Characterization of Nitrogen Flow in Lab-Scale Lyophilizers and Its Impact on Primary Drying

Collaboration with AbbVie

A series of experiments were carried out in partnership with AbbVie to investigate the role of the inert ballast gas on process and condenser chamber pressures during lyophilization. The study began by comparing chamber pressure throughout the cycle both with and without nitrogen ballast. In the latter case, the nitrogen ballast control valve was disconnected from the system, removing the lyophilizer's ability to regulate pressure. A second capacitance manometer was installed on the condenser chamber for both experiments to monitor the pressure drop across the duct. A comparison of the experiments is shown in Figure 1.

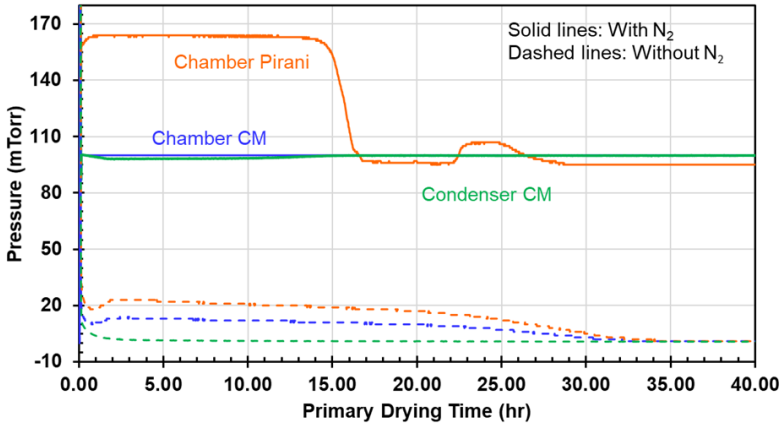

Figure 1: Comparison of process and condenser chamber pressures with and without inert nitrogen ballast.

The absence of nitrogen led to large (~10x) deviations from the pressure setpoint and increased the primary drying time by a factor of two, confirming the accepted view that the inert ballast is critical for both maintaining the chamber pressure and regulating heat flow into the vial. The reduction in base pressure also led to an increase in the pressure difference between the process and condenser chambers. This behavior is attributed to the reduction in Reynolds number, a nondimensional parameter representing the ratio of inertial and viscous forces acting on a fluid element, at lower base pressures and flow rates. The experimental study also explored the pumping dynamics of nitrogen and water vapor. The reduction in pressure drop across the duct following primary drying suggests the ballast flow rate needed to sustain the target chamber pressure is lower than water vapor. In this case, the flow of nitrogen is primarily dictated by the vacuum pump and foreline characteristics.

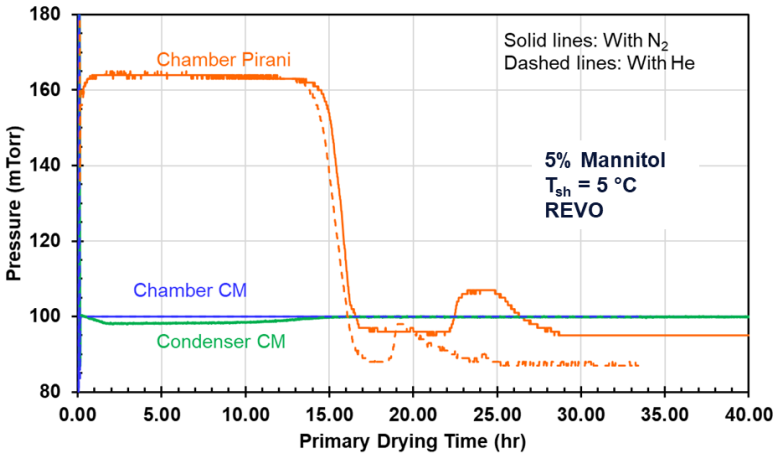

Figure 2: Comparison of drying performance using nitrogen and helium ballast.

Finally, the influence of inert ballast on drying performance was investigated. A comparison between nitrogen and helium is shown in Figure 2. Helium was chosen as a contrast species due to its high thermal conductivity and low molecular mass (large mean free path) relative to nitrogen. The data suggest that the primary drying and Pirani convergence rates are relatively insensitive

to the gas composition. Instead, the role of the ballast appears to be the regulation of back pressure, and ultimately, the partial pressure of water vapor in the vicinity of the vial pack.