

The sterility of the *ControlLy*TM process: reducing freeze dried product batch time without compromise to system integrity

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Introduction

Controlled nucleation is the most significant new development in freeze drying in quite some time. As is well known, in the typical freezing process of the freeze drying cycle, the contents of individual vials tend to freeze at different temperatures as the shelves cool (stochastic nucleation). As is also recognised, the temperature at which the product freezes affects the size of the ice crystals that are formed and the warmer temperature at which the product nucleates, the larger the ice crystals tend to be. In turn, when a relatively large ice crystal sublimates out of the product, it leaves behind a larger path for subsequent crystals to sublime and leave the vial. This reduces what is called 'resistance to drying' and can result in significantly reduced primary drying time.

How *ControlLy*TM works

*ControlLy*TM pressurises the freeze dryer chamber with filtered inert gas and then quickly depressurises the chamber. The quick depressurisation causes product that is slightly subcooled (that is, slightly below its melting point) to nucleate at virtually the warmest possible temperature, thus yielding the largest possible ice crystals and the shortest potential primary drying time.

SP Scientific has exclusive license for *ControlLy*TM nucleation on-demand technology and has supplied *ControlLy*TM on dozens of laboratory, as well as production freeze dryers (new and retrofits). For those systems that require sterile process environments, the *ControlLy*TM cycle is analogous to the pressurisations and depressurisations of typical and well-validated Steam-In-Place (SIP) cycles as well as the System Evacuation phase of the freeze drying cycle.

During a typical SIP cycle, during the steam purges and the final blowdown, the pressure in the freeze dryer is released by opening all valves in the main drain path. To maintain sterility, this path usually is closed when the chamber pressure reaches 16 PSIA (1.1 Bar), or about 1.3 PSI (0.09 Bar) above a standard atmosphere. Keeping the system pressure higher than that of the ambient pressure assures one that there is no backflow into the system from non-sterile sources, as is well documented in numerous SIP validations.

Likewise, the *ControlLy*TM process employs several purges followed by a final decompression. Instead of clean steam, an inert gas (Nitrogen or Argon), which passes through the same sterile filter used for gas-bleed pressure control during drying, is used to pressurise the unit. Here again the purges are used to remove air from the chamber and as in the SIP cycle, the *ControlLy*TM vent valve is closed before the point

the chamber pressure reaches 16 PSIA or higher for both the purges and the final depressurisation.

Additionally, an essential phase of the freeze drying process itself necessarily exposes the sterile boundary to a non-sterile gas exit path, that is, at the first valve which isolates the chamber from the vacuum system. During system evacuation, the vacuum pumps are energised and then the primary vacuum system isolation valve is opened. The side of the primary vacuum system isolation valve exposed to the chamber or condenser is considered sterile while the side exposed to the vacuum piping is not. However, it is well established that this event does not contaminate the product because the local pressure at the product is greater than that in the non-sterile piping. Consequently flow is always away from the product, just as it is during *ControlLy*TM.

The *ControlLy*TM process does not introduce any foreign elements into the vials which could potentially become a carrier for microorganisms introduced during aseptic processing to enter the vials. Given the improved quality attributes, product homogeneity, batch uniformity, reduced drying time, and minimal risk to product contamination, *ControlLy*TM is a technology that is consistently and easily scaled to any manufacturing freeze dryers.



Contact information

For more information on *ControlLy* or retrofitting *ControlLy*TM to your existing freeze dryer please contact **Leslie Mather**, Director of Pilot Freeze Dryers at Leslie.Mather@SPScientific.com, or **Paul Coiteux**, Director of Technical Sales, Production Freeze Dryers at Paul.Coiteux@SPScientific.com. For general media inquiries please contact **Shireen Scott**, Senior Brand Manager at Shireen.Scott@SPScientific.com, call 1-845-255-5000, or visit www.spscientific.com.

Reference

1. A video demonstrating stochastic versus *ControlLy* controlled nucleation can be accessed at: bit.ly/ControlLy



Further information:
SP Scientific
www.spscientific.com