Table 1 Initial formulations routinely used up until early clinical trials

Initial formulation options	Pros	Cons	Applications
Frozen liquid	Simple, rapid development and implementation, formulation change may not be necessary if stable in liquid state	Stability in frozen state can be difficult to assess, challenging logistics to establish a controlled cold chain	Products with known stability profile, stable in low ionic strength formulations
Lyophilized	Enhanced stability, potential to commercialize, flexible to modifications during development like manufacturing, dose, etc.	Longer development, additional cost of manufacturing	Products with known stability issues, proteases, good IP position
Liquid	Most convenient for patients and health-care professionals	Longer development time (real-time stability data), less flexible to changes in manufacturing, dose, etc.	Products with good stability

a good understanding of a product's stability profiles: susceptible stresses, major degradation products, stability indicating assays, and formulation "sweet spot(s)." If the product maintains stability during a couple of months of storage at 25 °C and against other pharmaceutically relevant stresses such as agitation and transportation, a refrigerated liquid formulation may be a good recommendation for an initial formulation. The expiry may be extended as real-time stability data from long-term studies become available.

One of the major disadvantages of the refrigerated liquid approach is its limited capacity to accommodate common but unexpected excursions. Such excursions could include accidental freezing, exposure to ambient temperature, exposure to ultraviolet (UV) or visible light, excessive agitation during transportation and/or handling, etc. Generating sufficient stability data to cover the full spectrum of potential excursions is often improbable to achieve during early stages of development.

Factors to consider while selecting proper initial formulations are summarized in Table 1.

Strategy for Commercial Formulations

Various drug delivery methods have been pursued to gain a competitive edge in the market. For example, controlled release products for less frequent administrations and noninvasive delivery methods such as oral or pulmonary applications have been considered for competitive purposes. Applications such as these have largely been