



**Fig. 2** General scheme for lyophilization cycle development and optimization

function of temperature. The temperature at which physical changes (viscous flow) are observed in the film is defined as the collapse temperature. Evidence in the literature shows that for some formulations differences exist between the collapse temperature of a thin frozen film and a frozen formulation in a vial. For example, Greco et al. have shown that a 25:75 bovine serum albumin (BSA)/sucrose formulation (5% total solids) can be successfully freeze-dried at 5 °C above collapse temperature of  $-28^{\circ}\text{C}$ , determined using LT-FDM [11].

Optical coherence tomography-based FDM (OCT-FDM) has been developed as an alternative to LT-FDM that has the advantage of accurate estimation of collapse temperature of a formulation [11, 12]. The advantage lies in the 3D OCT-FDM measurement approach wherein the collapse temperature of the formulation is estimated in a vial during the freeze-drying process rather than in a thin film. It should be noted that, every 1 °C rise in product temperature during primary drying decreases the primary drying time by  $\sim 13\%$  [13] and therefore, cycle time reduction achieved using accurate estimation of the collapse temperature by OCT-FDM should lead to cost reduction and in the overall life cycle of the product. In addition, accurate determination of the collapse temperature using OCT-FDM supports QbD-based development of lyophilization processes that are currently run above the collapse