TABLE 1 Heat Transfer Path and Mechanisms

From	To	Mechanism(s)
Bulk heat transfer fluid	Inner shelf surfaces	Convection (highly subject to the fluid type, shelf thickness, flow patterns, flow rate, temperature, viscosity), and conduction via the heat transfer fluid
Inner shelf surface	Outer shelf surface	Conduction
Outer shelf surface	Lower film surface	Gas-phase conduction (pressure dependent) and radiation
Upper film surface	Ice interface	Conduction through ice

surfaces by convection and conduction via the heat transfer fluid. Convection is extremely difficult to characterize analytically unless the flow paths are simple and fluid properties are well defined (and in the present case they are not well defined). Furthermore, the fluid properties are heavily dependent on temperature, which will vary widely over the course of sublimation tests. One may even encounter a turbulent to laminar flow transition in the heat transfer fluid as temperature is reduced, resulting in a step change in heat transfer properties. Heat transfer through the thickness of the shelf plate itself will be by pure conduction.

The case study below includes calculation of heat transfer coefficients from ice slab studies.

CASE STUDY

This case study covers the investigation and resolution of a projected capacity shortfall of freeze-dryer capacity for a particular product across 12 production freeze-dryers across three facilities on two continents. One of the facilities was in start-up mode with their three units.

Freeze-Dryer Time Analysis

The freeze-drying cycles run for this single product accounted for 58% of all freeze-drying time. The next largest block of time was spent on turnaround. A full 84% of this product's freeze-drying cycle was taken up with primary drying. In addition, in one facility there was significantly greater variability in primary drying time from batch-to-batch than in the other. This was later resolved by harmonizing thermocouple placement techniques and procedures for assessing the end of the step. Savings from this alone was estimated at $3.9 M/yr. Because almost half of all freeze-dryer time was being spent on primary drying for this single product, it became the focus of continued investigations described below.

Product Quality Attributes

The collapse temperature during primary drying is a critical parameter that must be firmly established. It is well-known that for a given formulation, the thermal history prior to primary drying can have dramatic impacts on how it behaves during primary drying. The product under consideration has a significant mannitol content in its formulation, so freezing and annealing studies were carried out to determine how these steps should be carried out across all of the freeze-dryers. A key result was that an annealing step was added to the process to ensure consistent, complete crystallization of the mannitol prior to initiating