Lyophilization in a Vial

Vial Heat Transfer Coefficient, K_v

A good understanding of heat transfer during primary drying allows for greater efficiency in process development and minimizes problems encountered during scale-up process [35]. The product temperature during primary drying is directly related to the heat transfer from the heat source (normally, the shelf) to the product itself.

Heat transfer may be defined as the ratio between the area-normalized heat flow and the temperature difference between heat source and heat sink [35]. The vial heat transfer coefficient, K_v, is defined by the following equation for a vial in direct contact with the shelf:

$$\frac{dQ}{dt} = A_v \cdot K_v \left(T_{shelf} - T_{product}\right), \tag{1}$$

where A_v is the external cross-sectional area of the vial, dQ/dt is the heat flow from the shelves to the product in a given vial, T_{shelf} is the temperature of the shelf surface and $T_{product}$ is the temperature of the product at the bottom center of the vial.

The vial heat transfer coefficient (K_v) consists of three mechanisms: (1) heat transfer due to direct conduction (K_c) between the contact points at the vial bottom and shelf surface; (2) radiation heat transfer (K_r) to the bottom, top, and sides of the vial; and (3) heat transfer due to gas conduction (K_g) in the space between the vial bottom and shelf surface. Therefore, the vial heat transfer coefficient (K_v) may be expressed as:

$$K_v = K_c + K_r + K_g. \tag{2}$$

The gas conduction term, K_g, is dependent on the pressure within the chamber during sublimation. This heat transfer is achieved by energy exchange during direct collisions of gas (i.e., H_2O) between vial bottom and shelf surface, and this is conduction through the dilute gas. It has been reported that the dominant mechanism for heat transfer for a center vial during primary drying is gas conduction [12]. The gas conduction mechanism has been expressed as a function of pressure [39]:

$$K_g = \frac{\alpha \cdot \Lambda_0 \cdot P}{1 + l_v(\alpha \cdot \Lambda_0 / \lambda_0)P}, \tag{3}$$

where Λ_0 is the free molecular heat conductivity of the gas at 0 °C, λ_0 is the heat conductivity of the gas at ambient pressure, P is the gas pressure, l_v is the constant "effective" distance characterizing the gap between the shelf and the vial bottom, and α is a term related to the energy accommodation coefficient (a_c) and the absolute temperature, T.