



# HOSOKAWA MICRON POWDER SYSTEMS

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## TECHNICAL ARTICLE

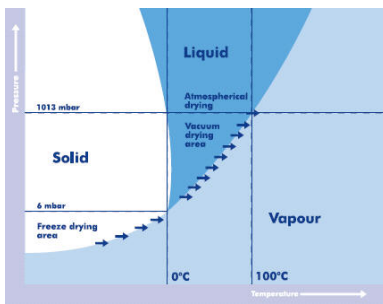
### STIRRED FREEZE DRYING

*A quicker and less labor intensive freeze drying process and the possibility of producing loose and free-flowing powder at low temperatures and low pressures, all in one vessel.*

*Even this short introduction illustrates that the newly developed Stirred Freeze Drying technology can be seen as a big step in the world of freeze drying and powder technology.*

### Freeze drying

Discovered about one hundred years ago freeze-drying (or also called *lyophilization*) has made a tremendous development in the previous century. From a curious lab experiment it has been evolved into a mature production technique for materials which are instable at room temperature when having their natural moisture content. Freeze drying involves the sublimation of a frozen solvent. After freezing the substrate is brought into trays in a chamber and by applying a deep vacuum the solvent is sublimated from the solid state directly into the vapor phase. Typical vacuum levels are between 1 mbar and 0.01 mbar. For example when water is sublimated such deep vacuum levels ensure sublimation temperatures of  $-20^{\circ}\text{C}$  degrees or lower.



By freeze drying a product can be obtained with good shelf stability and which will remain unchanged after reconstitution with the solvent. In other words by the freeze drying process the material to be dried is frozen in its original structure and the solvent is removed from this structure without changing this structure.

A disadvantage of the conventional tray-dryer type of freeze dryer is the lump formation when the material is dried on a larger scale. Despite the optimal structure of the individual product particles, the layer on the plates will usually form one piece of hard baked material. Another disadvantage could be the relative low heat transfer rate due to the quiescent state of the material. Often the product has to be crushed after freeze drying, which may lead to damage of the product structure. All these individual steps in the production process involve labor intensive handling of material in trays, making this unique technology one of the most expensive unit operations in pharmaceutical industries.

### Why a *stirred* freeze dryer?

Early experiments with a conventional vacuum dryer operated at low temperatures and low pressures showed that it is possible to operate a freeze dryer under stirred conditions. The result is a lump-free, free-flowing product. Stirred freeze dryers also exhibit a better heat transfer rate due to the continuous mixing of the product, which shortens the drying process. Finally the freezing step is simplified because all steps can be done in a single processing unit in stead of handling trays filled with product between freezing units, drying chambers and crushers. This results in easy handling of the product especially when compared to the traditional tray dryer equipment.

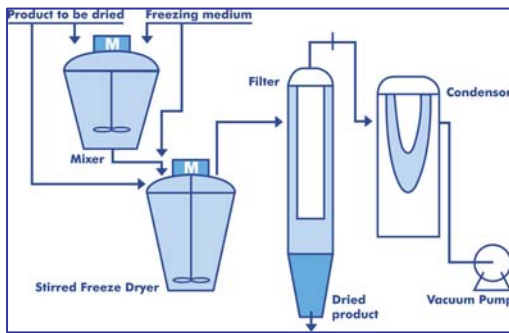
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The positive results of these initial experiments have led to the development of a commercial stirred freeze drying technology. In a dedicated designed stirred drying chamber the material to be dried is frozen. Due to stirring motion the material, being either a liquid, paste or solid, will be transformed into solid granules. The granules can have sizes and shapes which are controlled by the mixing characteristics of the machine. Once the freezing step is completed the drying chamber is closed and vacuum is applied. After evacuation of the freezing agent the sublimation process will start. From this stage the product temperature is dictated by the vacuum level. During

sublimation the heat is supplied through the jacket and efficiently distributed throughout the product by the stirrer. The initially coarse granules will gradually reduce in size due to the sublimation of the connecting ice structure in between the frozen material. The released dried particles will make up a loose powder. Towards the end of the drying process when most of the frozen solvent is sublimated the product temperature will start to rise. Finally the product temperature will equalize the wall temperature, indicating that the drying process is finished. By then all material is transformed into a fine and loose powder,

After breaking the vacuum the dryer can be discharged easily from the dryer vessel, assisted by the transporting characteristics of the mixing element.

## Applications



The main application of stirred freeze drying is found in the pharmaceuticals, e.g. 30% of all antibiotics, 90% of the macromolecules and 50% of the electrolytes are being produced by freeze-drying. Other products typically produced by freeze-drying are: proteins, hormones, viruses, vaccines, bacteria, yeasts, blood serum, liposomes and transplant materials like collagen sponge. Especially the drying of probiotics offers an excellent application of the stirred freeze drying technology. For all these products the

decisive factor to use freeze-drying is the preservation of the product structure, particle size and the minimal temperature load.

Another fast growing market for the application of stirred freeze drying on a larger scale is the materials business, in particular for nano-materials. By using stirred freeze drying for these wet base processed materials special advantages are obtained. The suspended particles remain separated during the freezing as well as the drying process. During the progress in sublimation single particles will become separated, but the continuous mixing of the material will induce the formation of weak agglomerates. The final product will consist of loosely bound single particles forming a fine cohesive powder.

## From lab-scale to bulk quantities

With the introduction of the stirred freeze drying technology a new type of production technology has been made available. Stirred freeze dryer batch volumes can range from a few liters for lab-scale and small scale production

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applications to bulk drying of a several cubic meters. In all sizes the advantages are obvious: rapid drying, simple product handling and an unique product quality.

For more information about the Freeze Drying Technology:

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