Lyophilization of Sterile Solution in Vials

Lyophilization process consists of three major stages: freezing (may involve additional annealing step), primary drying, and secondary drying, each of which must be completed before proceeding to subsequent stage for a successful cycle. Also, different mechanical and control systems of the lyophilizer equipment must maintain the process conditions within established limits to produce uniform dryness and quality for the complete batch [10–17].

Some specific considerations in lyophilization scale-up and transfer include:

1. Differences in lyophilizer units
2. Differences in cycle profiles from small to large lyophilizers
3. Determination of the end of various cycle stages at commercial scale
4. Consideration of nonuniformity of rate of drying in the chamber
5. Effect of stopper vent type and size during transfer of lyophilized products
6. Effect of load size on the duration of the lyophilization cycle

1. Differences in lyophilizer units

It is important to note that no two lyophilizer units are identical. There do exist some differences in supposedly identical units such as design, architecture, hardware, and controls, which may result into differences in the drying cycles. Table 1 shows the overview of some relevant technical characteristics of the lyophilizers. The list includes only those equipment parameters that are generally regarded as having the greatest influence on the course of a lyophilization cycle. It should be noted that the parameters that are most critical in maintaining a desired lyophilization profile are the shelf temperature, the condenser temperature, the chamber pressure, and the duration of various stages as well as the control/monitoring systems. As seen from this table, all of the critical hardware and the process control/monitor mechanisms between two units (transferring and receiving lyophilizer units) must be comparable. If such similarity exists, then it is fairly safe to assume that the independent programmable cycle parameters (shelf temperature, chamber pressure, and duration of various steps) will be executed identically in these units and the resultant lyophilization cycles will be equivalent as long as the process conditions do not overburden the system capabilities.

2. Differences in cycle profiles from small to large lyophilizers

Often, the lyophilization cycles are developed in R&D setup where the size of the lyophilizer unit is very small (shelf area of 2–10 sq. ft.). Additionally, these units are not insulated adequately and are located in a general laboratory environment. These conditions result in unintentional heat supply from the surrounding environment to the frozen cakes undergoing sublimation phase inside the relatively small chamber and the dynamics of drying becomes skewed. The drying vials receive heat not only from the shelf of the unit at the bottom surface of the vial but also additional heat from the door as well as walls of the chamber by radiation. In such case, the cycles are usually shorter than calculated or anticipated. If such cycle parameters are trans-