

Tofflon



Freeze Dryers

Tofflon

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Expertise in Pharmaceutical Industry



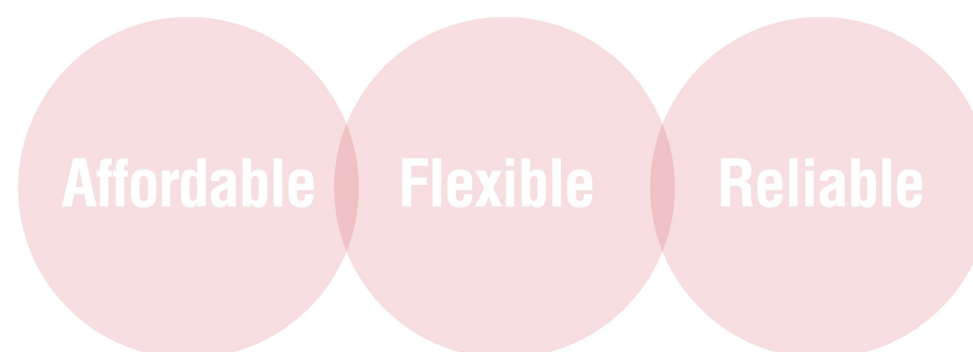
TODAY

Tofflon focuses on studying drug manufacturing science and process equipment manufacturing science, practices drug process knowledge integration with pharma equipment knowledge. Taking “Synergy Global Advanced Technologies” strategy, Tofflon builds comprehensive development institute in Shanghai headquarters, is building design houses and technical centers in USA, Europe and India, establishes joint ventures and technology collaboration with the technical partners from USA, Europe and Japan. Furthermore Tofflon has built five modern pharmaceutical equipments manufacturing bases with global competitiveness. It has been approved with all the international regulatory certifications like German TÜV ISO9001, ISO14001, OHSAS 18001, CE, UL, PED, ASME, etc. Thanks to 2000 Chinese and foreign employees professional works, it can provide competitive pharmaceutical equipment and system solutions valuable for today and future’s competence improvement of the pharma and biotech companies.

FUTURE

To commit to its mission “Expertise in Pharmaceutical Industry”, Tofflon will continuously work with pharmaceutical industry to face and meet the challenges and pressures in the industry through developing “innovative drug manufacturing science” and building “advanced drug manufacturing platform”. In the following years, Tofflon will dedicate itself to grow from “China Tofflon to Global Tofflon”, from “Equipment Supplier to Solution Provider” so as to grow up to a total solution provider of pharmaceutical manufacturing systems and engineering for the global pharma and biotech industry to contribute to the maximum benefits and welfare of its served stockholders, employees and their families.

Shanghai Tofflon Science and Technology Co. Ltd. (Short for “Tofflon”, Stock Code: SZ 300171) was founded in 1993. It is a comprehensive pharmaceutical equipment supplier to provide process support, core equipments, integrated system and pharma engineering for the pharma and biotech industry in the world. Since its foundation, Tofflon has supplied more than 8000 equipments and systems for 2000 pharmaceutical companies across over 40 countries and regions in the world which have been widely applied in the fields of liquid and lyo injectables, chemical API, bioengineering and pharma packaging, etc.





Supplies and Services

- Laboratory freeze dryers (LYO-0.5m²).
- Pilot freeze dryers (LYO-1 ~ 5m²).
- Production freeze dryers (LYO-7.5 ~ 20m²).
- Mass-production freeze dryers (LYO-25 ~ 50m²).

Strengths and Advantages

- Whole-life dedication to lyophilization technology.
- The largest and most modern freeze dryer manufacturing facility in the world.
- + 4000 freeze dryers across over 40 countries and regions since 1993 (single floor or two-floor, single side loading & unloading or pass through systems, external condenser or internal condenser, etc).
- Strength, Capability and Expertise to meet USFDA and EU-GMP approval.
- More than hundreds of FD + Loading Systems practical projects experience worldwide.
- Wide range of solutions for loading systems (Row-by-Row, AGV, Mixed and Semi-auto).
- Reliable, flexible and affordable technology.
- Quicker response, faster delivery and longer service guarantee.
- Locally-based sales and service.
- Cost effective manufacturing and documentation.

Technology and Qualifications

- Screw Compressor.
- VFD Screw Compressor.
- LN2 Refrigeration System .
- Low Temperature Trap.
- Backup or Redundancy Design.
- Dual Heat Exchanger (Both Shelves and Condenser Coils Cooled by Silicone Oil Circuits).
- Dry Pump.
- Water Intrusion Test (WIT).
- CIP External System (Tank and Pump).
- Slot Door and Constant Height Loading Mechanism.
- Cooling Heat Exchanger After SIP.
- Silicone Oil Jacket for Cooling and Heating.
- Vacuum Brazing Shelves.
- Condenser as CIP Buffer Tank.

cGMP Lab Freeze Dryer

- cGMP design.
- AISI 316L construction for all product contact surfaces.
- Cylindrical process chamber and external condenser located behind freeze-drying chamber.
- Air cooling and water cooling compressor for option.
- Thermal exchanger and circulation pump ensure homogeneity of distribution of temperature on and between each shelf.
- Control system based on PLC+PC+Touch Screen with 21 CFR Part 11 Compliance.



Range of Options Available

- Stoppering System.
- Installation Across Sterile Wall.
- SIP and CIP available for LYO-0.5.
- Sliding Door.
- Shelves Double Spacing.



Sliding Door(Optional)

Technical Specifications

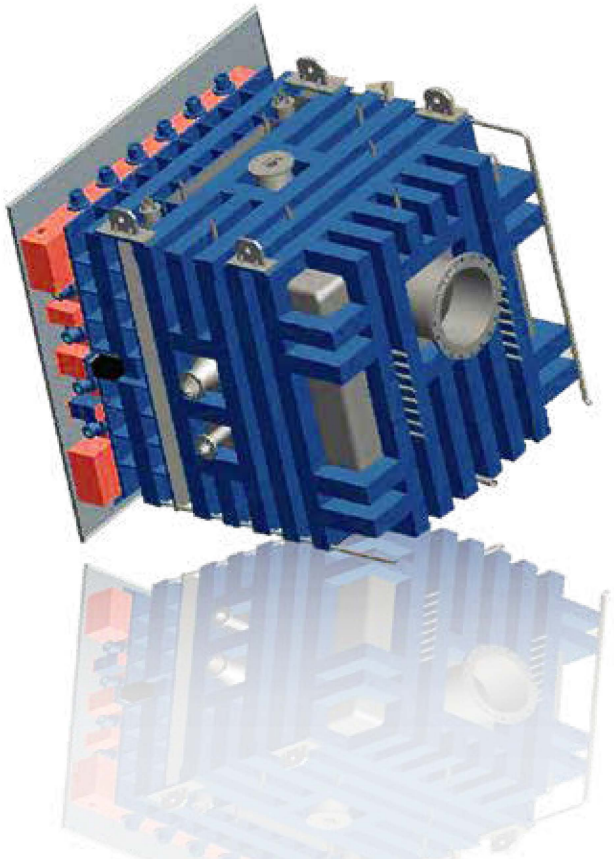
Model	LYO-0.5
Usable Shelf Area (m²)	0.54
Ice Capacity (kg)	10
Number Of Shelves	4+1
Shelf Dimensions(L×W) (mm)	450×300
Shelf Spacing (mm)	100
Shelf Temperature Range (°C)	-45 to +70 (Air cooling) -55 to +80 (Water cooling)
Condenser Final Temperature (°C)	≤ -45 (Air cooling) ≤ -75 (Water cooling)
Shelf Cooling Rate (+20 to -40 °C)(min)	≤ 60
Condenser Cooling Rate (+20 to -40 °C)(min)	≤ 30
Shelf Heating Rate (°C/min)(approx)	1
Evacuation Rate (min)(1×10³mbar to 1×10⁻¹mbar)	≤ 30
Final Vacuum (mbar)	≤ 1×10⁻²
Leakage Rate (mbar·lit/sec)	≤ 3×10⁻²
Overall Dimensions (L×W×H)(mm)	1600×1100×2100
Approximate Weight (ton)	1.5

Chamber

- GB-150/PED/ASME Code Pressure Vessel.
- cGMP guidelines and US-FDA recommendation.
- Leak tested with helium leak detector.
- X-ray weld tests.
- Piping connections with sanitary clamps.
- Sanitary clamp capped validation port on chamber.
- All edges and corners are rounded to facilitate cleaning.
- Dead-legs are limited to a length to diameter ratio L(length) / d(diameter)<3, and are sloped to ensure free draining. Where the length to diameter ratio can not be achieved, cleaning action is provided with spray-nozzle.
- Chamber bottom is sloped to drain.
- Cooling jackets for rapid cool down after sterilization with steam.

Type	Rectangular
Maximum design pressure	3barA
Maximum design temperature	134 °C
Sloping	2%
Finish	Ra ≤ 0.4µm
Material of product contact	AISI-316L

SS 304 cooling jacket on chamber for chamber reinforce (Option)

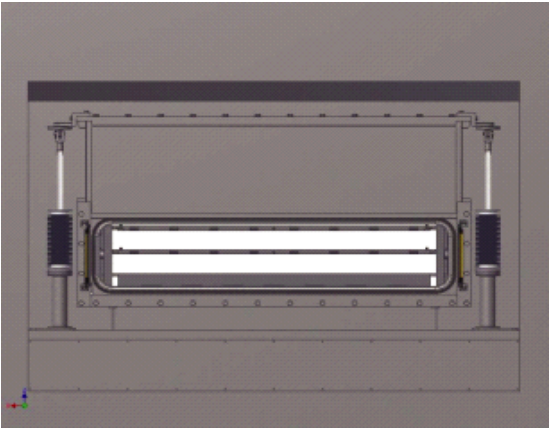
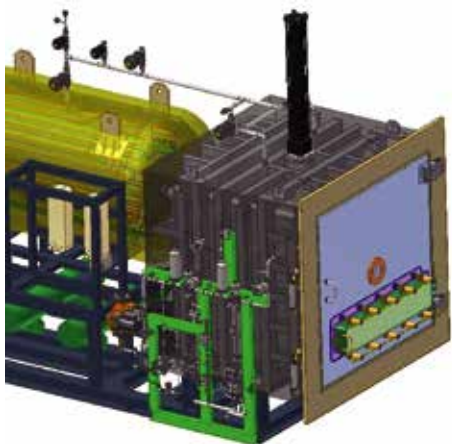


Door

- Door sealing is a solid single gasket designed for high vacuum and overpressure operation.
- Automatic locking mechanism is interlocked and controlled by PLC and its moving parts are in the machine room for easy maintenance.
- Interlocking mechanism: the door can not be opened in case the pressure in the chamber is higher than atmospheric pressure.

Finish	Ra≤0.4μm
Gasket	Silicone rubber single gasket
Locking arrangement	Automatic
Material of product contact	AISI-316L

Slot Door (Option)



Condenser

- Production dryers have a cooling jacket provided for quick cooling after SIP with steam.
- Designed for high vacuum and pressurization during SIP with steam.
- Piping connections are sanitary clamp type. Includes validation port.
- Condenser coils are made from polished and AISI-316L stainless steel tubing.
- The coiled piping design offers a high level of ice trapping.
- De-icing by pure steam.

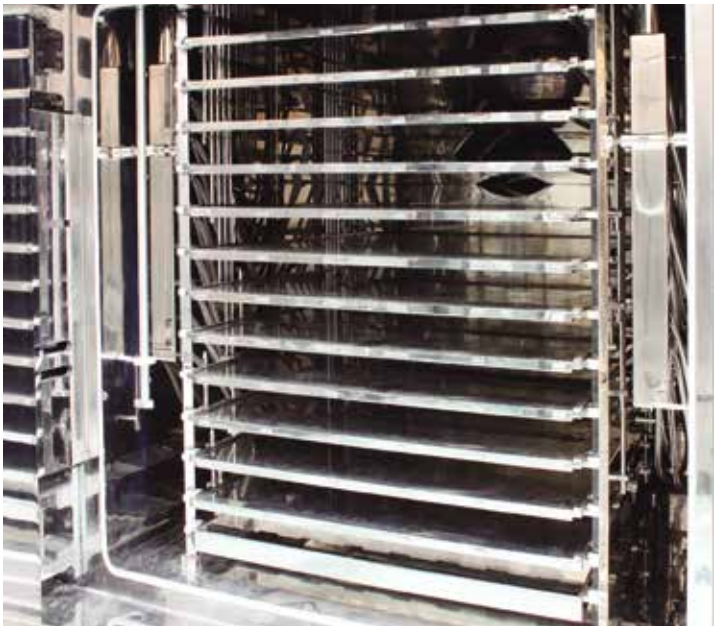
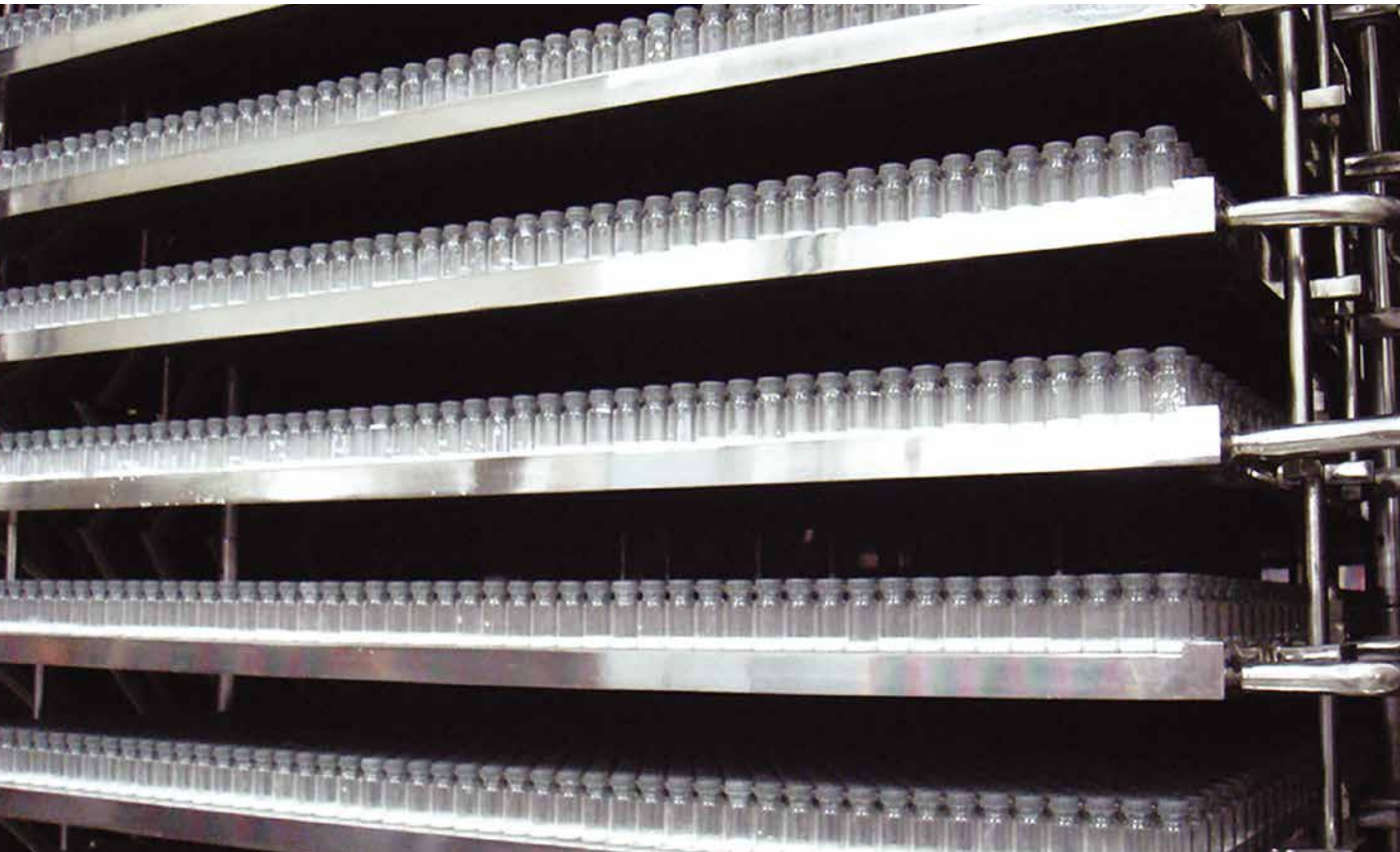
Type	Rectangular or Cylindrical
Maximum design pressure	3barA
Maximum design temperature	134 C
Final temperature	≤ -75 C
Condenser cooling time	≤ 30minutes (empty)



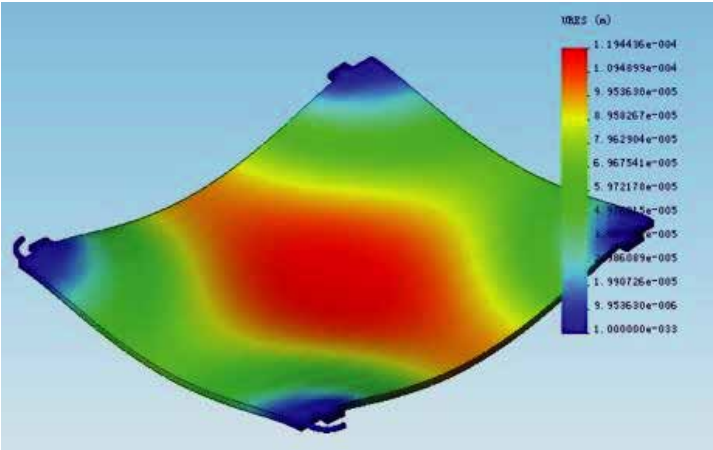
Shelves

- Shelves are cooled and heated by silicone oil circulation.
- Specially fabricated internal channeling not only strengthens the shelves but also ensures excellent temperature uniformity.
- Cooling and heating of shelves are PLC controlled.
- For production freeze dryers, there are optional shelf double spacing mechanism to meet requirements of different size vials.
- Force analysis ensures acceptable distortion after years of heating and cooling or full stoppering.

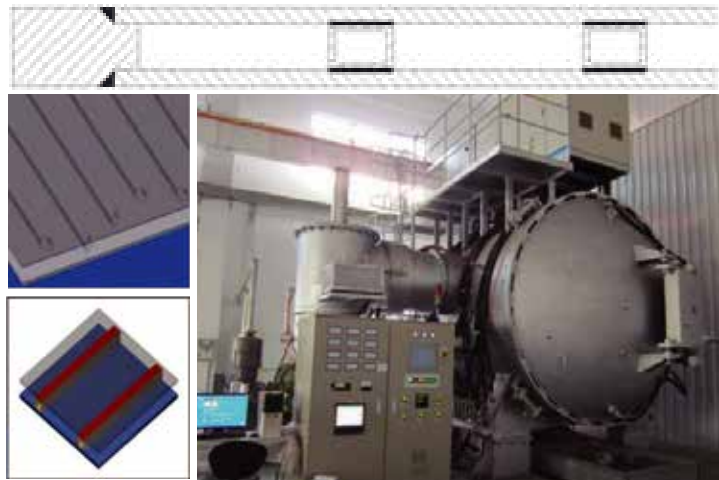
Temperature range	-55 °C to +80 °C
Finish	Ra≤ 0.4µm
Level	≤ ±1mm/m
Material of product contact	AISI-316L



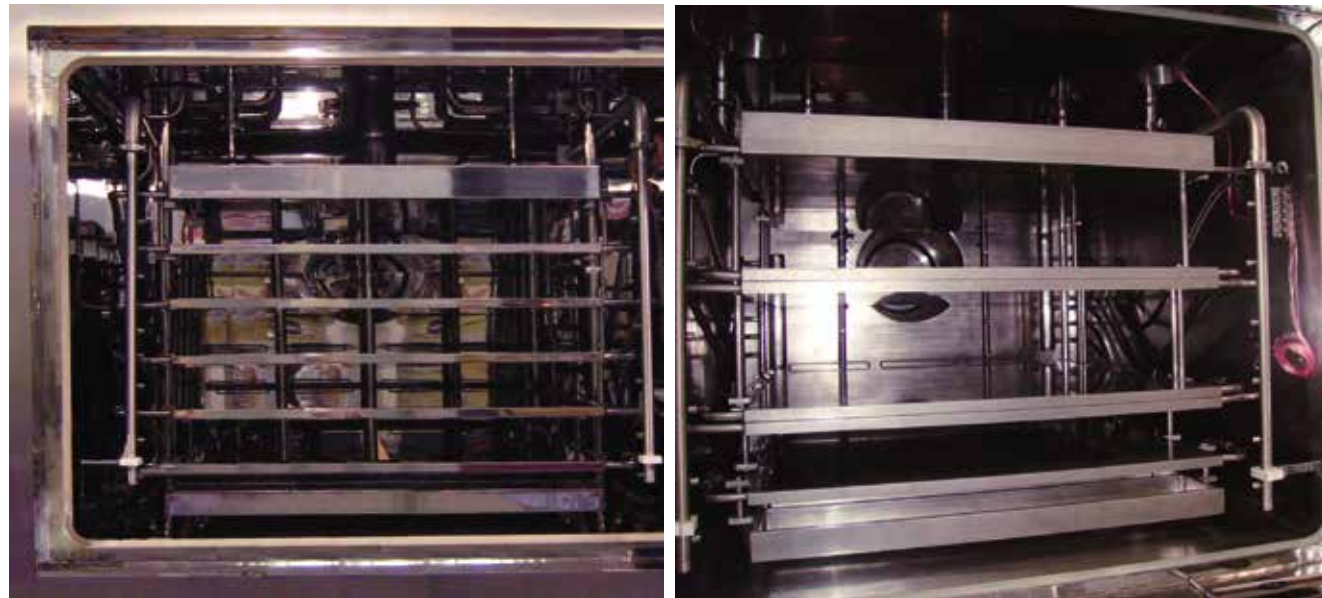
Shelf Pressure Analysis



Vacuum Brazing Shelves (Option)

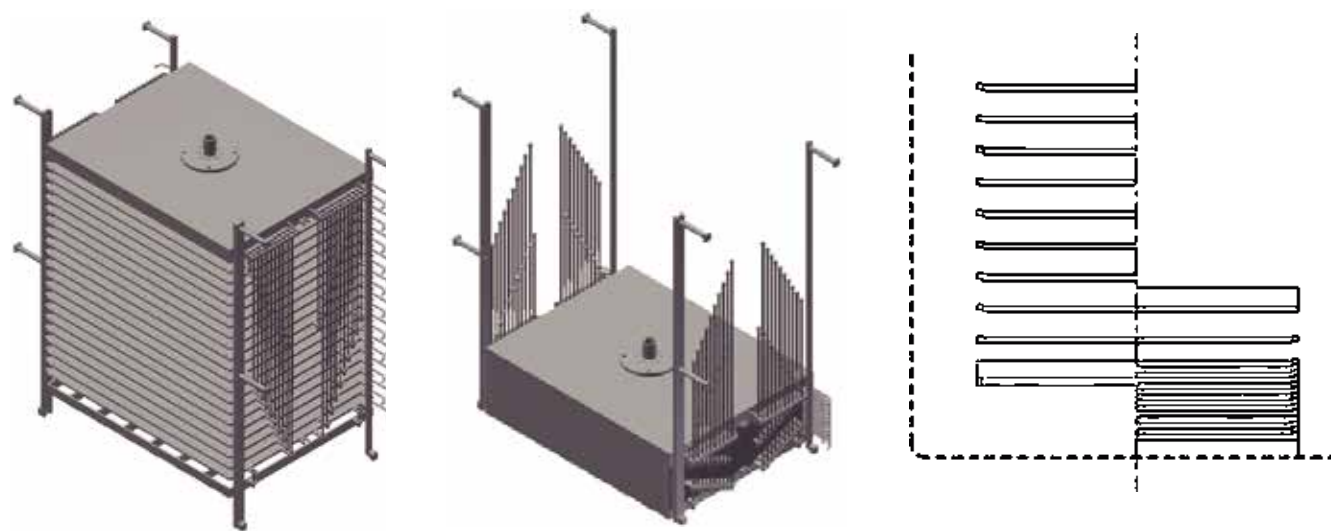


Shelves Double Spacing (Option)



Customized Shelves Design for Auto Loading Systems (Option)

- Shelves with two guided rails to control vial pack.
- Collapsible shelves to achieve zero clearance during full stoppering.
- Constant loading and unloading height.
- Stable position during loading and unloading process.



Chamber - Condenser Isolation Valve

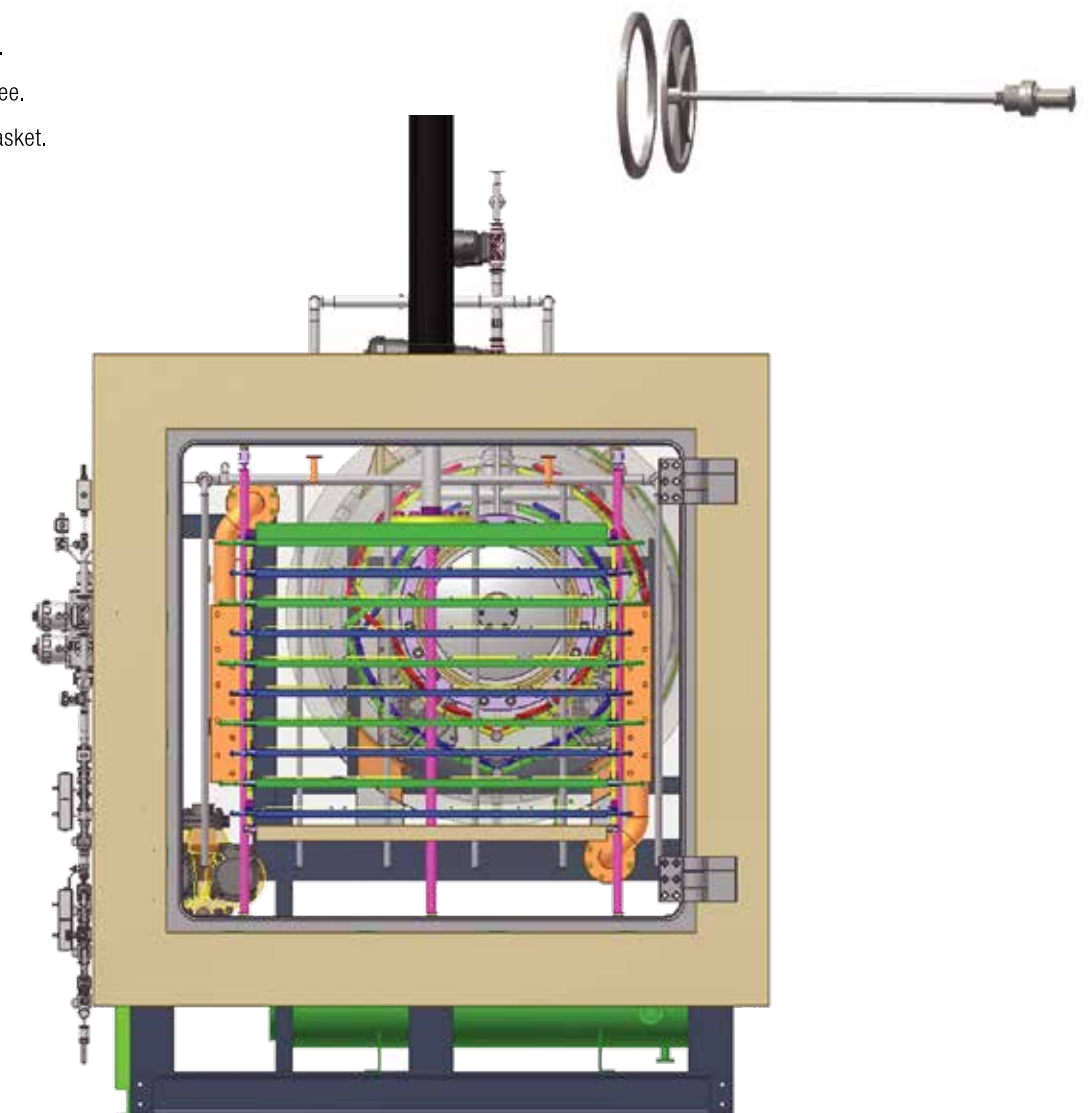
- Hydraulically or pneumatically driven.
- Feedback signal during the process so as to monitor position.
- Gasket in EPDM, silicone or fluorine rubber approved by FDA.

Butterfly Valve - Pneumatically Driven

- Simple design.
- High water vapor flow.
- Available for larger scale freeze dryers.
- Easy adjustments.

Mushroom valve -Hydraulically Driven

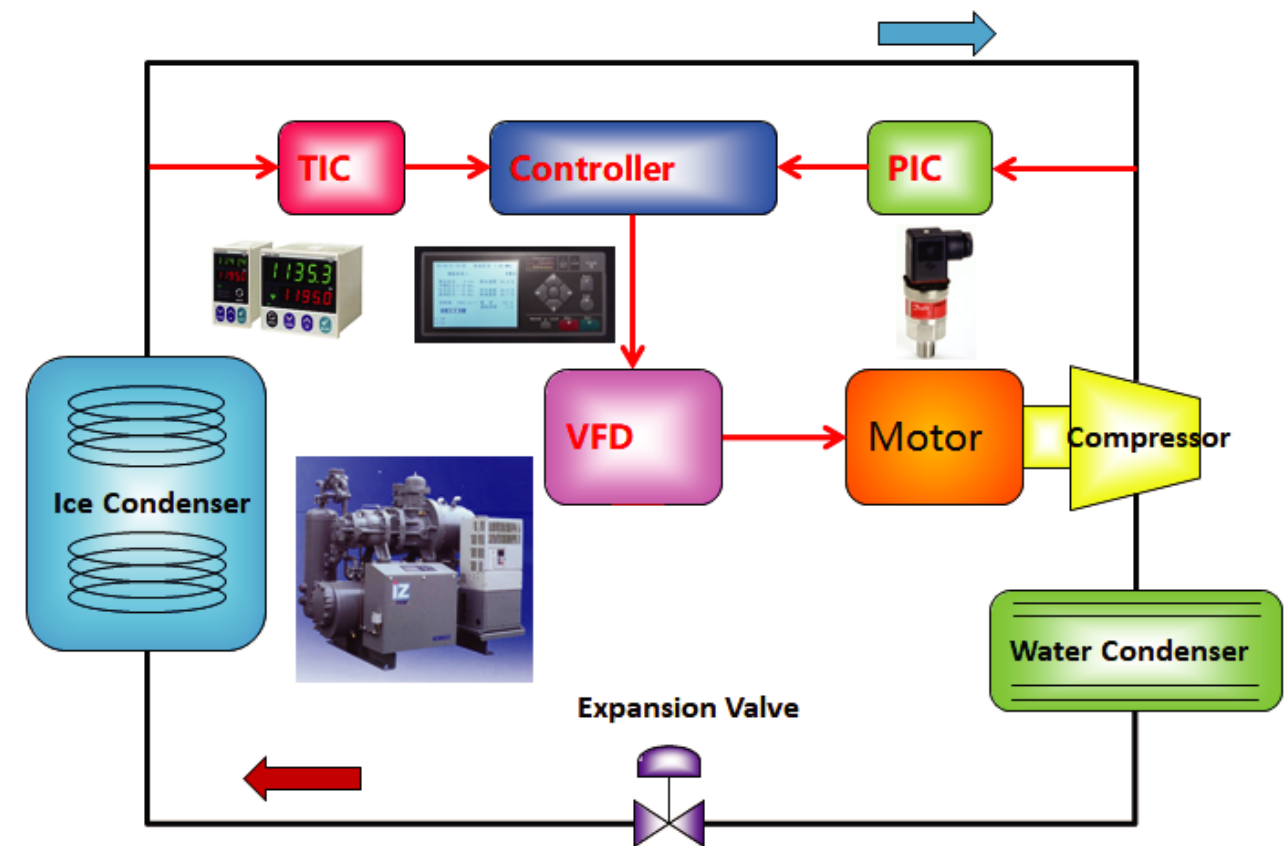
- High temperature resistant.
- Easy cleaning.
- Airtight sealing.
- Maintenance free.
- Easy change gasket.
- High reliability.



Refrigeration System

- Advanced pipeline process technology prohibits leaks.
- World-class refrigeration units ensure reliability with long service life.
- Each compressor has an independent circuit to cool shelves or condenser.
- Large main valve diameter, refrigeration capacity and condenser surface area to trap a large quantity of water vapor from product in primary drying.
- Safety protection for compressors in high head pressure, low pressure suction, motor over-temperature, differential oil pressure, unstable current, short circuit, lack phase and cooling water flow, etc,
- Environment friendly HFC refrigerant: free of CFC and HCFC.
- Vibration absorbers to reduce vibration and noise.
- The flow rate of refrigerant is controlled by an expansion valve to achieve the precise temperature.

Compressor	Bitzer®, Copeland® or Kobelco® , Mycom® 2 stage screw
Refrigerant	CFC-free R404 A or R507
Thermostatic expansion valve	Danfoss®
Solenoid valve	Danfoss®
Liquid filter and gas filter core	Alco®



Mycom Screw Compressor (Option)



Kobelco Screw Compressor (Option)



Vacuum System

- Vacuum pump plus mechanical booster pump (for large scale freeze dryers) used to evacuate the complete system. (i.e. less than 0.01mbar vacuum)
- Vacuum anti-suck back safety valve closes automatically in case of power outage to preserve system vacuum.
- Optional dry pump to avoid product contamination from back-streaming vacuum oil.

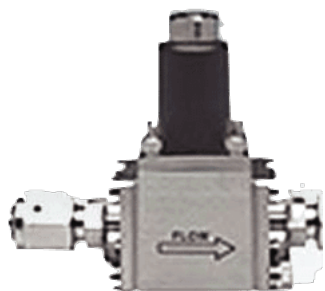
Vacuum pump	Edwards®
Final vacuum	≤ 1×10 ⁻² mbar
Evacuation time	≤ 30minutes (1×10 ³ mbar to 1×10 ⁻¹)
Leakage rate	≤ 3×10 ⁻² mbar·L/sec



Dry Pump (Option)



MKS PID Control Valve (Option)



MKS capacitance manometer plus Edwards Pirani APG-MP vacuum gauge (Option)



Circulation System

- Two "canned" circulation pumps provided: if one fails, the second one automatically switches on.
- Oil free sealing pump eliminates friction during operation.
- PID control can accurately control heating rate.
- Driven motors keep the lowest heat transfer to thermal fluid.



Circulation pump	Wilo® or Grundfos® or Speck® or Hermetic®
Plate heat exchanger	Alfa Laval®
Heater	PID control
Thermal fluid	Silicon oil (5cst or 2cst)
Shelf cooling time (+20 C to -40 C)	≤ 60 minutes (empty)
Heating rate	1 C/min (approx)
Shelf temperature uniformity	≤ ±1 C (steady state)

Speck magnetic pump (Option)



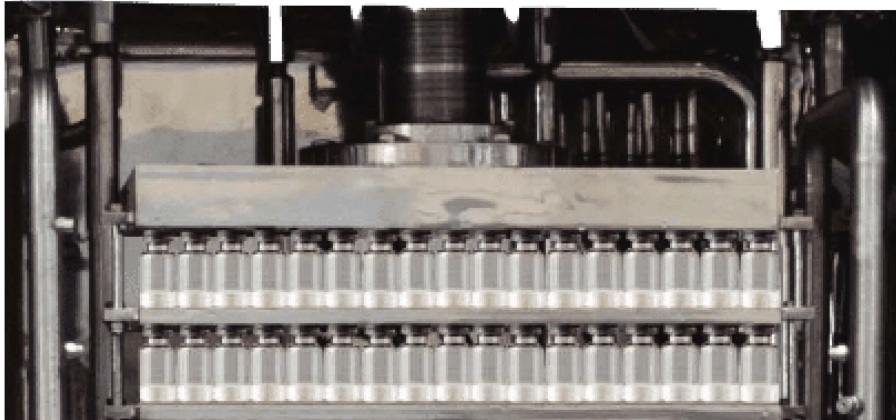
Hermetic low temperature pump (Option)



Hydraulic System or Stoppering Mechanism

- At the end of the drying process, vials loaded on shelves can be stoppered either under vacuum or under a controlled atmosphere of inert gas.
- The stoppering mechanism pressure is adjustable from 0 to 1kg-f/cm² for proper stoppering.
- Bellows covering the hydraulic ram prevent hydraulic oil from contaminating the chamber. Includes hardware and software integrity tests.
- The movement of the shelves can be operated either by means of a flush mounted operator's panel in the machine room or button on the flat sterile wall in sterile room.

Stoppering condition	Under vacuum or under inert gas
Operation location	Both in sterile room and machine room
Hydraulic motor	ABB®
Hydraulic units	ATOS®
Bellows	AISI-316L
Stoppering force	0~1.0kg-f/cm² (adjustable)



Documentation System

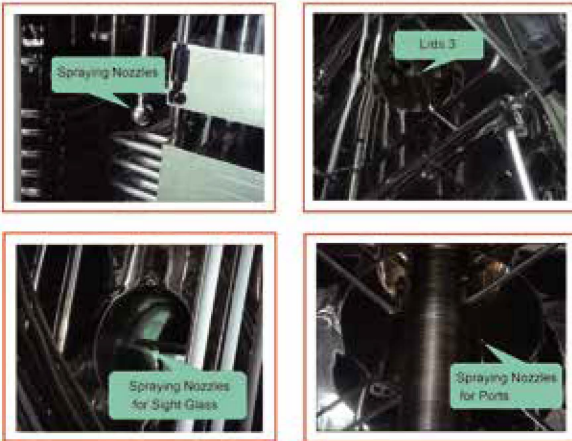
- Layout arrangement drawing.
- P&ID.
- Wiring drawing.
- Installation qualification protocol.
- Operational qualification protocol.
- Installation instructions.
- Operation instructions.
- Maintenance manuals.
- Materials certificates.
- Calibration certificates.
- Welding certificates and logs.



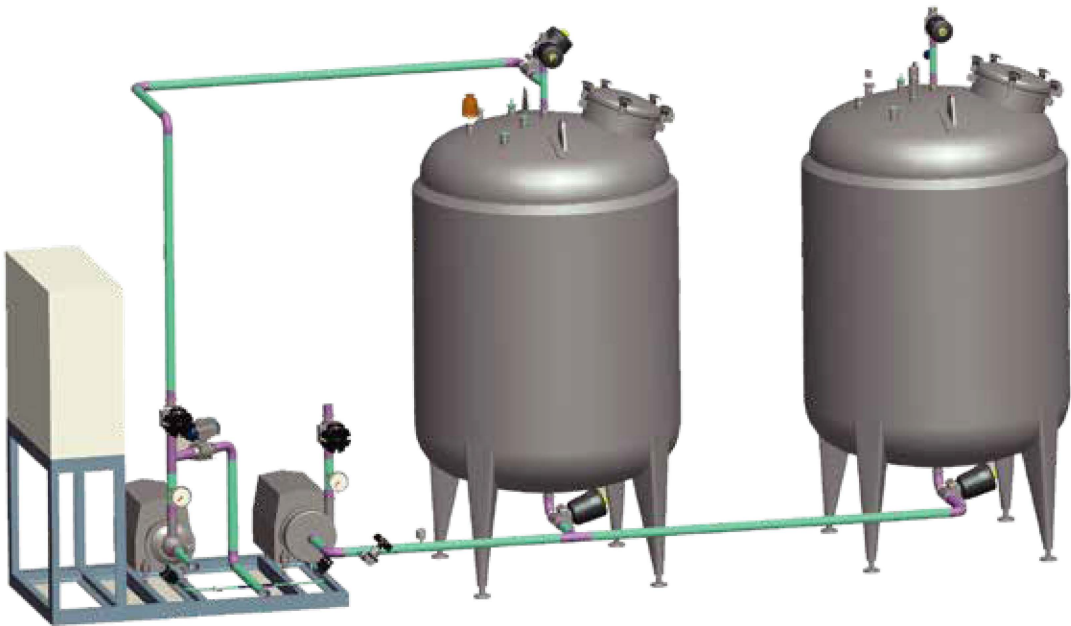
CIP/SIP System

- Rotary sprayer and fixed wide-angle nobles ensure maximum cleaning coverage.
- Pure steam sterilization minimizes contamination risks for sterile drugs.
- Ports, gaskets and viewing glasses are suitable for high temperature.
- The steam supply clean pipeline is made from polished stainless steel and is orbitally welded, tested and documented by endoscopic inspection.
- Temperature control and monitoring are done at the coldest point of the system.
- CIP/SIP runs automatically.
- Interlocking mechanism ensures safety during sterilization process.

Water-ring pump	SIHI® or Nash-Elmo®
Sprayer	Rotary type
Nozzle	Wide-angle type
Pure steam and WFI inlet valve	Burkert® (Diaphragm valve)



External CIP System (tank and pump) as option



Master Control System

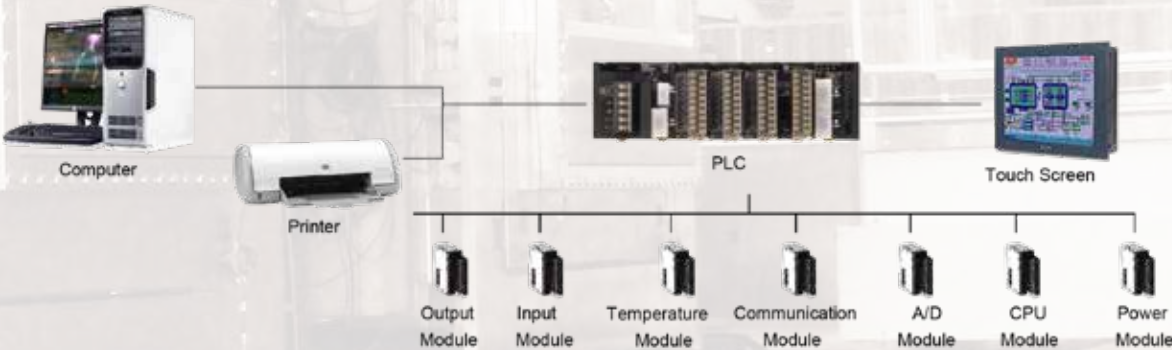
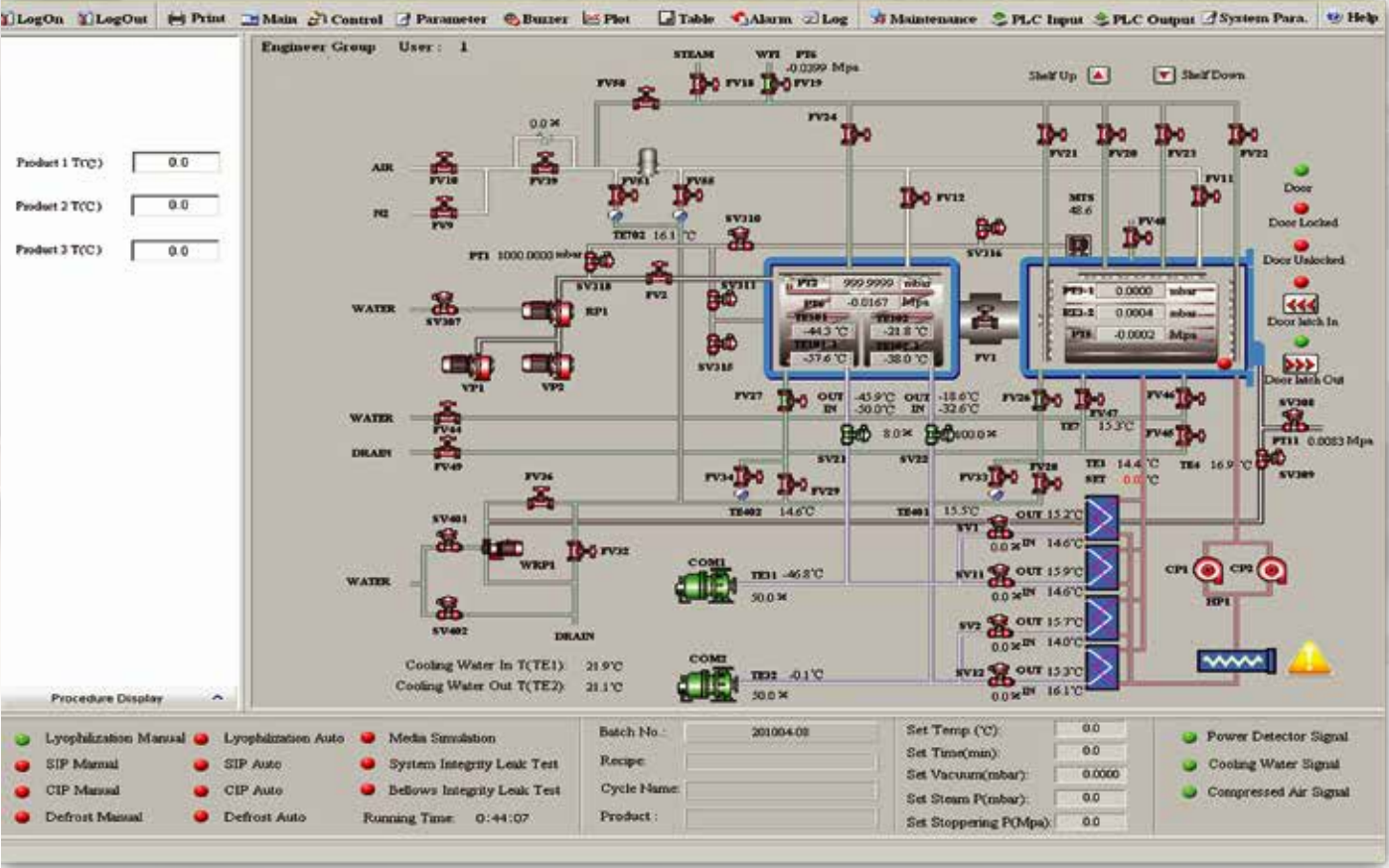


Meeting 21 CFR Part 11 and cGAMP Compliance

Control System

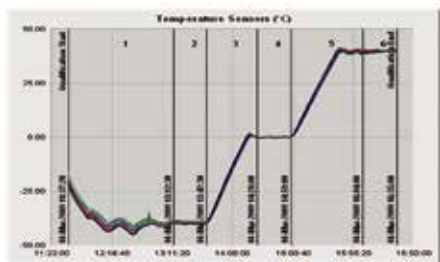
- 21CFR Part 11 and cGAMP compliance.
- Access control according to authority levels.
- Audit trail recording user actions and changes to process parameter.
- Query the curve and data table record.
- Query alarm record.
- Database management and maintenance.
- Available with manual or automatic control.

Software	Tofflon Master Control System (21 CFR Part 11 and cGAMP Compliance)
PLC	Omron® /Siemens® /AB®
Touch screen	Omron® /Siemens® /AB®
Computer	Dell®
Vacuum gauge	Edwards® or MKS®
Temperature probe	PT100
Breaker	ABB®
Contactor	ABB®

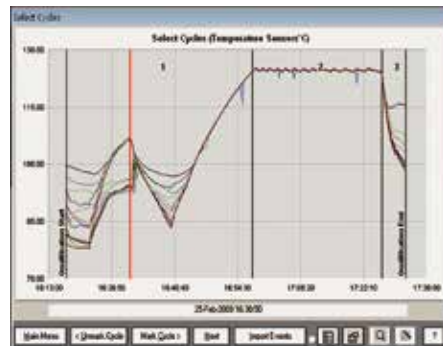


In-Process Quality Control

Shelves Temperature Uniformity Test



SIP Temperature Distribution Test



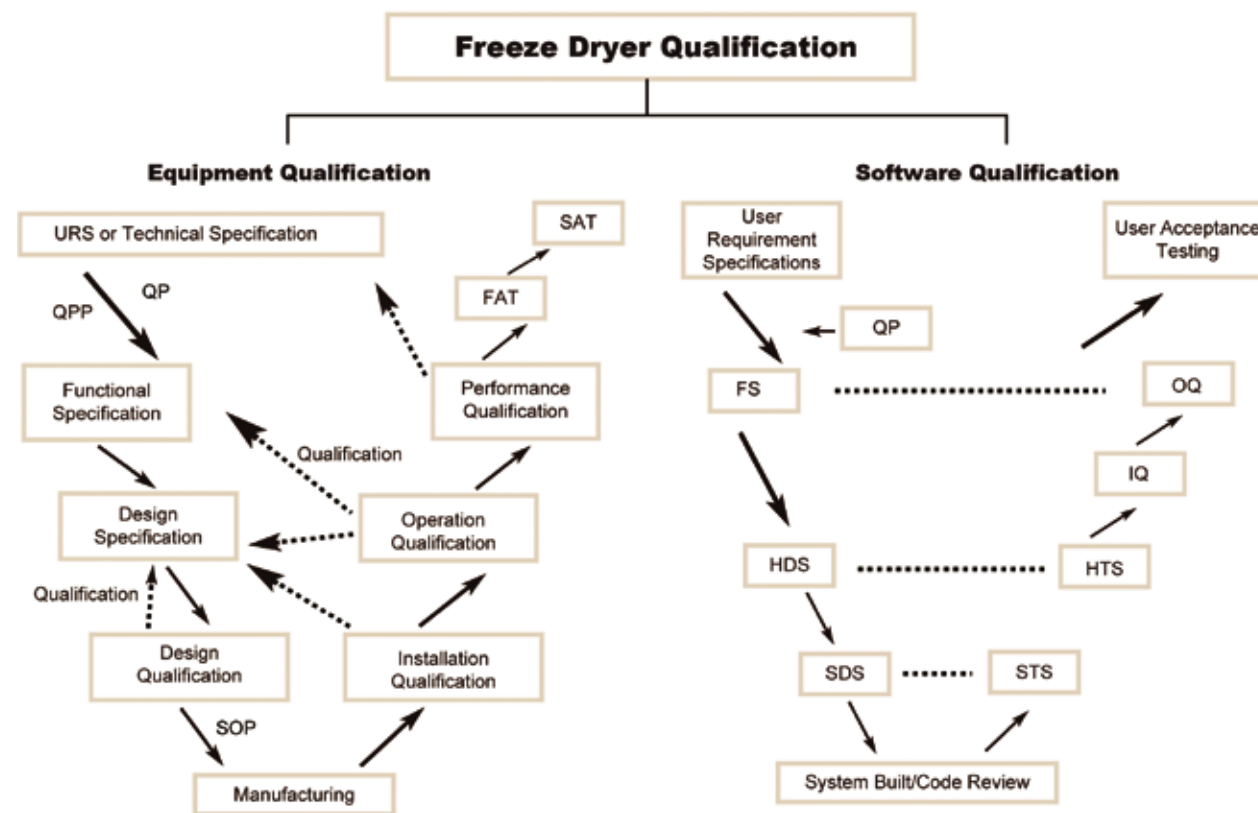
CIP Validation



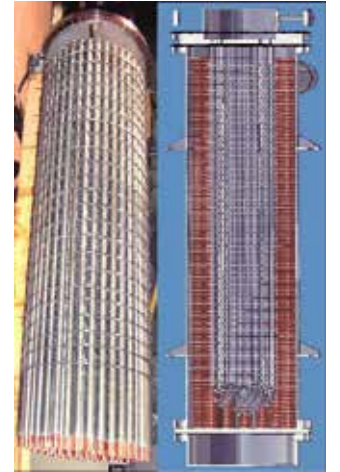
Filter Integrity Test (WIT)

- 0.22µm sterilizing filter, housed in a high temperature resistant enclosure.
- AISI-316L stainless steel pipework, orbitally welded, tri-clamp fittings.
- Filter Sterilization In Place available and all the valves and fittings to carry out Water Intrusion Test.
- Integrity test instruments as optional with FDA 21 CFR Part 11 compliance .

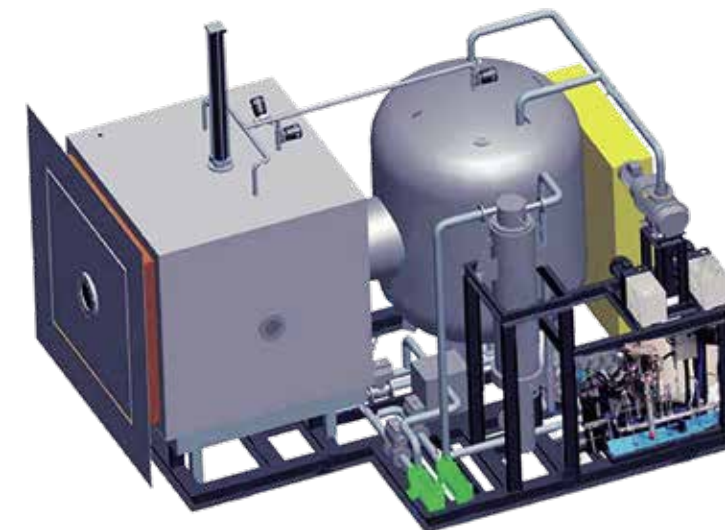
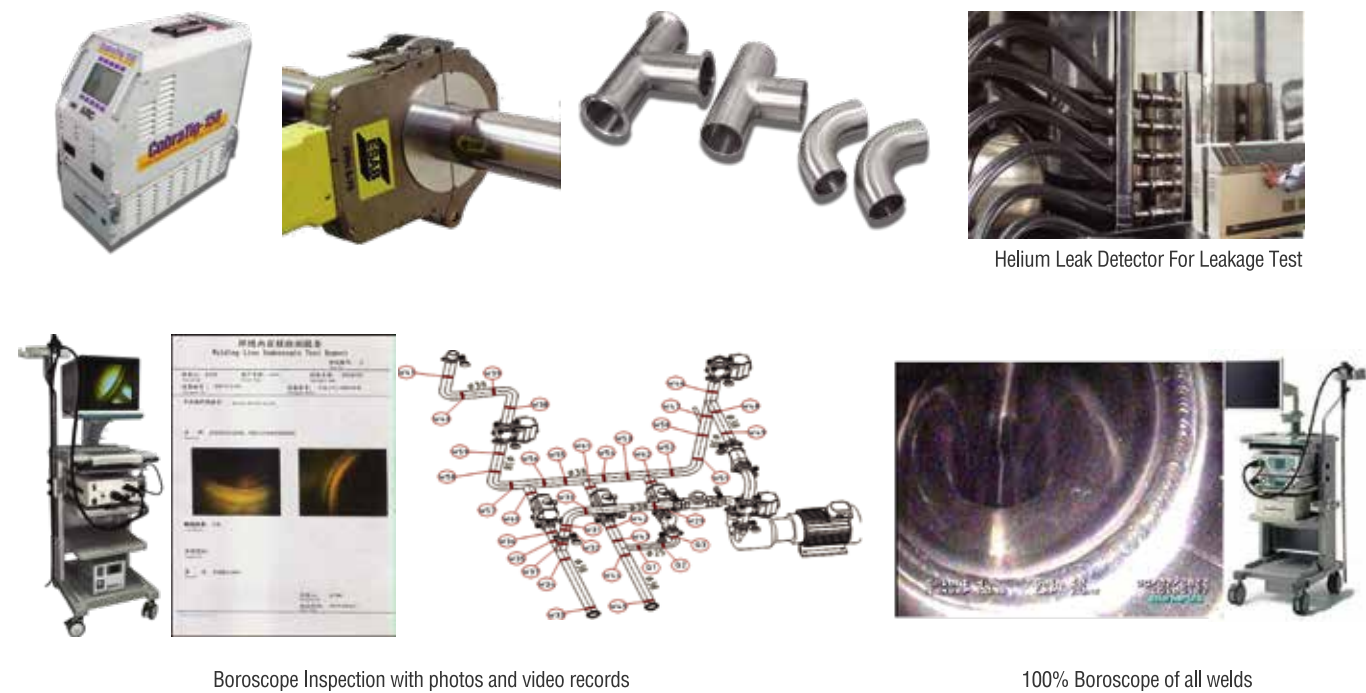




- Increases lyophilizer flexibility:
 - Achieves lower temperatures.
 - Precise temperature control (high reproducibility).
 - Provides faster cooling and/or freezing.
 - Improves reliability and requires minimum maintenance vs mechanical refrigeration.
 - Cost competitive with mechanics.
 - Smaller footprint than mechanics.
 - Environmentally friendly and quiet operation.
 - Nitrogen gas may be available for other uses.
-
- US Praxair NCOOL™ Heat Exchanger.
 - Samson® (Germany) LN2 control valve.
 - Hermetic® (Germany) low temperature pump.
 - Rosemount® (America) liquid level indicator and pressure sensor.
-
- Shelf Final Temperature: -60°C.
 - Condenser Final Temperature: ≤ -120 °C (For direct refrigeration by LN2).
 - Shelf Cooling Rate: 20 to -40°C ≤ 30min (Empty Loaded).
 - Condenser Cooling Rate: 20 to -40°C ≤ 30min (Empty Loaded).
 - Noise: 60-65 dB.



TIG Automatic Welding Machine



After-Sales Service



For many years, we have successfully established well-running after-sales service mechanism and system which make us earn customers' satisfaction and make us stay ahead of the competition.

Prior Delivery

We provide complete documentation with full details of the equipment. Standard documentation supplied with every freeze dryer includes:

- P&I Diagram, Layout Arrangement, Wiring Drawings.
- Erection and Operation Instruction, Maintenance Recommendations and Troubleshooting.
- Main Components List, Component Instructions.
- Factory Acceptance Test documents.

Supply of spare parts and accessories.

We are also able to provide standard IQ and OQ documentation package, as additional options to assist customers with equipment validation.

Post Delivery

- Installation and start-up of new equipment.
- Site Acceptance Test.
- Product training courses.

During Warranty

- Locally-based after-sales service.
- As local assistance, there are also factory-trained technicians.
- Preventative maintenance.
- Corrective repairs.
- Remote problem solving. (via telephone, internet, etc.)

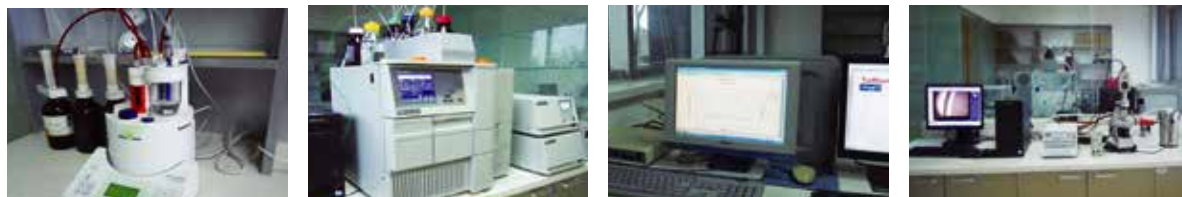
Lifetime Service

- Annual Maintenance Contract (AMC).
- Modification of existing equipment to optimize its performance.
- Sales and supply of spare parts and accessories.
- Product training courses.
- Remote problem solving. (via telephone, internet, etc.)



Mission

- To help customers know the risk in freeze-drying process and avoid it.
- To improve lyophilized drug quality, to reduce cost and to enhance productivity for the pharma and biotech industry.
- To introduce GMP concept into freeze drying process to ensure all the steps in compliance with regulatory expectation.
- Through studying lyophilization and process knowledge, to offer strong foundation for Tofflon freeze drying system solution for the pharma and biotech industry.
- Knowledge and Experience.
- Until 2014, more than 800 lyophilized drugs' thermal property detection and more than 700 lyophilized drugs' freeze drying cycle development.
- Strong experience to solve different lyophilized product defects and well-established database for tested lyophilized products.
- Sound experience on development of freeze drying cycle for different lyophilized drugs including chemical drugs, biological drugs, antibiotics, herbs as well as lyophilized tablets, pre-filled syringe and lyophilized films, etc.



Lyophilization Service

Contents	Period
Lyophilization training	Within 2 weeks
Parameter determination	1 -4 weeks
Cycle development and optimization	4 -16 weeks
Cycle scale up	2-8 weeks
Trouble shooting	4 -16 weeks



Lyophilization Research

A. Lyophilized Tablet

- Fast dissolving speed.
- Easy to deliver, no need water.
- Less hurt to stomach.
- Improve drug bioavailability, good for large molecules drug.



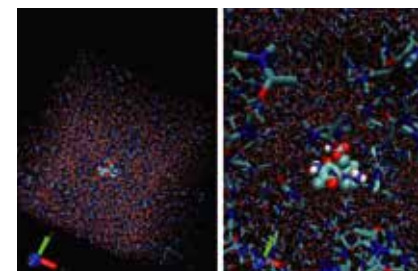
C. Spray Freeze Drying

- Faster sublimation rate.
- Reduce contamination risk.
- Simplify freeze drying process.
- Good for protein and peptide lyophilization.
- Particle size can be controlled as per reques.



E. Molecule Simulation

- To give prediction for freeze-drying cycle design or formulation design.
- To give ideas for formulation design.
- Explanation of the phenomenon in freeze-drying process.



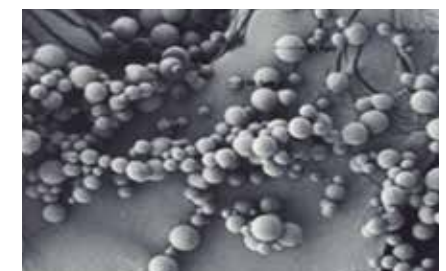
B. Dual-Chamber Syringe

- Easy to use.
- More safety to patient.
- Less contamination.
- Less residual.



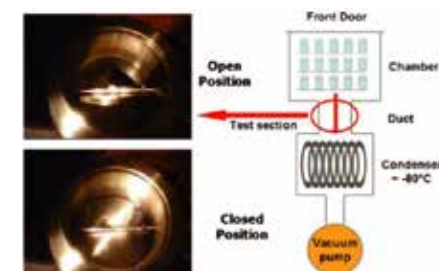
D. Microsphere Lyophilization

- Using membrane filtration process.
- Microsphere size controllable by membrane size.
- Uniform microsphere size.
- Closed process makes easy operation and aseptic protection.



F. MTM Development

- To monitor primary drying using the pressure increase in the freeze-dryer chamber during a shortest period.
- The results of each MTM measurement can be used for process optimization.



Freeze Dryers for Manual Loading and Unloading

LYO	Model/Unit	0.5	1	2	3	5	7.5	10	13	15	20	25	30	40	50
Usable Shelf Area	m²	0.54	1.08	2.16	3.24	5.40	7.56	9.72	12.96	14.40	19.73	24.59	29.60	41.86	50.83
Ice Capacity	kg	10	20	40	60	100	150	200	250	300	400	500	600	800	1000
Vials Capacity (Φ 22mm-10ml)	vials	1200	2400	4500	6700	11200	15700	20200	27000	30000	40400	52300	63300	87500	106500
Vials Capacity (Φ 16mm-5ml)	vials	2300	4500	8800	13000	22000	30800	39600	52900	58800	78400	100100	119400	171500	198900
Shelf Dimension (L)	mm	450	600	900	900	1200	1200	1200	1200	1200	1495	1495	1800	2000	2000
Shelf Dimension (W)	mm	300	450	600	600	900	900	900	1200	1200	1200	1495	1495	1495	1495
Number of Shelves	loaf	4+1	4+1	4+1	6+1	5+1	7+1	9+1	9+1	10+1	11+1	11+1	11+1	14+1	17+1
Shelf Spacing	mm	100	100	100	100	100	100	100	100	90	100	100	100	90	90
Power Supply	kw	6	14	21	29	43	54	66	85	85	117	133	152	184	230
Cooling Water	m³/hr	N/A	5	6.5	10	13	16	20	24	24	34	40	40	45	70
Overall Dimension(L)	mm	1600	2200	3600	3900	4500	4700	5200	6500	6500	7300	7300	7600	8000	8100
Overall Dimension(W)	mm	1100	1200	1750	2200	2300	2300	2200	2300	2300	3000	3000	3000	3200	4800
Overall Dimension(H)	mm	2100	2500	2850	3100	3100	3400	3800	3900	3900	4200	4200	4200	4600	4800
Approximate Weight	ton	1.5	2	3	4.5	7	8.5	10	12.5	13	17.5	20	25	30	32

Freeze Dryers for Auto Loading and Unloading

LYO	Model/Unit	2	3	5	7.5	10	13	15	20	25	30	40	50
Usable Shelf Area	m²	2.25	3.00	5.11	7.16	10.23	12.25	14.98	18.89	23.20	28.16	38.41	48.56
Ice Capacity	kg	40	60	100	150	200	250	300	400	500	600	800	1000
Vials Capacity (Φ22mm-10ml)	vials	5100	6800	11700	16300	23400	28100	34300	43000	53000	64500	87900	107000
Vials Capacity (Φ16mm-5ml)	vials	9700	12900	22200	31100	44400	53200	65000	81900	101100	122900	167600	201000
Shelf Dimension (L)	mm	960	960	960	960	960	1260	1260	1260	1535	1535	1535	1535
Shelf Dimension (W)	mm	900	900	1200	1200	1200	1200	1200	1495	1495	1800	1800	2000
Number of Shelves	loaf	3+1	4+1	5+1	7+1	10+1	9+1	11+1	11+1	11+1	11+1	15+1	17+1
Shelf Spacing	mm	120	120	120	120	120	120	120	120	120	120	120	120
Power Supply	kw	40	40	56	61	74	79	81	117	152	153	191	230
Cooling Water	m³/hr	5	10	13	16	20	24	24	34	40	40	45	70
Overall Dimension(L)	mm	6095	6095	7000	7000	7065	7065	7500	8320	9000	9310	9350	10000
Overall Dimension(W)	mm	2530	2530	2650	2650	2650	2650	2700	3000	3000	3000	3000	3000
Overall Dimension(H)	mm	4500	4500	4700	4940	5120	5400	5560	5200	5900	5900	6635	7000
Approximate Weight	ton	7	7	15	17	20	23	24	27	32	39	40	45

Utility Requirement

- 380V, 50Hz / 440V,60Hz,3-phase,5 wires.
- Cooling water for compressor (1.5 ≤ P ≤ 2bar,T ≤ 25°C).
- Steam for sterilizing or defrosting (2 ≤ P ≤ 3bar).
- WFI for cleaning (P ≥ 4bar,T=80 C).
- Compressed air for pneumatic system (5 ≤ P ≤ 8bar).
- Inert gas for vacuum release (0.5 ≤ P ≤ 1bar).

Technical Data

- Shelf temperature range: -55°C to + 80°C.
- Shelf cooling rate: 20°C to -40°C ≤ 60min.
- Shelf heating rate: Approx. 1°C /min.
- Condenser final temperature: ≤ 75 °C.
- Condenser cooling rate: 20°C to -40 °C ≤ 30min.
- Final vacuum: ≤ 0.01 mbar.
- Evacuation rate: 1000mbar to 0.1mbar ≤ 30min.
- Leakage rate: ≤ 0.03mbar·L/sec.