



- Increased cylinder spacing
- Best glass-to-metal contact
- Increased uniformity across load

FIGURE 15 Sleeve/post cassette loading configuration.

configurations. The posts on which the cylinders rest are located within the holes (sleeves) cut into a stainless steel or aluminum block. Cartridges are loaded into the holes that are in contact with both the sleeves as well as the support post. This provides stability during loading and unloading as well as improved homogeneity. Sleeve-and-post loading systems provide improved heat transfer characteristics over the other systems discussed due to greater heat transfer contact surface area between the syringe cylinder walls and the surface of the sleeve and post. Sleeve-and-post systems provide spacing between cylinders so that cylinders are not tightly packed against one another. This significantly increases the homogeneity within the batch.

Proper characterization of the drug product and an understanding of the fundamental stages of lyophilization are critical for the development of a suitable freeze-dry cycle for any product. DCS systems introduce a variety of unique considerations that can challenge even a veteran of lyophilization process development. Poor heat transfer due to low shelf-to-package contact surface area as well as distance between the shelf and the drug product are just a few significant factors influencing the drying of material in dual chamber packaging. The loading configuration is critical to the development of the process and should be identified and implemented in development studies as early as possible.

SCALE-UP AND OPTIMIZATION

Process scale-up and optimization are challenges for any lyophilization cycle design since numerous factors discussed previously can have a significant and sometimes difficult to predict impact on technology transfer between freeze-dry units. Cycle scale-up for dual chamber package systems can be particularly problematic since the impact of the contrasts between vials and syringes can vary significantly and unpredictably between small and large-scale lyophilizers. One should not expect laboratory or even pilot-scale cycle data to transfer well to commercial scale lyophilizers. Therefore, it is often necessary to move to large-scale development studies much earlier in the development process for dual chamber products than for traditional vial products. Typically a significant