

Praxair's NCOOL™ System offers a unique high performance liquid nitrogen based heat exchange technology. It can be successfully and economically deployed in place of mechanical refrigeration systems used to lyophilize/freeze dry biological and other active pharmaceutical products. Praxair's NCOOL technology is not only increasingly being used in new lyophilization systems, but it is also being applied to the conversion of existing mechanically based systems.

**Praxair's Proprietary,
High Efficiency NCOOL™
Liquid Nitrogen Heat
Exchange System**

Praxair's NCOOL™ cryogenic heat exchange system is specially designed to:

- Operate at very low temperature without freezing of the heat transfer medium.
- Minimize liquid nitrogen consumption.
- Ensure precise temperature control with high turn-down capability.



Praxair's NCOOL system employs proprietary, patented buffering technologies that minimize freezing during heat exchange between the cryogenic liquid nitrogen and the process fluid or cooling media.

Since the liquid nitrogen is used indirectly, with direct heat exchange taking place only between the cold gas and the heat transfer medium, the system greatly improves the efficiency of recovering the available refrigeration.

Praxair Technology Benefits

The advantages of Praxair's NCOOL technology versus other cryogenic heat exchanger designs include:

- Enhanced reliability: Minimal operation interruptions due to freezing, no defrosting required.
- Improved operating economics:
 - High liquid nitrogen efficiency, > 90% of available refrigeration utilized.
 - Low power consumption and minimal media pressure drop through the heat exchange system.
- Greater process flexibility: Can operate within a few degrees of the media freezing point.

Praxair's portfolio of lyophilization related technologies, processes and equipment are covered under U.S. patents 5,701,745, 5,937,656, 6,220,048, and 6,505,472.



BIO/pharma
LIFECYCLE TECHNOLOGY



Lyophilization (Freeze Drying) Process Basics

Lyophilization (freeze drying) is a manufacturing step often used to gently stabilize pharmaceutical, biopharmaceutical and food products and intermediates. A typical lyophilization process consists of three stages: freezing (solidification), primary drying (ice sublimation) and secondary drying (moisture desorption). Because lyophilization dries a product from the frozen state, the refrigeration system is a critical component of a lyophilizer.

Lyophilization Trends in Pharmaceutical Manufacturing

Lyophilization remains the process of choice for an increasing number of high value pharmaceutical products with more demanding process requirements.

These include:

- Biologic formulations.
- Formulations of non-aqueous solvent based drugs.
- High fill depth and high volume dosages.
- Vaccines.

There is an increasing need and demand for cost effective process improvements that provide:

- Enhanced reliability to minimize lost production of high value products.
- Greater operating flexibility to meet more demanding process requirements.

Liquid Nitrogen Lyophilization

Cryogenic liquid nitrogen has been increasingly used to provide low temperature refrigeration for lyophilization in pharmaceutical manufacturing because it provides a number of performance advantages over a conventional mechanical compressor based system:

Improved reliability.

- Refrigeration available during power failures.
- Reduced maintenance downtimes.
- Products can be kept frozen for some time, even in the case of full power or mechanical failure.

Colder process temperatures – enhanced process capabilities.

- Broader range of operating parameters, i.e., faster and constant cooling rate to lower temperatures.

- High condenser capacity.
- High shelf-cooling capacity.

Reduced complexity.

- Low maintenance requirement.
- Easy to operate.

Environmentally friendly and quiet.

Economically feasible.

- Low-capital requirement.
- Flexibility in refrigeration loading.
- Low electrical power and no cooling water requirements.
- Smaller installation footprint requirements.
- Low cost alternative to freon-based systems.
- Significantly reduced maintenance costs.

Convenient supply: Praxair can supply both the liquid nitrogen and related insulated delivery system required for this technology.



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