on the design space. Figure 1B shows a dashed black line over the −25°C curve to illustrate that boundary for a product that would have that as the maximum allowable temperature during primary drying. The case study below (and other chapters of this book) covers how to determine this temperature.

One would assume that the freeze-dryer itself has inherent limitations in the product drying rate that it can support. However, it was only recently discovered that the maximum drying rate that a given dryer could support is strongly influenced by the chamber pressure (6). The phenomenon responsible, choked flow, is explained in the next section. Briefly, exceeding the maximum allowable drying rate causes the chamber pressure and thereby product temperature to increase. Choked flow represents a second boundary on the design space depicted in Figure 1B as a bold black line.

The area within these boundaries constitutes a "safe zone" (Fig. 1B) within which the freeze-dryer will be able to support the product drying rate, and the product will remain below its collapse temperature. Note that the safe zone becomes more constrained as one moves toward higher drying rates. Therefore, one must be fully aware of appropriate boundaries within the design space to achieve both objectives of producing quality product while remaining within capabilities of the equipment.

CHOKED FLOW

It has recently been recognized that, given the design and operating conditions of pharmaceutical freeze-dryers, the water vapor velocity within them could be reaching the speed of sound (6). This is important because the flow of water vapor between the chamber and condenser can become "choked" if the water vapor reaches the speed of sound at any point between them. Choking can lead to the chamber pressure climbing above its set point (6).

The speed of sound is known as "sonic" velocity, and depends on the medium (e.g., water, air, water vapor) and is weakly dependent on temperature and molecular mass. For ideal gasses the speed of sound is

$$V_s = \sqrt{\frac{\gamma RT}{M}} \tag{1}$$

where γ is the ratio of specific heats (C_P/C_V) for the gas (1.3 for water vapor), R is the ideal gas constant, T is absolute temperature, and M is the molecular weight. Note that it is independent of pressure. The speed of sound of water vapor at 0°C is about 400 m/sec. One is in danger of choking the duct between the shelf chamber and condenser chamber if the velocity approaches this value in the duct between the two chambers (6). The limitation is on the gas velocity and not the mass flow of gas. At twice the chamber pressure, the same velocity of water vapor through the duct translates to twice the mass flow rate. Therefore for choked flow, higher chamber pressures also mean higher "carrying capacity" of water vapor.

There are two things one can do to prevent choked flow in freeze-dryers. One is to reduce the drying rate by reducing the shelf fluid inlet temperature, and the other is to operate at a similar (or even higher) drying rate, but at a higher chamber pressure where choking will occur at a higher mass flow rate of water vapor.