Indeed, as we have shown in Figures 1 and 2, freeze-drying deserves an accurate and continuous control of the pressure in the chamber during the whole operation.

With the exception of vacuum freezing (or "snap"-freezing generally used in the food industry), the *initial cooling* is always done at atmospheric pressure, sometimes in a separate cabinet.

Primary drying, to the contrary, is performed under vacuum. Whereas in the young days of the technique it was felt by most specialists that the higher the vacuum the better the process could be. It was shown by Neumann and Oetjen et al. that throttling the water vapor flow between the chamber and the condenser was increasing the speed and efficiency of the operations. Later on, Rieutord and I patented the air injection process, which could be applied to any equipment whether the condenser coils were placed in a separate chamber or in the drying cabinet itself. Since then, the "air bleed" has been used almost universally since a substantial rise in the pressure (0.1–0.5 mbar according to the T_{im} of the treated product) proved to increase considerably the heat transfer to the sublimation interface essentially by gas conduction-convection. As a consequence, the temperature of the heaters could be substantially reduced, which prevented melting of the still-frozen core and/or scorching of the already existing dry layer. Monitoring and control of this pressure is still an essential part of the process, and they can be geared to the intrinsic properties of the product such as its temperature or, better, its electric impedance. At any rate, during this whole sublimation period, the vacuum level is the master key to the heat transfer and can help to "rescue" a product that is becoming too hot and starting to soften dangerously. Indeed, in such a situation, pulling the vacuum down immediately works as a real thermal switch with an instantaneous result, whereas cooling the shelves requires a longer time.

Secondary drying is generally carried out under higher vacuum when the product has reached an above-zero temperature (or its electric impedance has reached the upper limit). Indeed, it has been shown by different authors that isothermal desorption was *faster* and allowed *lower final residual moistures* when the pressure lay in the level of 10^{-2} mbar but that higher vacuums (10^{-3} mbar) did not drastically improve the operation.

Final conditioning has always been much discussed and, in the last decades, vacuum and dry neutral gas both got their supporters. Today, stoppering the vials under a slightly reduced pressure of dry nitrogen gas looks to be the favorite option. Some experiments that we did in the past and that remained unpublished push us to think that stoppering under dry argon could give better results for long-term storage, as is the case, for instance, for international biological standards.

SOME CHALLENGING WAYS TO INVESTIGATE THE FINAL DRY PRODUCT

The dry freeze-dried cake undoubtedly has a very peculiar structure since, as we have already seen before, it has been "carved" under vacuum from a solid matrix (Fig. 3). At the end of this process and when it is still under vacuum its internal surface is quite "clean" and very reactive. It can be easily understood that its first contact with a foreign element, such as the gas used to rupture the vacuum, is determinant. This is, in fact, why the choice of this gas as well as the