Optimising Lyophilisation For Generics

All lyophilisation processes have the same ultimate goal, to provide active and shelf-stable product in as safe and efficient a manner as possible. However each product intended for lyophilisation will have different specific formulation and processing requirements.

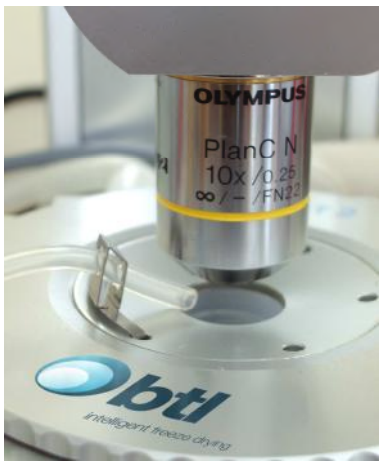
Considerations for generics

The development of products and processes for generic manufacture poses unique challenges. There is no longer the burden of proving efficacy through clinical trials, as with new drug development, but the expectation of lower prices and increased competition cause additional financial pressures. Product and process development must be completed as quickly and efficiently as possible without any resulting loss in efficiency in the final manufacturing processes. Unnecessary delays in development can delay launch to market, while inefficient manufacturing processes will add time and cost to a product in a market where the only differentiators are speed and price. Problems and setbacks must be resolved quickly to avoid losing market share or incurring further costs.

Inefficiencies in Lyophilisation

Across all markets and industries, lyophilisation processes are often developed without sufficient product data. Sometimes the process is copied across from one product to another without any consideration for their different processing requirements; at other times, product, equipment or batch specifications may be changed without understanding how this may affect the performance of the cycle.

However, ignoring the freeze drying stage when conducting process development is always a false economy and product failure may not be immediately visually obvious. Serious issues with product activity, shelf stability and batch consistency and repeatability can go undetected until late in development. Cycles that are too vigorous risk these sorts of problems as well as outright product collapse, but long, overly conservative cycles are an expensive drain on energy and manpower resources. Quality control and regulatory requirements can cause further setbacks, when raw data about the product is not readily available to explain the design of the process.



A Holistic View

Ideally, formulation development should be undertaken with lyophilisation in mind from the start. The choice, quantities and combination of different excipients will define the thermal characteristics of the formulation which will in turn define the processing parameters. Longer processing time reduces turnaround time, therefore reducing throughput. Lower processing temperatures are energy expensive and so formulations should be developed that raise the critical processing temperatures as much as is possible without endangering the active ingredients.

Biopharma Technology Ltd
+44 1962 841092
btl@biopharma.co.uk
www.btl-solutions.net

Empirical Product Data

Thorough product characterisation is always the first step in lyophilisation development. At the very least, collapse temperature (eutectic temperature in crystalline solutions) must be determined. Collapse is a catastrophic process failure which is often visually obvious. However formulations usually contain many components and therefore exhibit complex thermal behaviour. Other events taking place before, during and after freeze drying may be entirely invisible, and yet have serious implications for the product's activity and shelf life. Analyses such as DSC, freeze drying microscopy, and DTA and impedance analysis can be used in combination with sophisticated moisture analyses, such as FMS and Karl Fischer, to build an accurate and detailed thermal profile which will ensure product and process are aligned. They will also indicate where additional processing steps, such as annealing, may be beneficial.

Analysis for Process Optimisation

Even in instances where formulation and cycle are already completed and in use, thorough characterisation can prove invaluable. Seemingly small changes made to process or equipment can impact on the process overall. Analysis of the product and process together with details of batch and equipment specifications will highlight any potential risks and process inefficiencies and changes can be made to eliminate these risks before problems arise.

Any empirical data about the behaviour of the product throughout and after the cycle will also be invaluable for quality control and for any regulatory submissions, as well as saving time later should batch or equipment requirements change.

BTL's Expertise

We provide a complete freeze drying consultancy service from characterisation, formulation and cycle development through to, scale-up, optimisation and small-scale processing. Our freeze drying laboratory is equipped with a range of equipment to enable us to test, design, develop and validate to ensure optimal process conditions. We have significant experience developing and optimising products and processes for a wide range of product types in the pharmaceutical and biotech industries. We regularly collaborate with leading universities on freeze drying to ensure we remain at the cutting edge of this field.

Contact BTL now to discover how we can deliver intelligent freeze drying solutions.

btl@biopharma.co.uk www.btl-solutions.net +44 1962 841092