to evaluate this potential of new molecules. If during freezing, the solutes crystallize, the first thermal event detected using DSC will be the endotherm that corresponds to the melting of the eutectic formed between ice and the solute. This is usually followed by an endothermic event, corresponding to the melting of ice. Normally, freeze-drying of these systems is carried out below the eutectic melting temperature. Another way of detecting whether a solute or formulation crystallizes on freezing is to conduct subambient XRD. If there is no crystallization on cooling the solution of the drug, the supercooled liquid becomes more concentrated and viscous, leading to glass formation at a temperature known as the glass transition temperature (T_g). Generally, the freeze drying should take place below this temperature to avoid the collapsing of the cake, wherein high residual water remains and requires prolonged reconstitution time. There is an increased degradation as a result of increased mobility of molecules above T_g.

Testing of lead compound would preferably involve freezing and studying using DSC. In some cases, an endotherm caused by stress relaxation may be superimposed on the glass transition. It is possible to resolve these events using the related technique, modulated DSC (MDSC), or dynamic DSC (DDSC). The DSC is used to determine a wide range of physical properties of materials, including the glass transition temperature T_g, the melting temperature T_m, and solid–solid transitions. In this technique, a sample and a reference material are subjected to a controlled temperature program. When a phase transition, such as melting, occurs in the sample, an input of energy is required to keep the sample and the reference at the same temperature. This difference in energy is recorded as a function of temperature to produce the DSC trace. The MDSC provides the same qualitative and quantitative information about the physical and chemical changes as the conventional DSC and, in addition, provides unique thermochemical data that are unavailable from the conventional DSC. The effects of baseline slope and curvature are reduced, increasing the sensitivity of the system. Overlapping events, such as molecular relaxation and glass transitions, can be separated. Heat capacity can be measured directly with MDSC in a minimum number of experiments. Both MDSC and DSC measure the difference in heat flow to a sample and to an inert reference. The sample and reference cells are identical. However, MDSC uses a different heating profile. The DSC measures the heat flow as a function of a constant rate of change in temperature, whereas the MDSC superimposes a sinusoidal temperature modulation on this rate. The sinusoidal change in temperature permits the measurement of heat capacity effects simultaneously with the kinetic effect. Typical experimental procedure for an initial MDSC experiment includes a heating rate from isothermal to 5°C/min and a modulation amplitude from 0.01°C to 10°C. The modulation period can vary from 10 to 100 seconds or is expressed as a frequency, from 10 to 100 MHz.

The method of DDSC, such as using the PerkinElmer DSC 7 (18), along with the Pyris software platform, creates a modulated temperature profile applied to the sample, rather than a straight heating ramp, and the response of the sample is analyzed by Fourier transformation. The DDSC is particularly useful for separating overlapping thermal events, such as melting and recrystallization. Subambient operation of the DSC 7 normally employs a PerkinElmer Intracooler II, which allows reliable data to be acquired down to approximately −40°C; for even lower temperatures, a liquid nitrogen bath can be employed, which allows the collection of data down to approximately −150°C.