Table 1 (continued)

System	Subsystems	Difference type	Considerations
Temperature uniformity	Temperature mapping: within the shelves	Critical	Typically, ± 2.0 °C. Ensures uniformity of drying among vials in the load
	Temperature mapping: across the shelves	Critical	
	dT—Maximum deviation from set point	Critical	± 3.0 °C. Shelf surface temperature experienced by the vial bottom is the key. Not the set temperature

RTD resistance temperature detectors

ferred to the much larger unit where this radiation artifact is not encountered, then the cycle times are much slower than the ones observed in the laboratory. These differences in the dynamics of drying between the small laboratory units and commercial freeze dryers are the reason why many cycles fail in their initial attempts of technology transfer.

3. Determination of the end of various cycle stages at a commercial scale

A number of techniques are used to determine the end of primary and secondary drying stages of the lyophilization cycles. Some of these are listed below:

a. Measurement of product temperature
b. Pressure rise measurement
c. Differential pressure gauge responses
d. Remote sensing of product temperature
e. Others: dew point measurement (electronic moisture sensor), H_2O concentration from tunable diode laser absorption spectroscopy (TDLAS), manometric temperature measurement (MTM), sample vial extractor, residual gas analysis, near-infrared spectroscopy (NIR), etc.

All of the above are shown to be very effective by many research groups; however, these may not be always available at both the R&D site (technology transfer sending unit) and the commercial manufacturing site (technology transfer receiving unit). It is important that in a validated routine manufacturing process, end of drying should be independent of any variable. Ideally, it should be based on time duration parameter of the process alone. We discuss some of these more practical methods below.

a. Measurement of product temperature

The product temperature agreement with the shelf temperature is very commonly practiced in the industry using thermocouples and/or resistance temperature detectors (RTDs). As the end of the sublimation drying approaches, the product tempera-