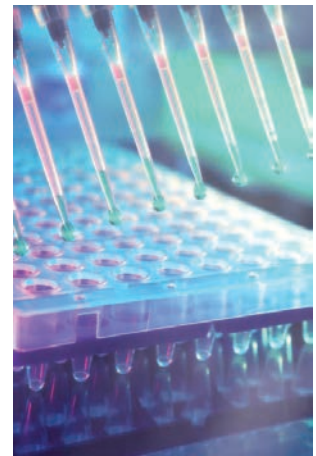


Laboratory Products

A 2020 Hindsight Look at How COVID-19 Has Affected the Freeze Drying Industry and What We Have Learned from It

Dr. Mattia Cassanelli, Biopharma Group

2020 proved to be a challenging year in the field of freeze drying/lyophilisation due to the rapidly shifting timelines required to get products to market. This was especially prevalent across the diagnostic and pharmaceutical sectors. In this article, we will be considering why freeze drying is important, how a limited cold chain affects getting products to climate sensitive regions, far from the source of production, and how outsourcing lyo R&D for tackling the freeze drying process efficiently has played such a fundamental part in successfully getting products to end users safer and faster than ever before.



How Biopharma Group and the Freeze Drying Industry Sought to Overcome Unprecedented Increases In Demand

The process of freeze drying, or lyophilisation, removes the liquid from a substance through sublimation to leave behind a dry product or 'cake' as it is known. This method is used for a wide range of applications including processing of pharmaceuticals, biologics, food, and nutraceuticals. It became apparent early in the pandemic, by the organisations who threw everything into diagnostics and vaccine R&D, that the importance of effective freeze drying methods on a large scale, would be integral to product storage and distribution.

Lyophilisation has been widely used for a range of applications during the COVID-19 pandemic including in the research and



development stage of covid specific vaccines and production of IVD tests (In-Vitro Diagnostic testing). In this instance, the difficulties faced by organisations involved in developing these vital resources, centres around the sheer volume and increased demand for products.

In 2020, we saw a significant increase in the demand for design and manufacturing of products for diagnostic applications, which later evolved in the second half of the year to focus also on the research and development of potential COVID-19 vaccine candidates. Below we examine how we overcame challenges for both diagnostic and pharmaceutical products.

The challenges faced when developing and producing freeze dried materials required for disease testing and vaccination products include:

- High customisation of product formulations that are suitable for required applications
- Design and technology transfer of lyophilisation processes
- High demand for large scale production in a short lead time
- Prolonging the shelf-life and storage capabilities of the products
- Quality retention of reagents and active ingredients in dried state

By working with our development partners to provide innovative solutions for large scale production and distribution in order to overcome the overwhelming production requirements, we found ways to increase capacity and product capability. This includes utilising lyo beads as a method to produce freeze-dried IVD products on a much larger scale. When using smaller freeze dryers for example, it is possible to accurately generate small batches of around 2,000 reaction units in well plates, which by comparison to up to 20,000 units using the lyo beads method - seemed like a 'no-brainer'. The next challenge was ensuring that the integrity of the product itself could be protected and quality maintained.

This involved working with Biopharma Group's research partners to develop optimised formulations which allow the materials to include added cryo and lyo protectants in correct measures followed by appropriate testing to examine the effects that these may have on the products in terms of quality, product activity and stability, reconstitution, storage and shelf life. In addition, lyo beads would also require high-performance mechanical behaviour to cope with the stress generated during handling, dispensing and shipment. This has been possible by using a proprietary technology, the MicroPress, to measure the strength and the elasticity of the dried beads. Finally, we also examined and implemented several standards and customised kitting and packaging solutions to ensure smooth large-scale production of high-quality materials.

In terms of vaccine development and production, Biopharma Group scientists are working with companies on the development of a product formulation suitable for both liquid and freeze dried applications. In the short-term, the global production of vaccines will rely on the liquid format, while in the mid- and long-term, we expect to some extent to utilise freeze drying methods to reduce the need for the cold chain in climate sensitive regions.

The Beneficial Results of Outsourcing Research and Manufacturing to the Freeze Drying Specialists

The unprecedented demand created by the pandemic posed many challenges for those in the medical, academic and pharma industries and it is an historic achievement to have arrived at this point. Ultimately, our work over the past year has contributed to large scale production and delivery of a successful COVID-19 diagnostic programme on a global scale, within a time scale that we would not have thought possible just a few years ago. Outsourcing both R&D projects and production campaigns have been proved to be highly beneficial for companies that consider time to market as a priority.

In addition to 'time is of the essence' tight deadlines, the need for skilled scientists in the freeze drying sector and a dedicated lyo lab has been a driving force in the desire and preference of companies to rely on contract research and manufacturing organisations like Biopharma Group. The research carried out in 2020 helped towards IVDs and vaccine development, but has also contributed advancing other medical applications based on freeze dried monoclonal antibodies and blood products. These advances in freeze drying will undoubtedly be beneficial for organisations that prefer to rely on such expertise for other products and applications. For example, this research is also leading the way for optimising freeze drying processing for other popular products such as bacteria and stem cells, antibiotics, small molecules for oncological use and customised treatments, such as for rare diseases.



Some 2020 major technical challenges that could be overcome by freeze drying specialists have been related to R&D, production, packaging and logistics. For example:

- R&D: Freezing protocol when processing bacteria and cells to retain the cell viability
- R&D: Overcoming 'blow-out' during freeze drying process
- R&D: Molecule degradation due to the freezing and dehydration stresses
- R&D: Limitation the moisture reabsorption by correctly designing the product formulation
- Production: Avoidance of pre-lyophilised product evaporation before the actual freeze drying stage, especially if there is a very little fill volume, which is typical for diagnostic products
- Packaging: Use of inert atmosphere to limit the moisture and oxidation
- Logistics: transportation, storage and cold chain

The risks associated to the above challenges could be limited or even eliminated through an extensive process audit, risk assessment, research and validation of lyo processes.

What Have We Learned and What Future Trends Are We Likely to See in the Freeze-Drying Industry?

In conclusion, outsourcing freeze drying research and development to the experts and tackling the freeze drying process efficiently and dynamically, has played a fundamental part in successfully getting products to end users safer and faster than ever before. Utilising the services of a contract research and manufacturing organisation gives the possibility to benefit from an end-to-end support for entire or partial product campaigns.

The advantages of continuing to develop freeze drying research in these fields, are that it will generate advantages which span across a wide range of industries. We anticipate some future trends for the freeze drying sector and for the advancement of medical treatments will include:

- More work in the field of freeze drying micro-organisms, bacteria and antibodies in the nutraceutical and pharmaceutical industries
- An increase in demand for investigating and developing methods for lyophilisation of human cells and tissues for various medical applications
- Development and progress in diagnostic applications, not just for COVID-19 but for other diseases including cancer.
- Increased diagnostic and pharmaceutical production needs due to the rise of exportation to climate sensitive regions
- Higher demand for projects using lyo bead technology

The last year has been a challenging time for many and much has been learned, so we look to the future and to discovering further optimal solutions to enhance methods used to combat a variety of diseases, including the fight against coronavirus.

To discover more, contact specialists at Biopharma Group today – www.intelligentfreeze drying.com