independent of the inside radius, the effects of a sharp outside radius are essentially the same. It is important to have the optimal radii that will lead to minimization of stress in the glass, yet lead to a reduction in the resistance to heat transfer. The optimal rounded diameter will help to absorb and alleviate the stress buildup that occurs during the lyophilization cycle.

Amount of Fill in the Container

The amount of internal pressure generated during the lyophilization cycle is directly related to the amount of fill in the vial. Fill levels of product up to a maximum of 35% of the vial's capacity are generally recommended as these proportions seem to create the fewest processing problems.

Plastic Vial Systems

Because of the introduction of cyclic olefin polymers (COP) and copolymers (COC), these types of materials are now being evaluated in various applications especially for biopharmaceutical and biological applications. These materials combine the inherent break-resistant nature of plastic with the clarity and inert surface that is beneficial to sensitive biopharmaceutical applications.

In addition to the benefits mentioned above, the use of a COC or COP vial brings the additional benefits of lower extractables resulting in a lower likelihood of leachables in the drug product. Glass contains free alkali oxides and traces of metals. At higher pH conditions glass can undergo delamination, as discussed earlier within this chapter. All of these things can lead to a negative impact on the stability of the drug product.

Cyclic olefin–based plastic vials have been studied for packaging lyophilized products. It has been found that lyophilization in some of these materials has led to more uniformity within the freeze-dried cake (3).

The major weakness of these materials is that, even though they have decreased moisture vapor transition rates versus other plastics, they still are not equal to glass from a moisture barrier standpoint. It would always be recommended that a secondary packaging barrier, such as an aluminum pouch, be used to assure adequate shelf life.

LEACHING AND DISSOLUTION OF GLASS

Several studies of glass vials have identified the potential of the glass to react in different ways with liquid products stored in the vials over time. Dissolution or leaching reaction between the liquid and the glass is very probable and is dependent on various specifics of the drug product and its processing in the vial. For instance, basic or high pH products can lead to dissolution of the glass surface.

The lyophilization process minimizes the potential for interactions between the glass and the drug product. In some circumstances, a pharmaceutical manufacturer may decide that lyophilization is the best alternative for extended product shelf life because a compatible glass container for the liquid product cannot be found. An example of this may be a strongly alkaline solution. For this reason, this chapter will briefly explain the concepts of leaching and dissolution as they relate to the glass vial; there will be more focus on the potential of the rubber closures to have extractables that may leach into the lyophilized drug product since this process is more likely to occur.