

Cryogenic cooling with CUMULUSTM LF.

Improved performance, high reliability and
low maintenance for your lyophilisers.



Improving performance of freeze dryers with cryogenic cooling.

The pharma industry is under constant pressure to improve the performance and reliability of its production processes while complying with ever-stricter environmental standards. Innovative cryogenic cooling technologies can help address these challenges.

Limitations of conventional freeze dryers

Freeze-drying equipment typically relies on mechanical refrigeration systems, which use compressors and refrigerants as the cooling agent. However, the performance of these systems is limited by the coldest temperature they can achieve and the cooling rate. They also require periodic maintenance and the refrigerants present a threat to the environment and climate.

CUMULUS™ LF by Linde – proven performance

Linde's advanced cryogenic cooling technology CUMULUS LF utilises liquid nitrogen (LIN) as the cooling agent to overcome the performance and environmental limitations of mechanical systems. CUMULUS LF is able to reach lower operation temperatures than previously thought possible and ramps down temperatures at much quicker rates. In addition, CUMULUS LF is simpler, more reliable and more efficient than conventional compressor skids.

Linde's partnership with IMA Life

Developed by Linde, CUMULUS LF is exclusively commercialised by IMA Life. A large global reference base confirms the success of this solution.



The benefits.

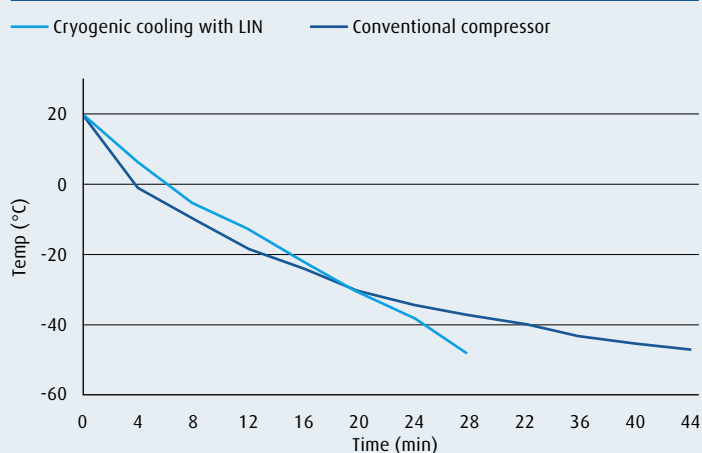
Reasons to choose CUMULUS™ LF.

Numerous successful installations confirm that cryogenic cooling with CUMULUS LF offers better performance, higher reliability and lower cost of ownership than conventional compressor refrigeration systems.

Key benefits

- Increased cooling performance vs. conventional mechanical refrigeration systems:
 - Faster cooling rates with near-linear cooling even at temperatures below -30°C (figure 1)
 - Significantly lower shelf temperatures can be achieved (down to -65°C)
 - Precise temperature control
- Increased reliability and low maintenance due to simplicity of the design and absence of moving parts
- Independent cooling of freeze-dryer shelves and ice condenser
- Mid- and large-scale systems require significantly smaller equipment footprint (figure 2)
- Very low noise levels
- Environmentally friendly with zero emissions
- Low capital investment required

Figure 1: Improved cooling rates



Cryogenic cooling with LIN vs. 4 x 50 hp screw compressors; same freeze dryer

- Near-linear cooling rate (°C/min)
- Faster cooling at lower temperatures

Figure 2: Smaller footprint

Dimensions in mm [in]	Length	Width
Compressor skid	4.267 mm [169 in]	2.240 mm [96 in]
CUMULUS LF skid	1.220 mm [48 in]	1.220 mm [48 in]

CUMULUS LF vs. compressor skid for LYOMAX 30 freeze dryer

The technology.

Cryogenic cooling with CUMULUS™ LF.

CUMULUS LF utilises liquid nitrogen (LIN) to cool commercial lyophilisers for (bio-) pharmaceuticals. It enables liquid or slurry products to be dried in a vacuum after initial freezing. At the heart of CUMULUS LF is a heat exchanger system that independently cools the shelves in the freeze-drying chamber and the coils in the ice condenser.



Cryogenic heat exchanger system

The specially designed cryogenic heat exchanger system (Cryo HEX, figure 3) converts liquid nitrogen into cold nitrogen gas, fully utilising the latent energy of this phase change. This cold nitrogen gas is then used to independently cool the shelves and the coils.

The system design requires only two control valves – one for the freeze-drying chamber, the other for the ice condenser cooling circuits.



Freeze-drying chamber

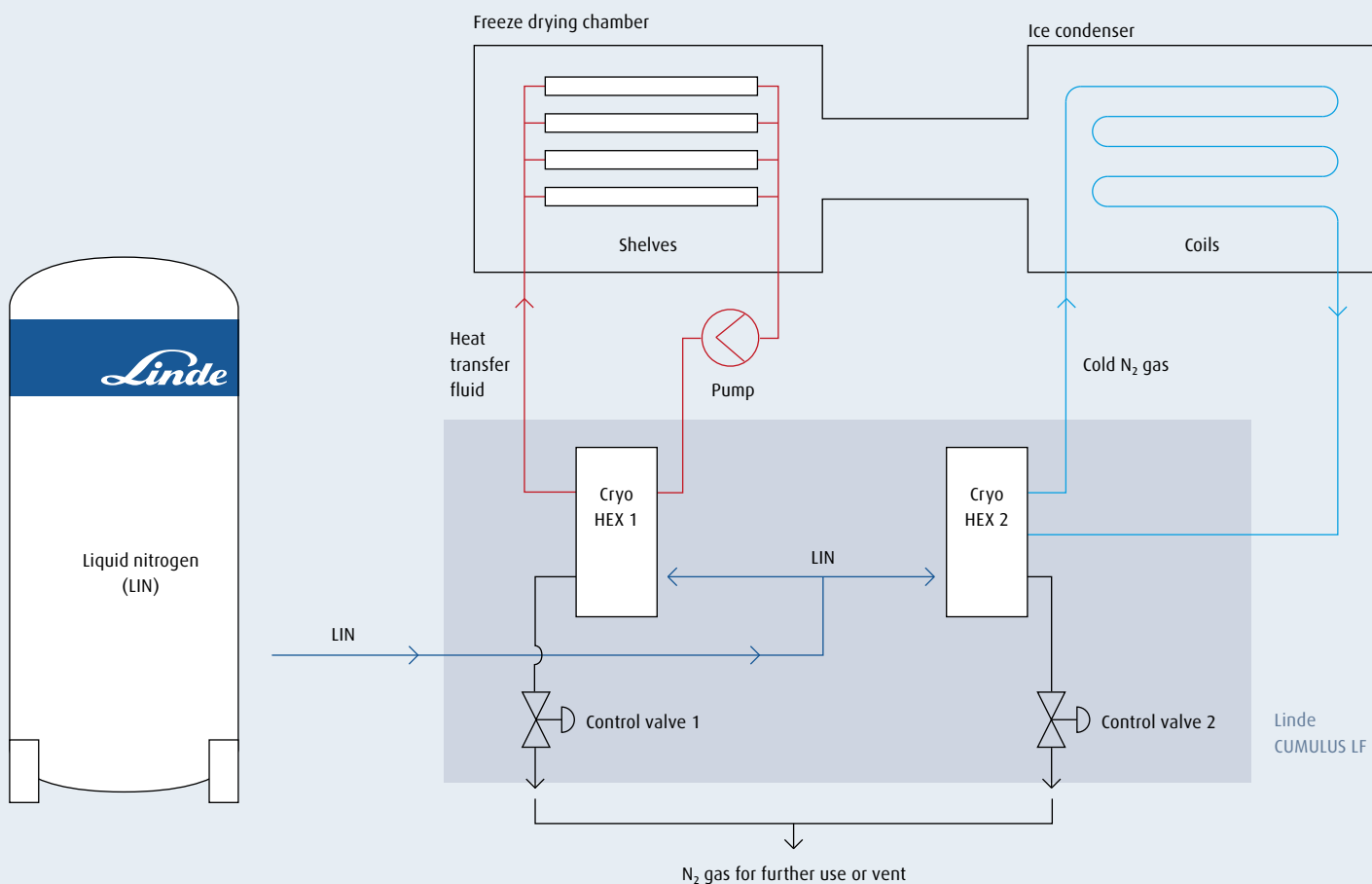
The heat transfer fluid which circulates inside each shelf (figure 3) is cooled by cold nitrogen gas rather than liquid nitrogen. Cold gas prevents heat transfer fluid from freezing, while quickly dropping the shelf temperature to -60°C and below at a near-linear rate.



Ice condenser

The coils (figure 3) are cooled directly by cold nitrogen gas, which is evenly distributed within each coil to eliminate the risk of large temperature gradients across the coils. Even distribution also ensures excellent temperature control. The setpoint can be as low as -100°C .

Figure 3: Schematic overview of CUMULUS LF supporting a commercial lyophiliser



Key features of CUMULUS LF

- Shelf and condenser cooling circuits can be positioned and operated independently
- System design only requires two control valves
- Excellent temperature control of both chamber shelves and condenser coils
- Cooling system works independently of the power supply
- Simple design with no moving parts
- Modular system for any size freeze dryer
- Successful operation demonstrated using various grades of heat transfer fluid

CUMULUS™ LF portfolio.

Perfect fit for every size freeze dryer.

CUMULUS LF can be implemented in any size freeze dryers. This solution can be integrated in new units or retrofitted in existing systems of various capacities.

CUMULUS LF

- By combining different modules, we can effectively serve freeze dryers of all sizes while ensuring the most efficient utilisation of liquid nitrogen
- Available modules:

	LF2512	LF5020	LF10050
Product shelves (cooling capacity in kW)	25	50	100
Ice condenser (cooling capacity in kW)	12	20	50

- Easy to retrofit with only minor modifications to the existing system
- Able to duplicate temperature profile to simplify re-validation requirements
- Low capital investment required
- We offer various liquid nitrogen supply schemes, on-site storage and distribution equipment

Proven partnership

- Successfully implemented to support various production-scale freeze dryers in partnership with IMA Life
- Design based on our proven and patented CUMULUS temperature control technology

Linde's technology for controlled nucleation

- Through our VERISEQ™ nucleation technology, we also offer a solution for controlled nucleation during lyophilisation. VERISEQ nucleation reduces overall cycle time, decreases vial-to-vial variance and improves product uniformity. This solution is also exclusively distributed by IMA Life.
Find out more at www.linde-gas.com/veriseq



A strong partnership.



CUMULUS™ LF has been developed by Linde. The technology is exclusively commercialised by IMA Life.

About Linde

The Linde Group is a world-leading gases and engineering company with a rich and sophisticated technology and service portfolio. Linde has been supporting the pharmaceutical industry with pharmaceutical-grade gases for many decades and has gained an in-depth understanding of the challenges pharmaceutical companies face.

Linde's offering for the pharmaceutical industry includes:

- VERISEQ™ process-grade gases – high-purity, traceable nitrogen, oxygen, carbon dioxide, argon, helium and synthetic air
- HiQ® specialty gases for calibrating gas monitoring equipment
- Process chemicals for applications like amination, catalysis and fluorination
- Gas applications for ozonolysis, inerting, purging, charging and mixing
- Gas applications for reactor cooling, cryogenic storage, transport and freezing
- Gas applications for freeze drying, cryogenic cooling and controlled nucleation in cooperation with IMA Life

About IMA Life

- Exclusive rights to market CUMULUS LF cryogenic cooling technology
- World leader in the design and manufacture of aseptic processing and freeze-drying equipment
- Five manufacturing sites across Italy, the US and China, and three service centres – in Italy, the Netherlands and Japan
- Worldwide network covering more than 80 countries
- Access to freeze-drying laboratory for development work with one laboratory-scale and one pilot-scale freeze dryer and other analytical tools including tunable diode laser absorption spectroscopy (TDLAS) instrumentation, a residual gas analyser and other re-configurable instrumentation ports





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