Table 5 Impact of lyophilization cabinet loading process on product rejection rates

Shelves in cabinet	Collapsed loading rejection rate (%)	Expanded loading rejection rate (%)
1–4	Not utilized	Not utilized
5–6	20.0	0.2
7–8	13.2	0.4
9–11	0.3	0.2
12–13	0.3	0.4
14–15	0.2	0.3
16–18	–	0.2

process and transition to new cabinet expansion with the manufacturing setting, a new method of loading the shelves where the majority of the shelves were collapsed during loading and shelves were indexed up during loading. This resulted in an increased product collapse on the top shelves of the cabinet and unacceptable rejects (Table 5). Through root cause investigations in the manufacturing facility, it was determined that the main cause was associated with unwanted annealing during loading. This annealing step resulted in ice structure changes as well as amorphous/crystalline state and ultimately leading to product collapse. Remediation of the cake appearance impact was to discontinue the use of the top few shelves of the cabinet, thereby causing underutilization of the full cabinet for long-term production.

This study clearly demonstrates the necessity to understand the process transfer between cabinets and ensure the formulation and process scientist understands the impact of annealing on product quality. It is highly recommended that proper temperature mapping studies and the corresponding correlation between the equipment and the facilities is documented to ensure proper technology transfer can occur in an efficient manner.

Case Study 2: Equipment and Facility Design Considerations

The freeze-dryer equipment design, facility, and their operation protocol (e.g., single shift vs. continuous operation, bottomless vs. perforated trays, etc.) must all be considered to achieve success during transfer and scale-up process. An illustrative example characterizing equipment and operational considerations is presented below in Table 6.

Choke flow measurements were quantified between the two industrial dryers. For example, the choke flow measurement in the industrial dryer using ice sublimation study revealed a value (1 kg h^{-1} m^{-2} at the target cycle pressure) much greater than the value obtained for pilot scale lyophilizer (0.34 kg h^{-1} m^{-2} at the target cycle pressure) suggesting that choke flow is not a concern during the scale-up. Besides