SPOTLIGHT feature

Sample Preparation & Processing

# Freeze Drying & Spray Drying: the Scalability of Your Process and Suitability for the Pharmaceutical, Diagnostic and Vaccine Industries

Elliot Gibson, Biopharma Group

This article will assess the different processes of freeze drying and spray drying and consider which is the most applicable for particular requirements. Additionally, we will also explore the ease of scalability of these drying processes and the benefits of the end products.

The demand for dried products with a long shelf life is increasing across all sectors. This increased demand is driving practitioners in the industry to consider the benefits of drying technologies such as freeze drying and spray drying.

## Freeze Drying & Spray Drying – what are the key differences in each process?

Freeze drying or lyophilisation, is the drying process which consists of the sublimation of ice crystals into vapour. This process produces frozen samples, the pressure is then decreased and ice is removed by sublimation. Freeze drying is especially popular in the pharmaceutical sector, due to the better API retention and its end product viability, whilst limiting any damage to the product. It avoids degradation of the molecules and can be carried out in various containers such as vials, plastic tubes, trays and well plates; it can also be achieved in different formats such as traditional lyocakes or lyobeads, also known as freeze dryable spheres.

Spray drying can be considered as an alternative or complementary drying process to freeze drying. In the past, spray drying has been perceived as not as effective as freeze drying, however, this is not necessarily the case, and spray drying has become an increasingly popular drying method in recent years. When appropriately and correctly used, it can be as effective as freeze drying, subject to the product or samples the process is being applied to due to the high processing temperatures and shear forces it demands; spray drying is best suited to robust samples. Freeze drying is widely preferred in the pharmaceutical and biotechnology industries, as the process is generally better suited for the more sensitive nature of the products at hand.

Like freeze drying, spray drying is performed on a suitable liquid formulation, which will eventually result in a dried material. Before spray drying, the product must go through the wet process to optimise the yield of the spray drying process. Various techniques such as heating and evaporation of your solution may be used to optimise its viscosity and yield.

These approaches can be used in diagnostics, food, biotech, and pharmaceuticals. In monetary terms, spray drying is a highly desirable option owing to it offering continuous runs and a quicker drying method. It is however, always advisable to conduct comparative studies of both freeze drying and spray drying to help choose the best and most viable or sustainable method for your product or project requirements. Both freeze drying and spray drying can present unique advantages to dry materials while preserving them from degradation.

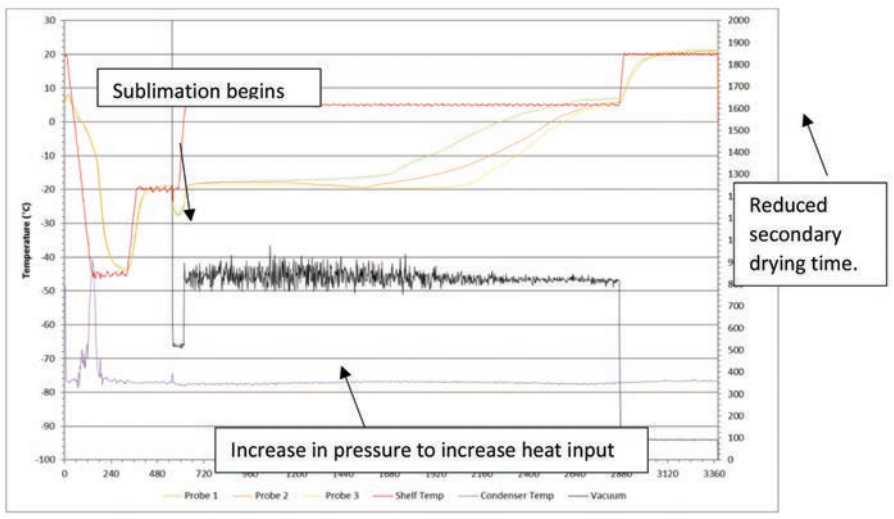
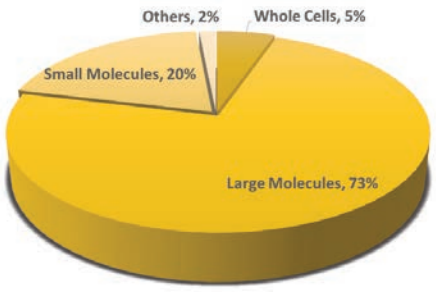



*Figure 1. Freeze Drying Product Drying Cycle.*

The graph above shows an example of a successful freeze drying cycle after developmental work. The following were achieved: shorter cycle length, high collapse temperature, low moisture content and a good overall final appearance.

## Growing demand for product drying services

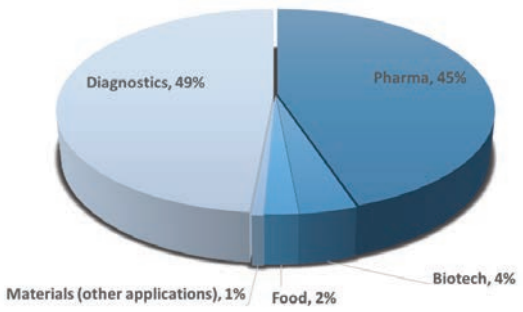
As mentioned, for the freeze drying and spray drying industries there has been a substantial growth in demand across a large variety of sectors. In 2020, the overwhelming growth areas were, unsurprisingly, in diagnostics and pharmaceuticals. In examining the further product segmentation, we saw a huge growth in demand for large molecule related projects with nearly 75% of the sector being dominated by this requirement. Within this sector there was growth in demand for diagnostic products such as PCR particularly and an increase in biotherapeutics and pharma projects related to antibodies, blood products and vaccines.




Trends in 2020:

- +28% increase in large molecule related projects
- Increased demand in diagnostic products, such as PCR
- Increase in biotherapeutics and pharma projects related to antibodies, blood products and vaccines

*Figure 2. Biopharma Group Market trends.*




Trends in 2020:

- Diagnostics +40 projects more than 2019
- Total of +35 projects more than 2019
- +7 manufacturing campaigns (NEW)
- Development and production of lyobeads

*Figure 3. Biopharma Group Market trends graph.*

The growth has been across the whole cycle of these products, with increases being recorded in formulation development, in overall drying services and product manufacturing. This growth in demand across the industry, means that innovation of our manufacturing processes has been necessary to enable increased workflow, efficiency and overall speed of the process. Additionally, with an increase in contract manufacturing requirements, the scalability of product processing and projects has had to stay in line with that growth.

However, with such an unparalleled increase in the demand for and scalability of freeze drying and spray drying services, our science teams ran into specific issues that needed to be resolved accordingly.

## Scalability of Freeze Dry and Spray Dry Processing

When it comes to scaling up your manufacturing requirements for freeze drying and spray drying processes, if your upstream or early development of formulation is complete on the small scale, it can be scaled up and optimised to the next level. There are nevertheless, some key areas that you will need to consider in order to increase the workflow, efficiency and reduce the overall costs of your product/project.

Freeze drying and spray drying share some drying process benefits:

- ***Improving the storage & shelf life of products***
- ***Processing temperatures can be controlled***
- ***Rapid reconstitution for delivery***
- ***The product is always processed to the highest quality***
- ***Being suitable for both small & large companies***

So let's at some of the other areas on an individual process level.

When scaling up your freeze drying manufacturing capability, it is prudent to review and assess whether the use of traditional lyocakes or, the newer 'lyo-process' of lyobeads is best suited for your needs. With this in mind, we have considered, below, some common contributing factors:

### Lyocakes

In order to scale up your process into a full manufacturing cycle, there will be some obstacles that to address. When scaling up, you may see a degradation of reagents and this is a very common issue. The best solution is to first gain a full understanding of the liquid state stability (levels of oxygen, light sensitivity etc.) plus ascertain a definition of the hold time and storage temperature. When you bulk up your manufacturing you will have to have the framework in place to run tests to manage and control your consistency intra- and inter- batch. To increase your workflow, consistency and reduce your run-time per batch, you can potentially introduce automation into your manufacturing process, this can be calibrated robots or dispensing tools, allowing you to increase the stability of your formulation and overall efficiency.

Freeze drying in the form of lyocakes can be beneficial because:

- ***The sample does not need to be heated for the process to work which can be problematic in spray drying***
- ***Freeze drying is a better match for more products, including sensitive samples and those with expensive APIs, than spray drying***

### Lyobeads

The traditional end product in freeze drying is the production of 'lyocakes' in vials. However, within the freeze drying sector there has been a marked shift toward the use of lyobeads, also known as freeze dryable spheres. Lyobeads offer the best possible ratio of volume to surface area, which results in fast reconstitution, reducing run costs and increasing workflow efficiency. Lyobead formats require no aliquoting and no freeze-thaw cycles after reconstitution, which helps reduce batch variation and degradation of your product; a common issue encountered when working with conventional lyocakes. Lyobeads can be produced at a much faster rate than lyocakes too allowing increased manufacturing output. Lyobeads can be very adaptable and flexible with your process or formulation cycle to boost your specific needs. However, even though lyobeads have plenty of positive properties, they are still relatively new to the market, so still need careful consideration prior to any change.

Freeze drying in the form of lyobeads can be beneficial because:

- ***No aliquoting & no freeze-thaw cycle, which speeds up your process***
- ***Faster sublimation***
- ***Faster production rate, which increases workflow***
- ***Reduced running costs***

### Spray Dried Products

Typically, spray drying has not been seen as an alternative to freeze drying due to specific challenges created by the drying process i.e. heat and shear, and was only looked at as an option of drying when freeze drying was not feasible. With shifting trends and demands within the market, we have seen a growth in the demand for products to be processed via spray drying; specifically for products which have powder properties important for functionality or the organic properties of the product.

Spray drying can be more beneficial because:

- ***It is time and cost effective***
- ***It is a continuous process***

Freeze drying, lyobeads production and spray drying can all be scaled up effectively. While developing a roadmap for process development and scale up, different factors must be taken into consideration for scaling up both freeze drying and spray drying, as outlined above. Freeze drying is typically performed with product directly filled into vials and other containers, which means that this scale up is best suited to formulations that do not require further drying processes. Spray drying on the other hand, is often used for products that require encapsulation, or projects that are looking to miss out a milling step to save costs.

| Factors | Lyocakes | Lyobeads | Spray Drying |
|---|---|---|---|
| Formulation of Product | 2 | 1 | 3 |
| Speed of Reconstitution | 3 | 1 | 2 |
| Batch Uniformity | 2 | 1 | 3 |
| Volume of Equipment for Formulation | 1 | 2 | 2 |
| Running Cost of Equipment | 3 | 2 | 1 |
| Scale-up equipment | 1 | 2 | 2 |
| Biologically Sensitive Materials | 2 | 2 | 1 |
| Length of product creation/cycle to packaging | 2 | 1 | 1 |
| Cost of materials | 1 | 2 | 1 |
| Staff costing to run | 3 | 1 | 3 |
| Cost of installation | 3 | 2 | 3 |
| | | | |
| Scale: Best (1) - Worst (3) | | | |

*Figure 4. Comparative Table of each process.*

## Conclusion

In conclusion it is clear that both processes have their benefits, but it all comes down to the needs or your product specifications and the goals you are trying to achieve. At Biopharma Group, with over 30 years in the industry, you can discuss your requirements with an independent team of specialists who can help you with your formulation, perform comparable process studies, scaling up process and any other enquiries around these questions; get in touch today - https://biopharma.co.uk/intelligent-freeze-drying/intelligent-freeze-drying/contact/ or visit www.intelligentfreezedrying.com