surface of an uncoated stopper. Fluoropolymer-coated stoppers are more slippery, and, all other things such as the vial remaining the same, are more sensitive to displacement in halfway down position and also are more seen to more easily lead to rising of stoppers after full stopper insertion and before capping. This in turn can lead to a transient CCI failure that ends when the stoppered vial is crimped, but in the meantime may have led to effects on the composition of the vial headspace and potentially to lack of sterility assurance. Altogether, the behavior of the stopper/vial combination in transport phases right after filling, during loading and unloading of the freeze-drier, and between unloading and vial crimping shall be closely observed.

Vials

In the area of lyophilization vials, a lot of attention has been paid in research and literature to the role of the vial in mass and heat transfer and its impact on sublimation rates, e.g., [1] and [15] and the references cited there. Noteworthy is that some new types of vials are offered to the market that specifically target a use as lyophilization vial. An example of such a vial is a tubular vial that is subjected to a plasma impulse chemical vapor deposition (PICVD) process [16]. In this process, a transparent Si-O-C-H layer is deposited on the inside of the vial. The coating has a hydrophobic character. Claimed advantages are better cake appearance and prevention of cake collapse, as well as a better emptying of the vial leaving less residue of the reconstituted product, opening the way for reduced overfill. The vial bottom geometry is claimed to be optimized allowing reductions in freeze-dry process times. A second example is a reduced weight molded vial that thanks to its flat bottom is equally claimed to have an optimized heat transfer and a better cake appearance. A comparison of both vial types with a polymer molded vial in cyclic olefin copolymer (COC) is presented in [18]. Through sublimation tests with pure water at varying low pressures, it was shown that the above-cited molded vials have a very similar performance in comparison with the PICVD-coated tubular vials. Both vials clearly outperformed the polymer vials that were used in the study.

Secondary Packaging Components: “Integrated Rubber/Plastic Caps”

In the elastomeric closures section of this chapter, it was pointed out that the closure/vial seal area is not in the same location before and after crimping of the vial with an aluminum cap. Before crimping of the cap, the seal area is between the plug of the stopper and the “vertical” portion of the inside of the vial neck. After crimping, the seal area relocates to the position between the underside of the flange of the stopper and the “horizontal” rim of the vial neck. After lyophilization, vials thus leave the freeze-dryer with a seal between vial and stopper that lacks robustness.