed by low viscosity silicone oil through plate heat exchangers. This solution allows full condenser redundancy
Enhanced heater	Capable of heating shelves from -40°C to +40°C (measured when shelves are empty) at a rate of 2 °C/minute
Back-up vacuum pump	For systems supplied with a single primary vacuum pump, dual pump are supplied to provide back-up should the duty pump fail
Dry vacuum system	To eliminate the possibility of oil back streaming from rotary pumps and reduce maintenance, dry vacuum pumps may be substituted for the standard oil sealed type

LYOCORE Series

Option and Accessories

UPS	An uninterruptible power supply to provide electrical powder to the control system for at least 20 minutes when the main power supply fail
eSignature	Software compliant with 21 CFR part 11
GAMP5	Documentation regarding the control system compliant with GAMP5 standard
Alternate layout	The refrigeration group may be mounted on a discrete frame and located separately from the chamber and condenser, including separate floors. Configurations may also be adapted to accommodate loading and unloading requirements
Solvent handling	LYOCORE may be configured to handle non-aqueous solvents. Your sales contact will be pleased to arrange a proposal for specific requirements
Potent product	LYOCORE may be configured to handle toxic materials. Your sales contact will be pleased to arrange a review to enable a proposal to be provided for specific product requirements
Liquid nitrogen refrigeration system	Shelf and condenser be cooled by liquid nitrogen instead of compressor refrigeration. The redundant magnetically driven seal-less centrifugal pumps will be utilized in liquid nitrogen system for shelf circulation. Ultimate shelf temperatures: -65°C (in conjunction with 1.6cSt silicone oil); Condenser ultimate temperature, direct liquid nitrogen cooled: -100°C

LYOCORE Series-Freeze Dryer Condenser

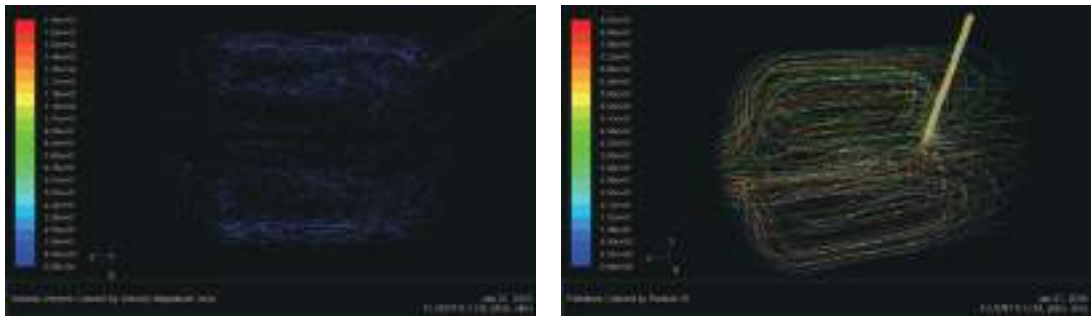
Condenser Design

The design of condenser has direct influence on ice capture efficiency, freeze-drying period and load of refrigerating system.

- Non-uniform ice capture will decrease coil refrigeration area, and affect ice capture efficiency
- The ice density is big, which eradicates“snow ice”, and has higher heat exchange efficiency
- High efficiency ice capture technology can reduce refrigerating unit load, and avoid water vapor entering into vacuum pump to cause damage

Air Pattern Test for Coils

Study the air flow pattern in freeze dryer by using 3D mock test technology to prevent the formation of turbulence.



Highlights



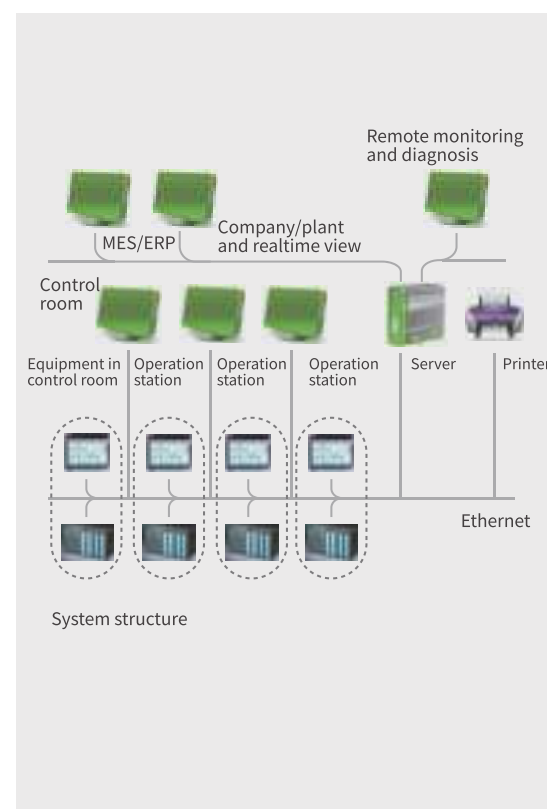
Freeze-Drying curve is smooth and steady, vacuum and temperature control is uniform and stable.

Ice-capture Picture, AUSTAR Freeze Dryer

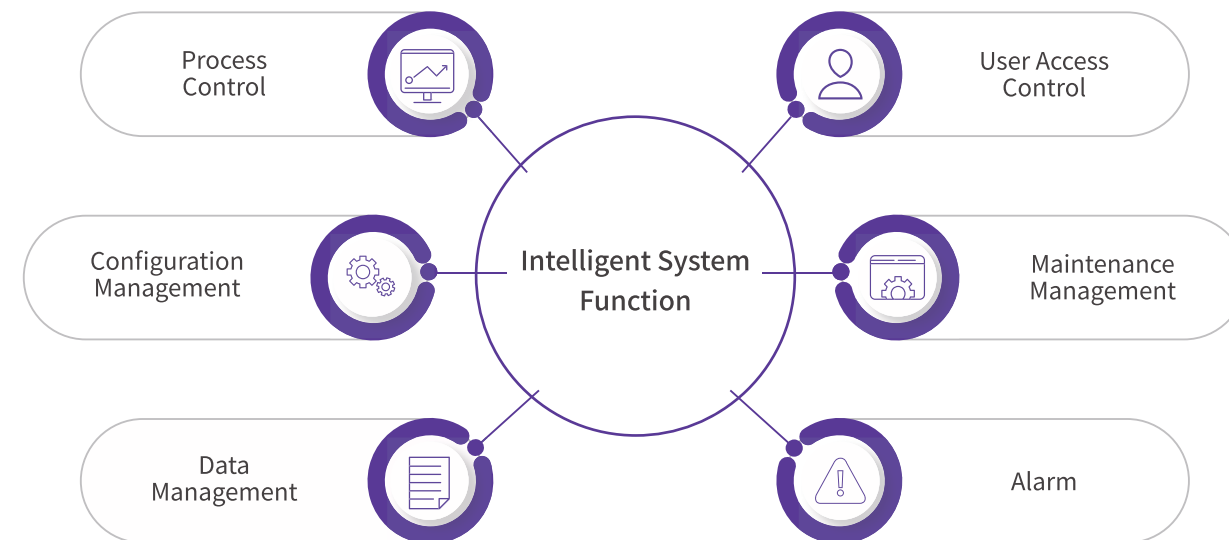
LYOCORE Series-Intelligent Freeze-Drying Control System

General

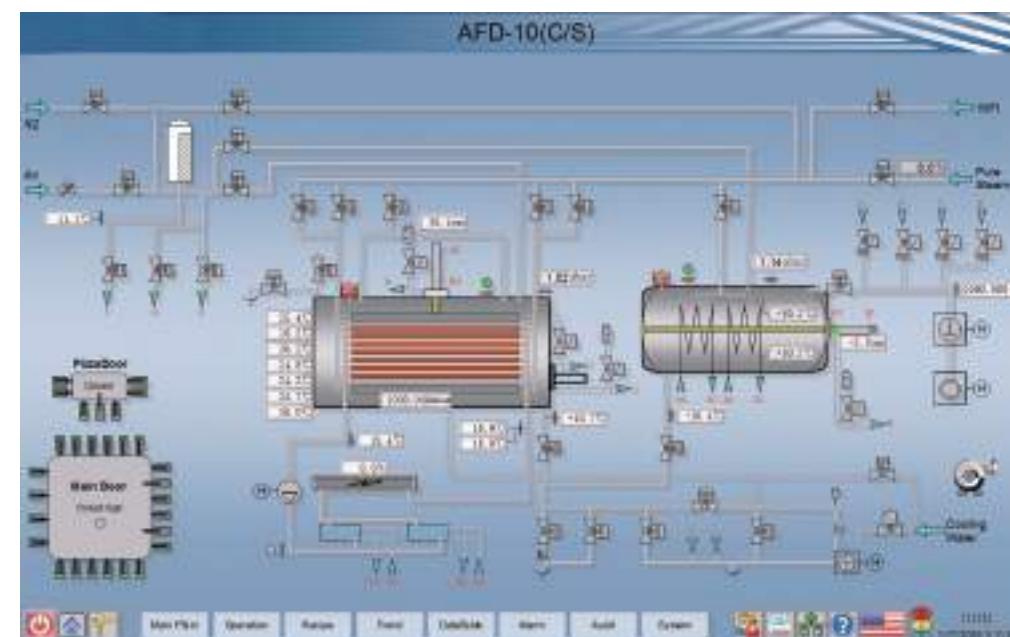
- AUSCON series software is specially designed for AUSTAR freeze dryers used in pharmaceutical industry. The control system allows the freeze-drying control through a user graphic interface HMI. It adopts international advanced control technology to optimize the batch duration and guarantee repetitive and reliable processing
- Key control software is developed on the basis of Siemens platform, and integrated strong automation and process capability of AUSTAR
- Advanced refrigeration and vacuum control technology to ensure stability of process control
- AUSCON series software has been programmed following GAMP 5 requirements, meets the requirement of FDA's 21 CFR Part 11, and complies with increasingly strict requirement on computer validation
- Equipment is able to conduct interlocking and protection at the same time to prevent personnel misoperation
- The program is developed with the purpose of product protection, so as to protect product characters as maximum as possible in failure conditions



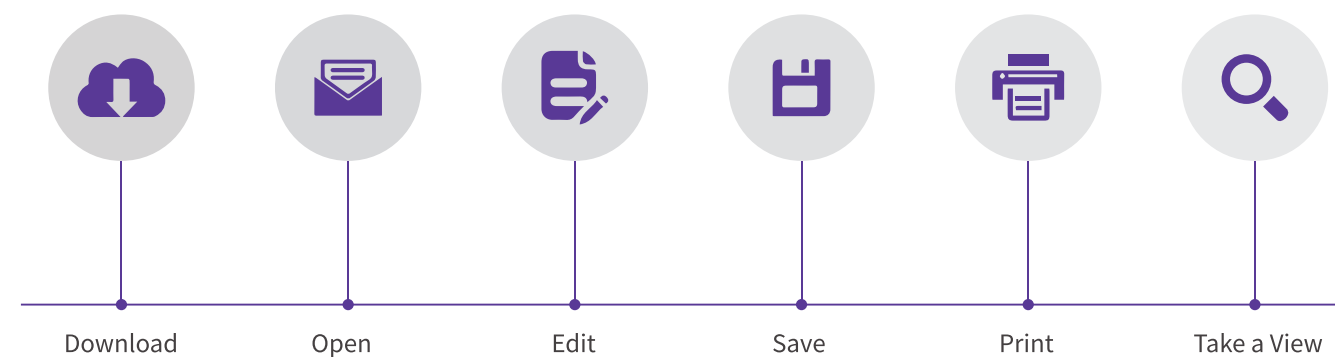
Schematic Diagram of Freeze - Drying System



Process Control



Formulation Management



LYOCORE Series-Intelligent Freeze-Drying Control System

Data Management

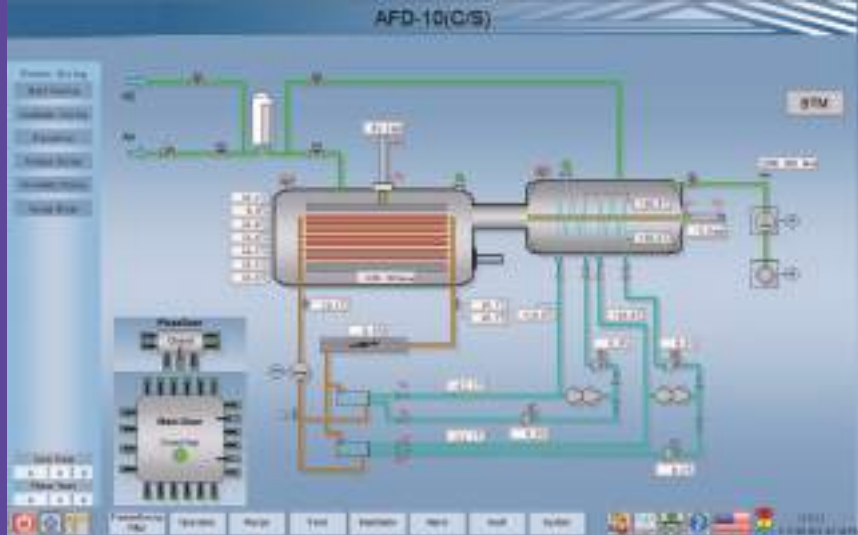
- Batch Data
- Operation Record
- Trend Data
- Alarm Record
- Export and Print Data
- Intelligent Maintenance Reminder



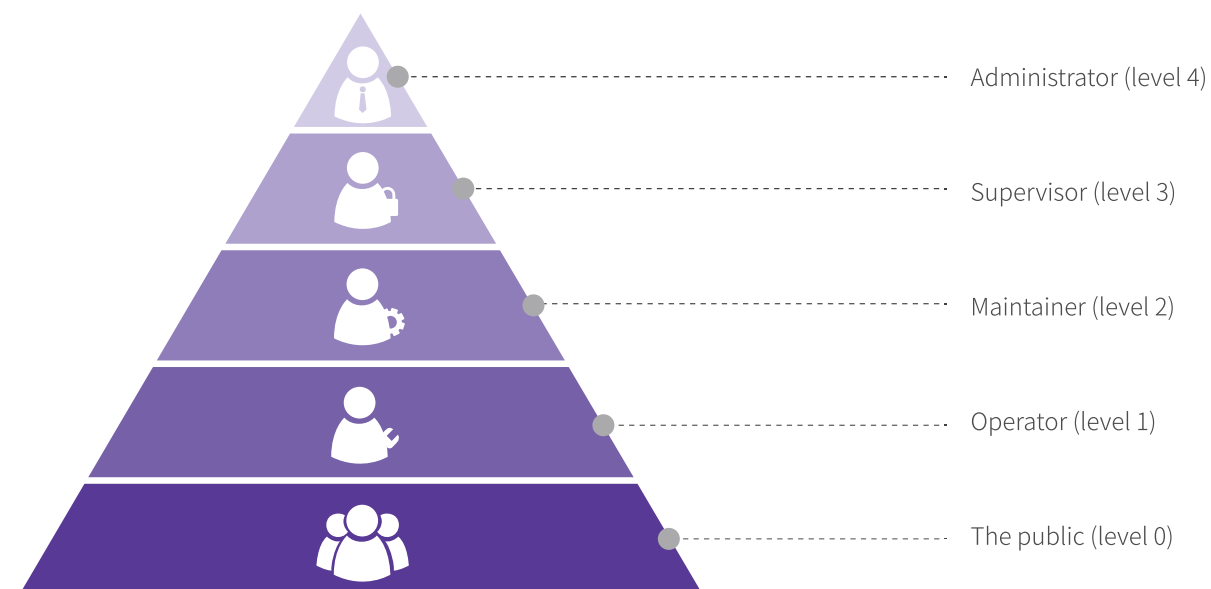
Maintenance Management

Intelligent test function conducts overall inspection for freeze dryer.

- Manual test for valve and pump
- Sensor test
- System integrity leak test
- Stoppering bellows test
- Chamber-condenser isolating valve bellows test
- unloading pushrod bellows test



User Access Control



Alarm System

1 Multi-level Alarms

- **Level 1**
Alarm having impact on the product (vacuum is abnormal during freeze-drying process)
- **Level 2**
Alarm having no impact on the product, but to be verified by manual
- **Level 3**
Reminding alarm

2 Intelligent EMAIL Short Message Reminder (option)

Set critical alarm parameters, timely inform administrator, record and raise response speed, reduce quality risk

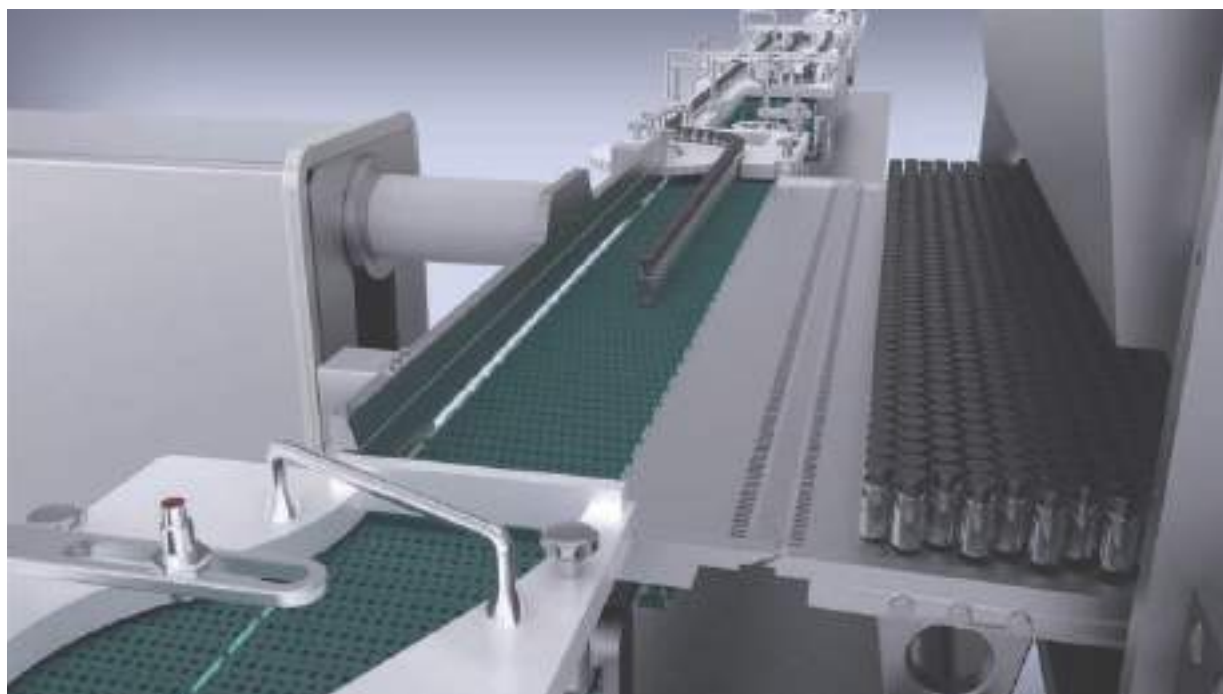
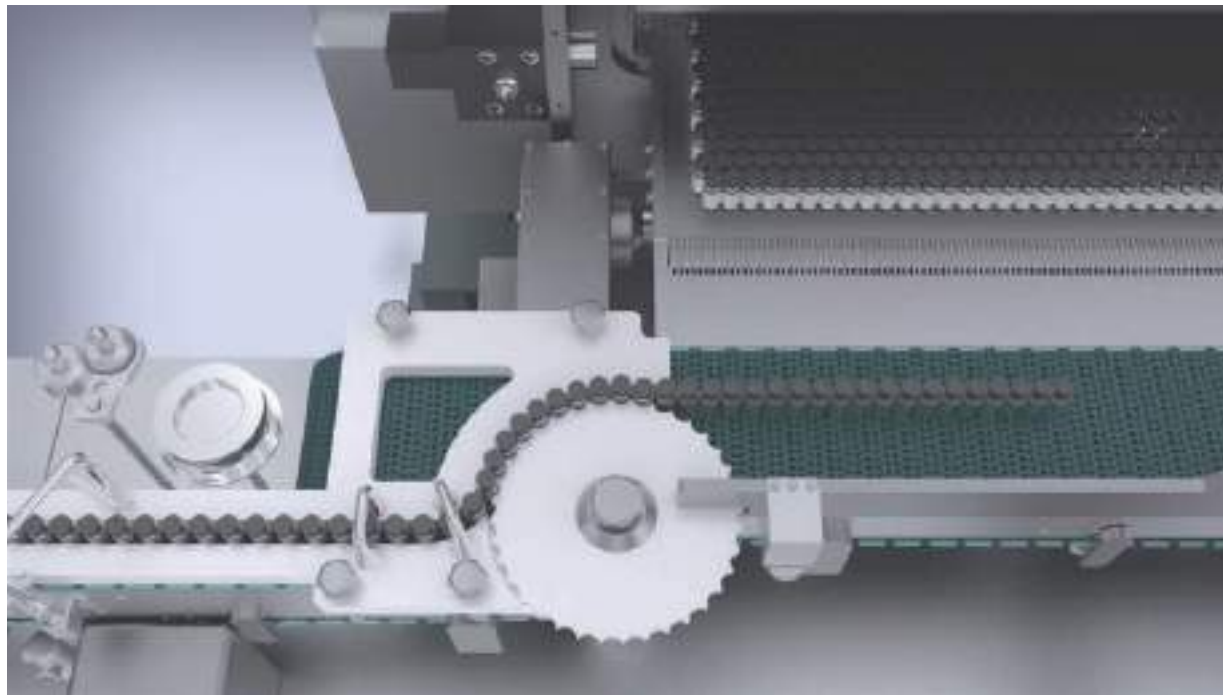
3 Alarm Verification

Password input to verify information intelligent reminder about the actions/measures to be taken and possible reason

Automatic Loading and Unloading System

Product Description

AUSTAR freeze dryer can be integrated with automatic loading & unloading system to segregate product and operator and provide productivity benefits while maintaining consistent standards of aseptic processing. The use of AUSTAR ALUS enables to reduce the risk of contamination, helps to assure the quality of the product while protecting operators from potent substances.



Highlights

1 Fast Accessible Docking

The moving infeed conveyor of loading system is able to be fast docked with upstream sterile filling line (any brand) to collect containers and feeds them to the loading system for continuously loading into the process chamber of freeze dryer at constant height.

2 Compact Design

The automatic Loading & Unloading System is modular designed and engineered with compact configuration and therefore suitable for use with barrier isolation and RABs technology as well as in more classical laminar flow installations.

3 Loading with Low Temperature

The loading system not only meets the requirements of routine loading manufacturing process, but also meets the requirements of loading manufacturing process at low temperature.

4 High Productivity

The unloading system adopts many kinds of unloading methods to meet the production requirements of single and multiple high speed capping machines.

5 High Stability

Driven by several servo motors + variable frequency motor, which have high stability, and can avoid risk caused by starting control.



Freeze-Drying Laboratory

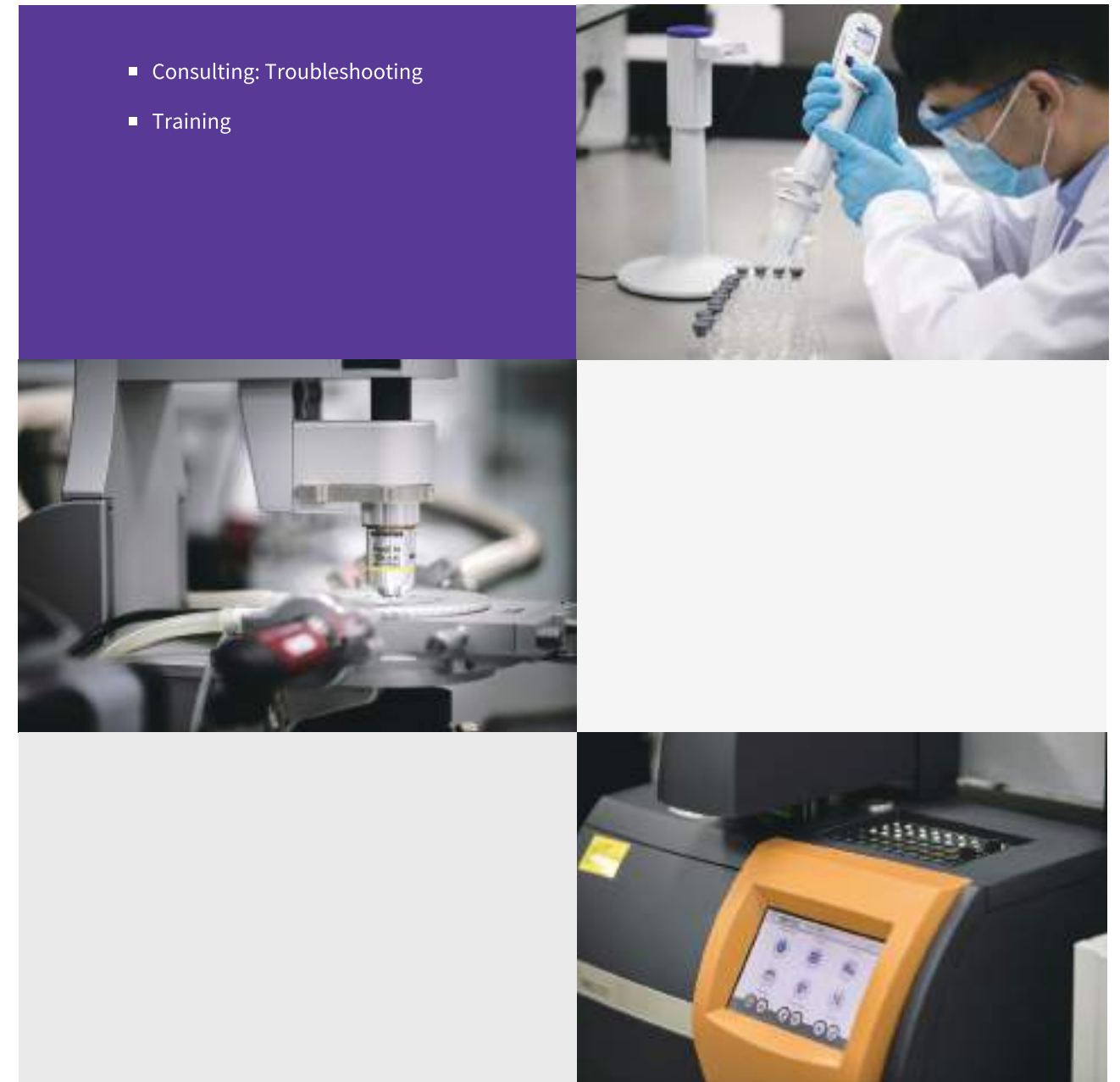
Technical Services

- Determination of the physicochemical characteristics of the product:
 - Eutectic temperature
 - Glass transition temperature
 - Collapsing temperature
 - Residual moisture content
- Optimization and development of freeze-drying cycle
 - Established procedure of development that is based on the characteristics of the product and equipment
 - Calculation of optimal process parameters with mathematical modeling: less trial and error



Other Services

- Consulting: Troubleshooting
- Training

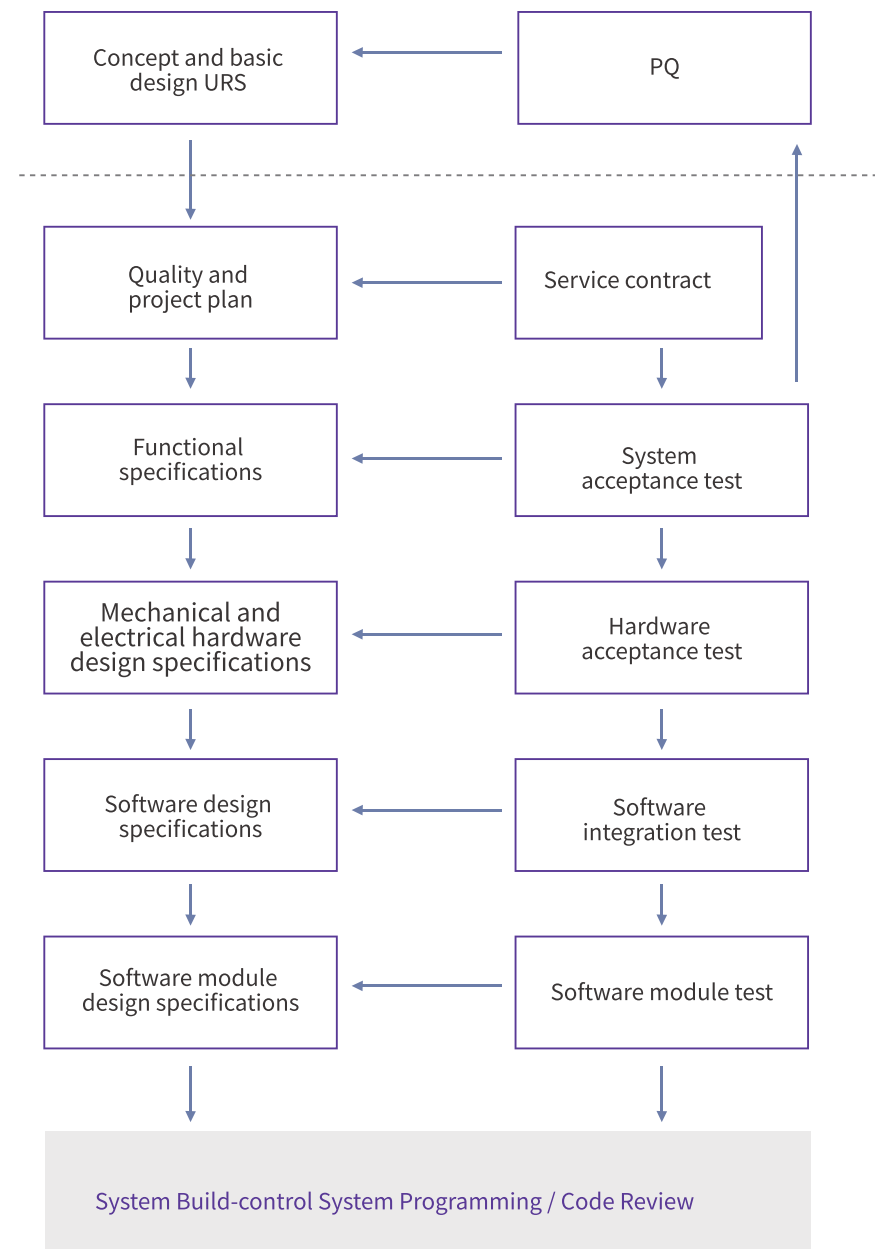


Validation

GAMP5

Control system is designed and tested according to the requirements of GAMP5.

- Validation team consists of international and domestic GxP experts recognized by global pharmaceutical industry, and several senior international registration consultants
- Professional GxP service experience gained from previous validation project with more than 100 pharmaceutical enterprises
- Leverage industry resources in global scope, closely cooperate with many international consulting agencies
- Provide professional and comprehensive GxP compliance consulting service to support client to comply with relevant standard and regulation such as FDA/EMA/CFDA/WHO.etc.



- Provide comprehensive validation services to clients with validation plan throughout the equipment lifecycle
- Highly qualified technicians guarantee professional validation service
- Rich validation experience on FDA projects assure the clients of reliable documentation system



Successful experience on validation over years not only originates from the understanding on certification, but also originates from the meticulousness to validation execution.

After-sales Service

Training Plan

AUSTAR has a dedicated after-sales service team to provide a complete technical service to ensure your equipment is working correctly and efficiently at all time. Our after-sales service team is made up of 50 specialist technicians, who are specially trained and most of them have 20 years of after-sales service experience on imported freeze dryer.

A wide range of training program is provided for machine operators, electrical and mechanical engineers, maintenance engineers and supervisory personnel. The programs are designed not only to improve the participants' overall understanding of the production equipment, but also to enhance their confidence and performance levels to provide a beneficial return for their business.

Training Plan

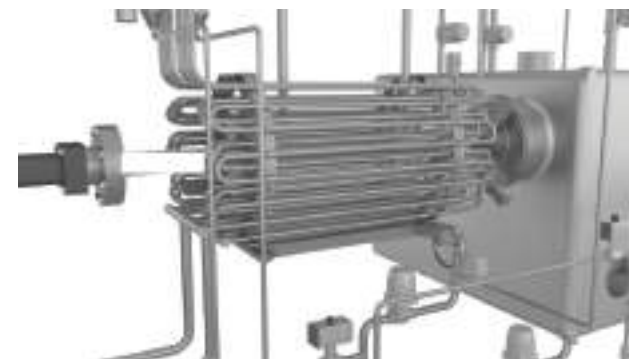
- Practical explanations / demonstrations of the operation and maintenance of the equipment, which is supported by the standard O&M manual
- Periodic maintenance plan
- Troubleshooting



Preventive Maintenance Program

AUSTAR can provide a full 'After-sales' support for the installed equipment, including regular/periodic maintenance service visits. Routine maintenance is an integral part of AUSTAR's cGMP approach. All maintenance activities are properly documented to provide support during corporate audits and regulatory inspections.

- Assure compliance and continuity of validated equipment status
- Ensure equipment reliability
- Minimize downtime and extend the equipment lifecycle.



AUSTAR Freeze Dryer Technical Specifications

AUSTAR LYOCORE Series

AUSTAR masters the core technology of freeze dryer. The LYOCORE range of freeze dryers meet GMP requirement and all your lyophilization requirements. LYOCORE guarantees superior quality, shortens lead times, and is cost effective. The specifications of the based model meet all leading industry standards and the broad range of standard options enable LYOCORE freeze dryers to be your specific requirements.

Model	Type	Manual Loaded							Auto Loaded									Approx Utilities And Dimension						
		Usable Shelf Area	Shelf Space	Shelf Size		Number of Shelves	Batch Capacity (PCS)		Usable Shelf Area	Shelf Space /mm	Shelf Size		Loading Size		Number of Shelves	Batch Capacity (PCS)		Min Condenser Capacity	Total Power	Cooling water flow rate	CIP water flow rate	SIP Pure Steam	Weight	Dimension
		m2	mm	(W×D)mm			∅ 16	∅ 22	m2		(W×D)mm		(W×D)mm			∅ 16	∅ 22	kg@15mmice	Kw	m³/h	L/min	Kg/Batch	Kg	(L×W×H)mm
LYOCORE 2	GMP Manufacture	2.2	110	600	900	4	8832	4512	2.0	120	650	900	600	840	4	8880	4560	40	26	5	160	50	400	4000*1800*3500
LYOCORE 3	GMP Manufacture	3.2		600	900	6	12348	6768	3.0		650	900	600	840	6	13320	6840	60	30	10	160	70	5000	4250*1800*3200
LYOCORE 4	GMP Manufacture	4.1		900	900	5	16560	8460	3.8		950	900	900	840	5	16650	8600	80	40	11	160	90	6000	4400*1900*3100
LYOCORE 5	GMP Manufacture	5.4		900	1200	5	22050	1125	5.1		950	1200	900	1140	5	22755	11800	110	48	15	190	110	8000	5600*1900*3225
LYOCORE 7	GMP Manufacture	7.6		900	1200	7	30870	15750	7.2		950	1200	900	1140	7	31857	16520	150	54	20	220	130	10000	5600*2000*3800
LYOCORE 10	GMP Manufacture	9.7		900	1200	9	39690	20250	9.2		950	1200	900	1140	9	40959	21240	200	72	25	220	200	12000	4800*2650*4800
	GMP Manufacture	10.1		1200	1200	7	41160	21000	9.6		1250	1200	1200	1140	7	42763	22320							6500*2650*4500
LYOCORE 15	GMP Manufacture	15.8		1200	1200	11	64680	33000	15.0		1250	1200	1200	1140	11	67199	35046	320	86	30	220	320	16000	7200*2650*6000
LYOCORE 20	GMP Manufacture	19.8		1200	1500	11	80080	41888	19.0		1250	1500	1200	1440	11	84414	44550	400	110	35	220	400	20000	8600*2800*6400
	GMP Manufacture	20.3		1500	1500	9	81900	42840	19.4		1550	1500	1500	1440	9	86211	45567							8960*2700*6000
LYOCORE 25	GMP Manufacture	24.8		1500	1500	11	100100	52360	23.8		1550	1500	1500	1440	11	105369	55693	500	125	40	220	500	24000	9100*2800*6400
LYOCORE 30	GMP Manufacture	29.3		1500	1500	13	118300	61880	28.1		1550	1500	1500	1440	13	124527	65819	600	148	45	250	600	28000	9600*3200*6400
	GMP Manufacture	29.7		1500	1800	11	119460	63360	28.7		1550	1800	1500	1740	11	127875	67573							10000*3200*6400
LYOCORE 40	GMP Manufacture	40.5		1500	1800	15	162900	86400	39.2		1550	1800	1500	1740	15	174375	92145	800	188	50	250	810	32000	10500*3200*6830
performance parameter	shelf temperature range		Shelf heating speed			Shelves temperature uniformity				Shelf cooling time				Stoppering force			Condenser coil temperature Min							
	-55℃~80℃		1℃/min			±1℃				20℃~-40℃≤60min				0~0.1Mpa/cm²			≤-75℃ (R507/R448A)							
	Condenser cooling time		Evacuation time			Final vacuum				Leakage rate				Shelf flatness			Finish of shelves/maintenance door							
	20℃~-40℃≤30min		1atm~0.1mbar≤30min			≤0.01mbar				≤0.01mbar*L/S				±0.5mm/m			Ra≤0.4 μm							

AU STAR

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