



Fig. 3 Expanded view of time–temperature profile of a typical lyophilization cycle. Product temperatures from vials located at various places were monitored. Nonuniformity of product temperature in large lyophilizer is evident

seen from the expanded view in the Fig. 3. During scale-up and transfers of the lyophilization cycles, considerations must be given to the slowest drying vials and cycles should be designed to ensure completion of primary drying step of these slow drying vials before moving on to the next stage of secondary drying where the shelf temperatures are sharply raised.

5. Effect of stopper vent type and size during transfer of lyophilized products

Many a times, it becomes necessary to transfer an existing lyophilization cycle using a different kind of stopper—in type or in the number of vents due to many operational reasons. It becomes a question, if the existing cycle will have to be changed due to such change. A recent paper has described the effect of vent size on the drying rates during lyophilization [17]. Using precisely governed vent area, the authors concluded that as the water vapor transfer across the vents diminishes as the vent area is decreased and the drying rate profile follows choked and non-choked regimes. They further showed that as long as the vent areas were greater than the critical mass transfer restriction threshold, there should not be any difference in the overall drying behavior, and substitution of stoppers within the range should yield similar drying cycles. In very aggressive cycles, where the water vapor flux across the stopper vent is very high, then the dimension of the vent may become rate limiting and impede mass transfer. This may result in accumulation of water vapor inside the vial and become choked flow across the vent resulting in rise in the product temperature and adverse effect on the cake quality.

6. Effect of load size on the duration of the lyophilization cycle

It is often asked if the total duration of a cycle depends upon the load size in the chamber or if the cycle will be longer for a fully loaded chamber than a partially