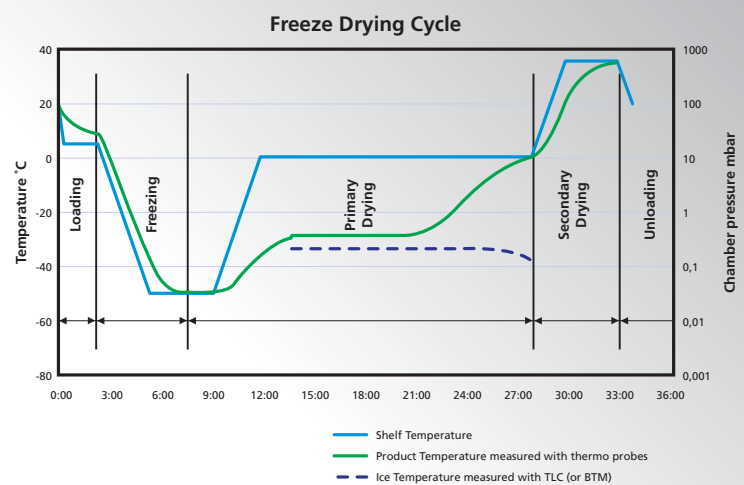


Enabling
PAT

Thermodynamic Lyophilization Control - TLC®



During the freeze drying process, the ice temperature is the key parameter to monitor and control!

A safe, reliable, reproducible process is essential to ensure that pharmaceutical and biological products have the specified properties and quality. In fact the FDA's PAT (Process Analytical Technology) initiative demands thorough process understanding, careful monitoring and control. Also with the continuing trend towards more process automation; with automatic loading and unloading systems and in some cases, isolators in an effort to minimize contamination risks and meet sterile processing and validation regulations. This trend depends on increasingly sophisticated monitoring methods to control the freeze drying process.

Lyophil Technologies

Advantages

- Applicable for all freeze dryers
- Ideal for sterile processing
- Ideal with automatic loading and unloading systems
- Ideal when isolator technology is used
- No need for mechanical modifications at the freeze dryer
- No risk of contamination
- Reproducible measurements
- Direct & accurate lyophilization monitoring and control
- Monitoring of the complete batch during the whole drying process
- Enables optimization of the freeze drying process cycle
- No influence on the product by short measuring times
- Process data easy to scale-up
- Delivers comprehensive data for better process understanding



Ice temperature during primary drying

Thermodynamic Lyophilization Control TLC®

A process analysing, monitoring and control tool for Freeze Drying in R+D applications and for full-scale production.

GEA Lyophil has developed TLC as an in-line, non-invasive method of:

- Monitoring the primary (main) drying
- Determining the end of the main drying
- Monitoring the secondary drying
- Determining the end of the secondary drying

TLC enables a dynamic control of the drying process: minor variations – e.g. of the raw product or the filling height of the vials – will be identified and the process will be adjusted accordingly.

Principle

The TLC method is based on the relationship of ice temperature to vapour pressure. The ice temperature is measured using pressure rise analysis BTM (Barometric Temperature Measurements) during main drying. The point at which to switch from main to secondary drying can be determined by tracking and analysing the different BTM measurements. During secondary drying the process is monitored and the end point is determined by DRM (Desorption Rate Measurements).

Main drying

TLC provides accurate temperature control during the entire sublimation process without temperature probes, making the control of the drying process easy and reliable. Compared with other pressure rise methods, TLC needs only a short measuring time therefore prevents any warming influence on the product and the drying cycle. The end point of the sublimation process can be determined by monitoring the trend of the ice temperature. This makes the TLC method an ideal development tool and provides reliable data for the production process to help optimize the process cycle.

Secondary drying

The desorption rate is determined during secondary drying by measuring the pressure rise over a pre-determined period. The measuring time is longer than during the main drying process but has no impact on the product as only adsorptively-bound water is present. The desorption rate is calculated using the chamber volume of the freeze dryer and the mass of the dry product.

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