The unit is isolated from the freeze-dryer before and after the nucleation process and is fully compatible with laboratory freeze-dryers of any size and brand.

The VERISEQ® Nucleation system can be easily sized based on the volume of the freeze-dryer, as opposed to the area, to ensure adequate ice-fog filling and circulation within an acceptable period of time. System design considerations include location of inlet/outlet ports and their size to ensure optimal ice-fog distribution within the chamber, as well as available space limitations.

Results and Discussion

Experimental detection of nucleation inside the vials can be assessed by a combination of direct observation and temperature measurements. Measurements are taken using wired and/or wireless temperature sensors attached to the external surface of selected vials or placed inside the vials. Figure 3 below shows a comparison between temperature profiles during uncontrolled (random) and ice-fog-controlled nucleation using water. Note, that some of the variation between vial temperatures is due to the fact that some temperature probes were placed on the outside of the vials. While accurately reflecting the time of nucleation, this may introduce some uncertainty with regard to temperature.

As can be seen from the provided temperature curves, uncontrolled nucleation of vials takes place over the interval of about 27 min within the temperature range between −8 and −15 °C. In the case of controlled nucleation, all the vials nucleate almost instantaneously at a temperature close to that of the shelf (about −7 °C, based on internal temperature sensors).

To demonstrate ice-fog nucleation utilizing different vial/stopper sizes, tests were performed using the combinations shown in Table 1 (see also Fig. 4):

Consistent ice-fog-induced nucleation was demonstrated in all vials.

In addition, the water intake during ice-fog-induced nucleation was evaluated based on the weight measurements. The results are shown in Table 2.

These results indicate that the water intake is minimal and practically does not affect the duration of primary drying.

Ice-fog-induced nucleation at a lower-degree supercooling results in much larger ice crystals and, hence, pore size, which reduces resistance to mass transfer and decreases the primary drying time.

Case Studies

As with anything related to lyophilization, many of the potential benefits of controlled nucleation vary from product to product, and indeed for the same product, from presentation to presentation. In order to better understand these variables, a number of studies were performed.