



Control. Every step of the way.

Praxair's *ControLyo*™ nucleation on-demand technology can deliver improved process control, uniformity, quality, and yield. Helping you reproduce results from the lab to manufacturing, while reducing lyophilization cycle times.

Take control of your time, your costs, your product.

Until now, the freezing step of lyophilization was unpredictable due to the random nature of the nucleation process. In a typical pharmaceutical lyophilization process, the contents of individual vials nucleate over a broad range of temperatures, usually spanning 5° to 20°C below the formulation's freezing point. However, Praxair has developed a new and scalable method that can make nucleation control a reality.

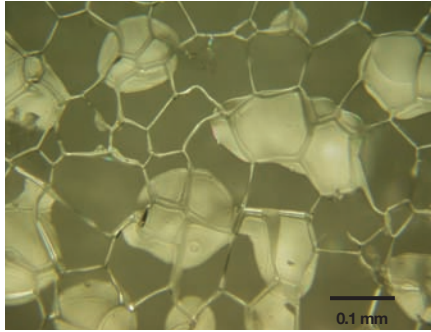
By being able to consistently and uniformly nucleate at warmer temperatures, significant improvements in product quality and drying rate can be achieved. Warmer nucleation causes larger ice crystals to form, which increases pore size and reduces interfacial ice surface area. Increased pore size can considerably

reduce drying time, while a reduction in surface area can lessen protein aggregation. With improved ice structures and process consistency, product uniformity and cake elegance benefits can also be realized.

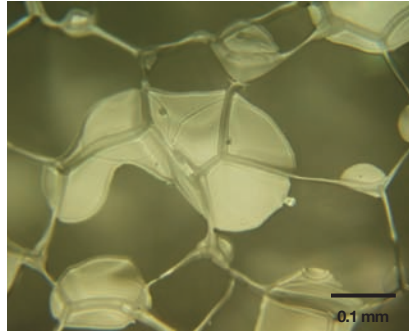
Scalable process control and improved product uniformity allow manufacturers to simplify their formulation and scale-up effort, potentially reducing the time to market. Gaining improved control of process parameters also facilitates the application of the FDA's QbD (Quality by Design) initiative.

Since Praxair's technology requires no changes to existing drug formulations and can be retrofitted to most freeze-dryers with minimal impact on established lyophilization protocols, it is a viable technology for everyone.

Comparison of Cake Pore Size



Conventional, stochastic lyophilization.



Praxair-controlled lyophilization.

Take Control of Your Process

Lyophilization helps preserve and stabilize sensitive, high-value, sterile products with a three-step freeze drying process: freezing, primary drying, and secondary drying. Despite many advances in freeze-drying equipment, the freezing step remains unpredictable due to the normally random nature of nucleation (i.e., beginning of freezing).

This phenomenon negatively impacts lyophilization processes, resulting in longer cycle times, reduced yields, and quality issues. Complex formulations and conservative freeze-drying cycles are commonly used to mitigate the negative effects of unpredictable nucleation.

Praxair's new *ControLyo* technology adds improved control and uniformity to the lyophilization process, making the age-old nucleation control problem a thing of the past.

Praxair *ControLyo*™ Technology Benefits

Improved process control and reproducibility

- Provides predictable process scale-up and transfer
- Reproduces results from the lab to manufacturing

Increased lyophilization capacity

- Reduces primary drying times by up to 40%
- Lowers operating costs
- Lowers capital costs

Improved product quality

- Improves vial-to-vial uniformity
- Improves cosmetic appearance
- More homogenous cake
- Reduces protein aggregation
- Aligned with FDA's QbD initiative

Improved product yield

- Reduces freeze damage for APIs
- Reduces vial cracking

Actual results may vary.

To learn more visit, www.fastprecisecold.com or call 1-800-PRAXAIR.



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