Freeze-drying or lyophilisation is the latest technique of dehydration for a long-time preservation of enzymes, bacteria and other biotechnological products. The product being dehydrated is subject to preliminary freezing and then processed at pressure lower than 1 mbar. The water contained in the product and transformed into ice is sublimated and removed from the condenser. This process is also known as “dehydration by sublimation” or “cryo-drying”.

Freeze-drying has the following advantages with respect to conventional dehydration techniques:

• Better preservation of the distinctive properties of the product;
• Possibility of instant re-hydration
• Total recovery of consistency, taste, flavor and color of the product

Freeze-Drying Technique
Speaking about the freeze drying technology, we need to examine a few technical points related to:
• Freezing
• Drying
• Preservation

Freezing
The process depends on the following two parameters:
a) Freezing speed
b) Lowest temperature achieved
The freezing speed is most important to the final result of the process.
There is plenty of literature on physical and chemical phenomena involved with it; however, a precise knowledge of this phenomenon has just a merely theoretical value: unsatisfactory results in freeze-drying can actually be corrected through suitable “adjustments” during the freezing phase.
On its course, the freezing process first concerns part of the water crystals entrapped in the fibers or in the liquid being treated.
Large crystal of ice can visibly develop at freezing speed of 1°C per minute.
On the contrary, if the freezing speed is much higher (10 to 50 °C per minute) the ice crystals cannot be seen even at the microscope under normal light conditions.
Let us examine the influence of the formation of ice crystals on freeze-dried product:
• The ice crystals may have a destructive effect on the cell lining
• Separation of ice crystals may alter the concentration of salts.

Drying
Drying consists of two stages:
• Main drying
• Final drying
The first stage lasts until a frozen area still remains, i.e. until there is ice in the product still to melt in water.
The second stage eliminates intra-molecular linking water.
During the main drying stage, the product can have mixed areas with and without ice.
The areas containing ice mainly have water crystals, salts and proteins which in turn contain intra-molecular-linked water.
This area can melt if the work temperatures are high, thus affecting the freeze-drying process.
In fact, the pores of the already dried layer may be obstructed by the liquid material this causing the reduction of the amount of evaporation.
This automatically starts the “circle” consisting in the termination of the sublimation under-cooling which produces the final defrost of the ice core and the formation of foam in the product being dried.
In spite of the so many studies carried out, it is still unknown what should be the quantity of liquid in the dried product to get the best out of the lyophilisation process and what are the factors determining this phenomenon.
However, generally the temperature admitted for the ice core can vary from -10 °C to –60 °C and that such temperature can only empirically be determined.
The concept of “admitted ice core temperature” is in any case most important to control of the lyophilisation process. Of course during sublimation internal areas will still have ice while the outer part is already dried.
Such area contains only the absorbed water and the intra-molecular water.
The resistance of freeze-dried proteins to high temperatures, which was considered rather surprising when first announced years ago, has since been proved by...
many experiments. Likewise, some freeze-dried bacteria are extremely resistant to temperature.

**Aggregation of water according to pressure and temperature**

Under the theoretical work conditions the relation between the ice temperature and the steam tension is easy. In the practice, during the freeze-drying process, the steam is continuously sucked and the already dried layer of product stops the exit of the steam. Therefore, it will be more difficult to determine the relation between the temperature of the area containing ice and the partial pressure of steam. As to the speed of the freeze-drying process, the principle is that the higher is the temperature of the ice core, the higher is the pressure of steam coming from the product. Also the higher is the pressure fall towards the condenser, the faster will be drying. This means that the volume of 1g of steam sill be lower. As a consequence, the ideal temperature of the ice core should be as high as possible. The knowledge of the ice core temperature admitted for individual items being freeze-dried is therefore most important to determine the freeze-drying speed. If this value is unknown, it is recommended to carry out the process slowly and at low temperature, so as to ensure a good final result. The factors acting on the temperature of the ice core in freeze-drying are:

- Adduction of heat from external sources
- Energy absorption during outcome of water from the product being treated.

**Preservation**

The main factors which can affect preservability of the products are the contents of oxygen on the dried material and the contents of humidity in the dry product. Packing under vacuum or under inert gas atmosphere is in all cases recommended. As to the influence of high residual humidity on preservability, researches meant to establish the exact limits of tolerance showed that only in few products residual humidity can substantially exceed 1/2 % approx. With regard to variations in the enzymatic and microbic contents during
preservation, it is generally assumed that microbic proliferation as well as metabolic activities may be neglected: bacteria proliferation actually begins when humidity is much higher than observed under the most unfavorable conditions of preservation of freeze-dried products. Finally, enzymatic reactions may take place only if free moving water is available.

**Conclusion**
Each Lyophilized products is different and clearly our article is indicative. This technology currently meets a second life because the global market requests flexibility and availability of the different products everywhere and most of the time far away from the production site. This technology is still seen as the best way to transport sensible products that will be recombined, it guarantees the final quality in every condition.