There are other phenomena that will limit the maximum possible sublimation rate. At very high sublimation rates (irrespective of pressure) one should be concerned about limitations imposed by

- available heating capacity for shelf heat transfer fluid,
- the heat transfer coefficient from the shelf heat transfer fluid to the top of each shelf,
- available condenser coil (or plate) surface area,[a]
- the heat transfer coefficients within the condenser coils, and
- available cooling capacity for the condenser coils.

Regardless of the nature or cause of a given limitation, one should test lyophilizers to determine their maximum drying rate capability over the range of expected operating pressures.

MEASURING FREEZE-DRYER DRYING RATE CAPABILITIES

A freeze-dryer is first and foremost a dryer. Its principal function is to move water out of the product and onto the coils of its condenser. The rate at which the freeze-dryer can do this should be measured periodically. For modern freeze-dryers with separate product and condenser chambers, the maximum drying rate that the dryer can support increases substantially with chamber pressure. This section outlines procedures for measuring the maximum possible drying rate over a range of chamber pressures.

Freeze-dryer drying rate capability studies are often referred to as "ice slab sublimation studies" because they use slabs of ice on the trays instead of product-filled vials or trays. The ice slabs are easily formed by freezing 2.5-cm depth of water on each shelf, held in place by shelf border rings into which plastic film has been installed. One note of caution—do not attempt to reuse ice slabs or use a given set of them for more than about six hours of sublimation because after that period of time the ice tends to lose contact with the top of the plastic film, having "burned off" those areas first. In addition, each freeze-dryer must be tested separately. Even nominally identical dryers may have differences that can only be detected by these tests.

The tests are conducted in two parts. In part A, a characteristic data trend of chamber pressure versus shelf fluid inlet temperature is generated. These data are used to decide shelf fluid inlet temperatures to use for separate subsequent executions of part B in which the (maximum supportable) drying rate is measured for each selected chamber pressure.

The rationale behind the conduct of part A bears some explanation. Figure 2 shows data from three separate experiments in the same laboratory-scale freeze-dryer. After the water was frozen on the shelves, vacuum was pulled and the shelf fluid inlet temperature was increased at 0.5°C/min. This figure shows the resulting trend of chamber pressure for three cases: chamber pressure set to 0, 100, and 200 mTorr (0, 13.3, and 26.6 Pa).

For the latter two cases, at a point during the ramp, the chamber pressure began to climb above set point. This is because at that point, the rate of ice

[a]A rule of thumb is that the condenser coil area should be greater than the shelf area used for product, but the effect of condenser coil surface area on condenser performance has yet to be explored and published.