Elegant Cake Every Time

ControLyo® Technology

Patented technology from SP Scientific

con·trol

kənˈtrōl/ noun

1. the power to influence the course of events: "The operation is under the control of the Production Manager."

synonyms: jurisdiction, sway, power, authority, command, ... more

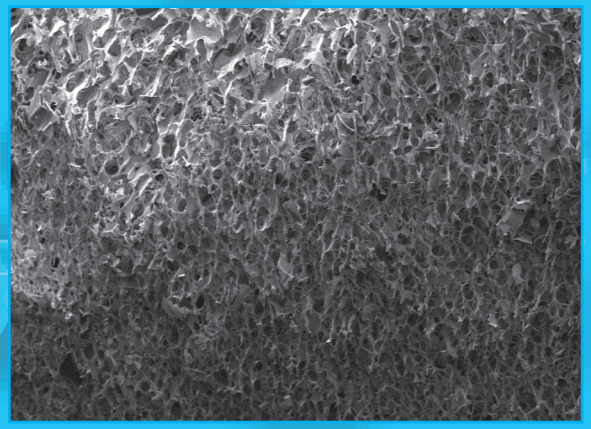
Oxford Dictionaries oxforddictionaries.com

ControLyo® Technology changes the act of nucleation (initiation of crystallization) within the freeze dryer from a stochastic process with wide inter and intra batch variability to a controlled, higher temperature event that can be reproduced with confidence.

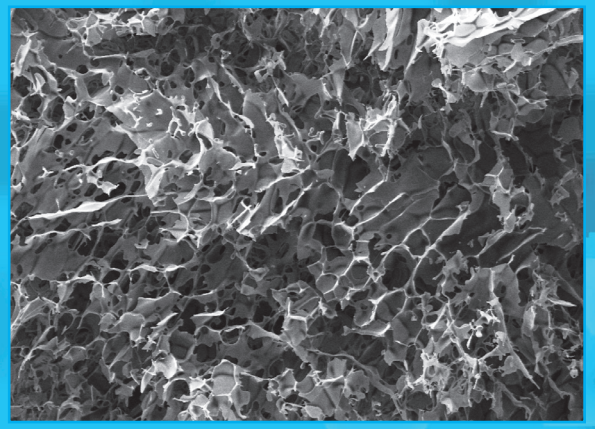
By controlling the ice nucleation temperature, ControLyo® Technology can control the supercooling effect, reducing primary drying time and increasing product homogeneity. In short, this patented technology offers an effective solution to one of the most common freeze drying scale-up challenges and does so without significant addition of utilities or risk of introducing foreign particles into the vials as may occur with other technologies.

Crystallization Comparison

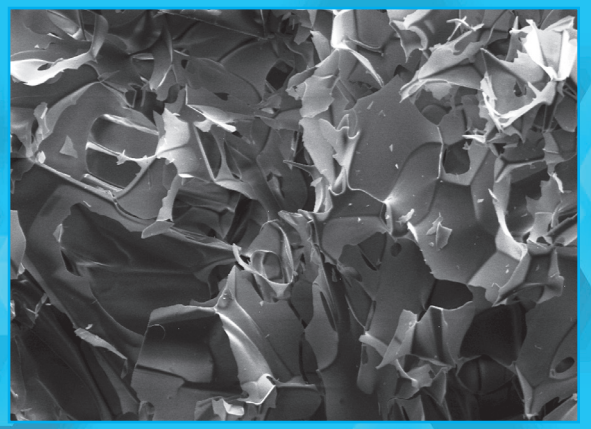
SEM Photography captures Sucrose, 75 mg/mL, processed under the following conditions:



Uncontrolled: 1°C/min shelf cooling rate



1°C/min shelf cooling rate plus annealing



***ControLyo® Technology* at -3°C**

Except for the freezing regimen, all other drying conditions were kept the same.

ControLyo® Technology Benefits

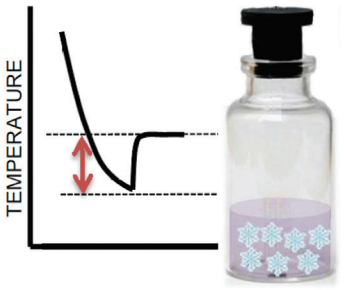
Freezing all vials at the same time, at a higher temperature creates larger, more consistent crystal sizes that will dry more uniformly.

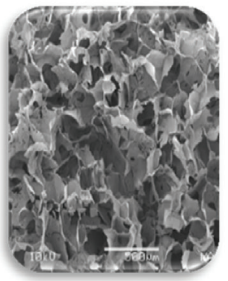
- ***Improved product qualities - product homogeneity, cake appearance, cake morphology, and reconstitution time***
- ***Less aggregation and better stability of protein formulations***
- ***Conforms to regulatory framework for QbD by controlling process inputs***
- ***Can be replicated from one freeze dryer to another enabling scale-up***
- ***For every 1˚ increase in nucleation temperature, primary drying time is reduced by 3%[1].***

Crystallization Comparison

High degree of super-cooling
Smaller ice crystals
Smaller pores in dried matrix
Increase in product resistance Rp
Decrease in rate of sublimation
Longer freeze drying cycle times

Low degree of supercooling
Larger ice crystals
Larger pores in dried matrix
Decrease in product resistance Rp
Increase in rate of sublimation
Shorter freeze drying cycle times



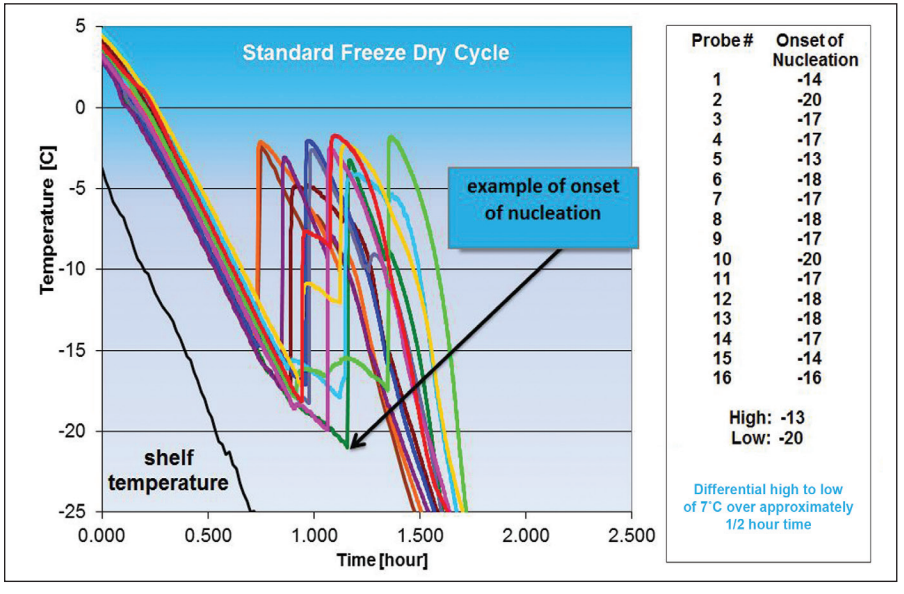


ControLyo® Technology is an option on SP Scientific clinical, pilot and production freeze dryers and may be retrofitted on qualified existing units regardless of manufacturer.

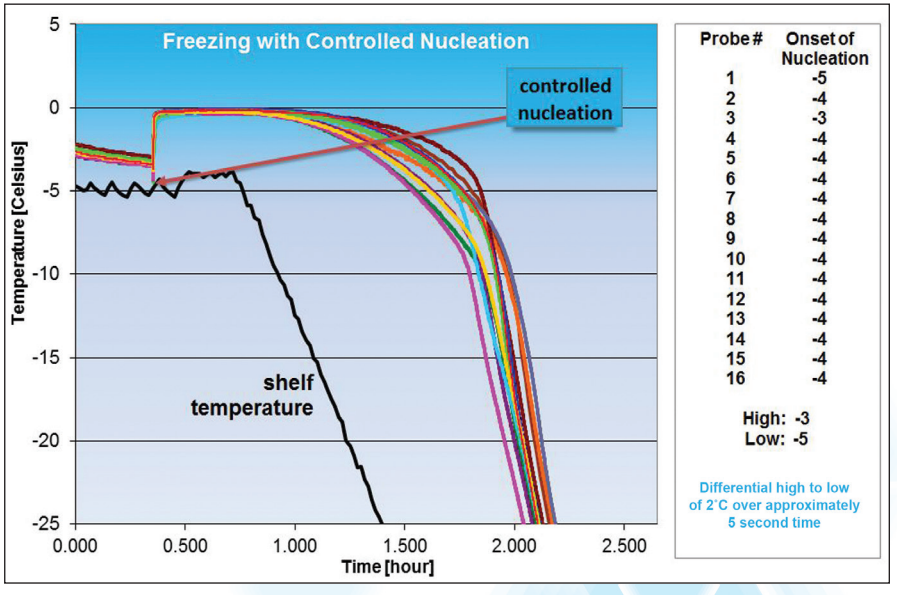
1. Searls, J.A., Carpenter, T., Randolph, T.W. (2001). The Ice Nucleation Temperature Determines the Primary Drying Rate of Lyophilization for Samples Frozen on a Temperature Controlled Shelf. J. Pharm. Sci., 90:860-871

Freeze dryers without controlled nucleation will produce product with varying degrees of supercooling, resulting in less homogeneous products. Controlled nucleation shows significantly less variation in the degree of supercooling and results in inconsequential variation in ice crystal morphology.

Uncontrolled Nucleation



Controlled Nucleation



Characteristics of Nucleation in a Production Environment

Without control over the nucleation process:

- Nucleation rarely occurs at the thermodynamic freezing point of formulation
- Nucleation is a stochastic process, with nucleation occurring up to 20˚C below the thermodynamic freezing point in a class 100 (Grade A) production environment
- The degree of supercooling can create variability in crystal size with significant impact on the drying process
- Freeze dryers without controlled nucleation will induce nucleation at arbitrary times and temperatures across the batch causing a lack of product homogeneity

ControLyo® Technology Process

ControLyo® Technology utilizes an inert gas and a series of pressurization and depressurization steps to create consistency of temperature and pressure throughout the freeze drying chamber at the controlled shelf temperature. This controlled environment induces nucleation across all vials at a higher, more consistent nucleation temperature. Stabilization of the products after nucleation then allows complete freezing of the vials.

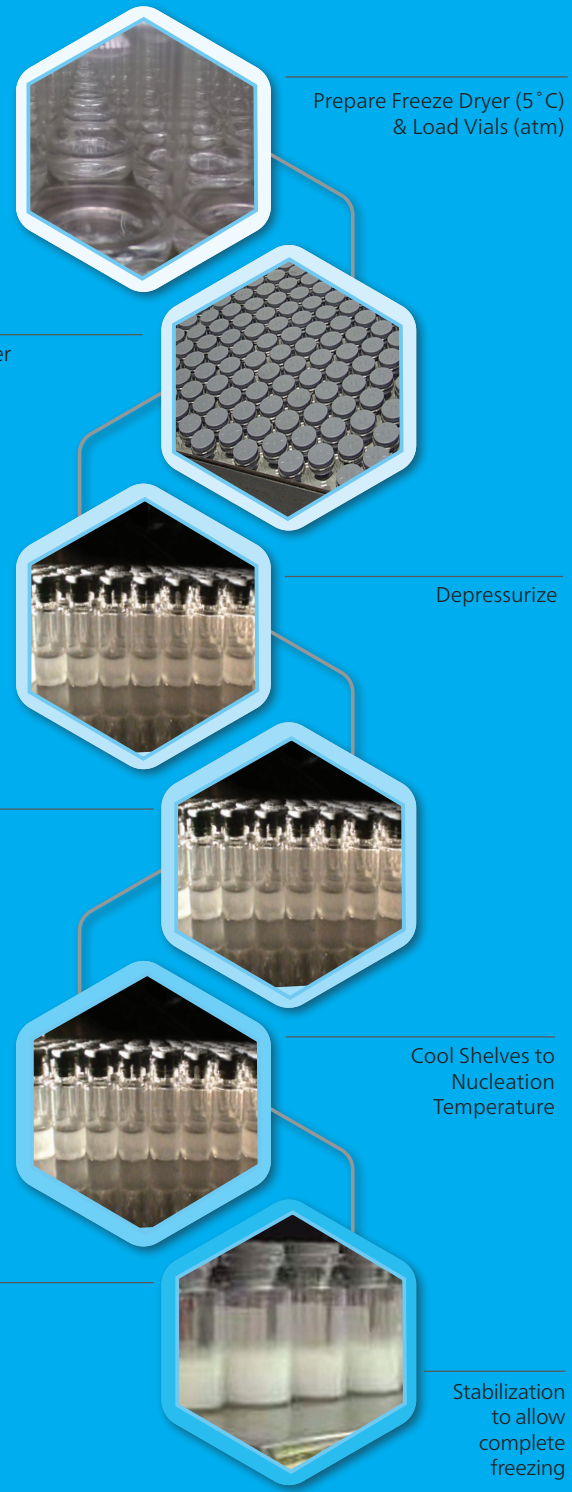
During the ***ControLyo® Technology*** process, purges with sterile inert gas are used to remove air from the chamber while maintaining a sterile boundary. The ***ControLyo®*** vent valve is closed before the point at which the chamber pressure reaches 16 PSIA or higher for both the purges and the final depressurization. ***ControLyo®*** flow is always away from the product, just as it is during a steam-in-place (SIP) process. Higher local pressure is maintained to prevent backflow and the pressure differential is similar to SIP.

No significant addition of utilities are needed to implement ***ControLyo® Technology***. It can be retrofitted onto qualified existing units regardless of manufacturer.

- No modification needed for chamber or condenser – no baffles or nozzles required
- Use of existing utilities – sterile nitrogen
- Other cycles can be run by deselecting ***ControLyo®*** functionality with no interference
- Compatible with auto loading or unloading systems with no modification needed
- Easy to validate, no complex control system
- No need for wall temperature control

http://bit.ly/ControlledNucleation

ControLyo® Technology in Action



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