

IMPROVING LYOPHILIZATION PRODUCTIVITY AND RELIABILITY



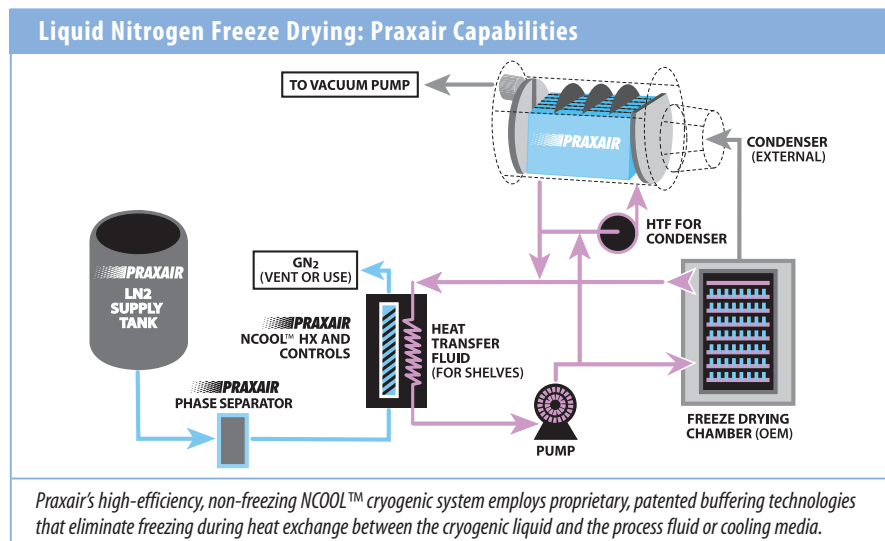
The increasing number of high value biologic and synthetic formulations and products has created the demand for dependable lyophilization techniques and equipment. This makes the process capabilities of the refrigeration system all the more critical to a successful commercial lyophilization operation. Fortunately, new advances in lyophilization technology are putting more control in the hands of manufacturers, while keeping costs in line. The performance advantages of cryogenic liquid nitrogen make it particularly suitable for lyophilization of biologic formulations, vaccines and non-aqueous, solvent-based drugs. A look at the capabilities of these systems shows how liquid nitrogen lyophilization is ready for mainstream processing operations.

Flexible operation and enhanced process control

Lyophilization is a unique process from a refrigeration point of view. Not only does it require ultra-low temperature refrigeration below -50°C , but during a processing cycle the refrigeration load is also extremely variable, often requiring a system turn-down in excess of 10:1. Both of these processing characteristics favor cryogenic refrigeration over mechanical systems.

Cryogenic systems are capable of providing a rapid and constant cool-down rate in any temperature range of interest. Mechanical systems typically cannot maintain the initial cool down rate throughout the entire production cycle. Therefore, the increase in operating flexibility and the precision of cool-down and freezing obtainable with advanced liquid nitrogen systems offer manufacturers significantly improved product structuring capability. This is especially important in developing formulation models and lyophilization cycles where the added control over parameters such as freeze rates, shelf and product temperatures and sublimation rates enables manufacturers to determine and employ optimum settings to attain ideal moisture levels and shelf-life for their lyophilized products.

Additionally, the later stages of the lyophilization process call for maintaining ultra-low temperatures in the condenser for extended periods to remove the vapor originating from the sublimating ice from the product. Indirect cryogenic heat exchange systems can hold very low temperatures at a precise point over any period of time without



Praxair NCOOL™ Non-Freezing Cryogenic Heat Exchanger System

Improved efficiency and lower costs over many alternatives

- Highest performing heat exchanger
- Greater than 90% efficiency
- Negligible power consumption

Greater process flexibility and control

- Maintains very low temperatures
- Precise control and fast and constant run-down rates
- Expanded processing window

freeze-up. This heightened level of control makes temperature specifications more easily reproducible. Dependable and precise temperature control can also help with cGMP documentation and compliance.

Improved reliability, reduced complexity

Lyophilization typically requires ultra-low temperature refrigeration at temperatures below -50°C ,

sometimes as low as -100°C . The reliability of mechanical systems deteriorates as the refrigeration temperature drops. Compressors and related equipment, in fact, account for 80% of service problems associated with mechanical systems. Inherently simple and reliable cryogenic systems, with practically no moving parts, are not subject to catastrophic compressor failure, making them much more reliable than complex mechanical systems. Liquid nitrogen-based systems also provide constant cooling power throughout the temperature ranges of any lyophilization cycle. Finally, these systems can maintain refrigeration during power failures, maintenance and other downtimes, providing additional operational flexibility to support valuable products.

For more information

Contact Praxair at 1-800-PRAXAIR (1-800-772-9247) or log on to www.praxair.com.