bulking agents have to be added to "build" that structure if the initial solution is too diluted. Lactose, sucrose, mannitol, PVP, dextrose, methyl cellulose, glycine, and many others have been used to fulfill this task.

New Carriers

In some cases, however, the introduction into the formulation of these "foreign compounds" might be undesirable and, ideally, it would be by far better to do without them and handle the active substance alone. An interesting option might then be to enclose the liquid to be dried into a porous matrix where it will be kept in the course of drying and thus prevented to fly away with the water vapor stream. Porous polymers, sintered metals, ceramics, porous glass, inorganic textiles, multilamellar pads, even small silica or glass beads, etc., could, at first glance, be resorted provided they demonstrate simultaneously a certain number of properties.

- They can adsorb the liquid solution easily as a hydrophilic material and withstand freezing and drying without mechanical rupture.
- They do not interact with any element of the formulation.
- They are clean and deprived of residues, particles, or contaminants.
- They hold enough liquid per unit volume, which means that they present at least a 30% to 50% porosity.
- They can be shaped as well-defined geometrical units: disks, rods, and spheres to be incorporated into the vial.
- Their pore structure is thin enough to hold the solution but wide enough to let the water vapor escape from the frozen liquid, which means an open-pore structure, a "sponge" with interconnecting interstitial channels.
- They release the adsorbed active product when they are flooded with the reconstitution fluid.

To our own experience, fulfilling these requirements is not an easy task and, actually, very few products are susceptible to provide this complete set of properties. While most of the structural issues can be solved, the most difficult, by far, remains the latter one: The "carrier" should release the totality or at least a major known amount of the active substance at the time of reconstitution. To that end, developments have been made to "exhaust" the carrier by percolating through it the dissolution fluid under pressure, as would be done with a conventional online filter. Special syringes have been manufactured where the original solution to be dried is pumped through the carrier, then allowed to dry there, and finally extracted by the reconstitution fluid using the same type of mechanism.

Today, the inert carrier issue is still under development, and it is more than likely that the enormous amount of research, which is currently devoted to new materials, whether glass and glass derivatives, polymers, fibers, etc., might help us to find new supports with almost nil adsorption properties and still an open porous structure.

OPERATING PRESSURE

Numerous books and papers have been written on the physics of primary and secondary drying. However, we would like to stress one single point that has not always been clearly understood—the central role of the operating pressure.