

## Issues Specific to Lyophilized Formulations

As nearly 60% of biopharmaceuticals, including antibodies, vaccines, and plasma products, are lyophilized, optimization of lyophilized formulations should concern most biotech professionals. Nevertheless, the value of extra investments in an optimized formulation may differ by indication and geography, so it is important to evaluate the product within different populations.

For example, many orphan diseases require patients to take medication starting at a young age for their entire lives. Suboptimal reconstitution devices can directly and indirectly impact treatment efficacy and patient quality of life [13]. The pediatric population also has other considerations, such as different safety and tolerability issues for certain excipients or device components as adults.

Lyophilized drugs have a great advantage with regard to geography, since a cold chain encompassing storage, distribution, and use may not be necessary for a stable lyophilized formulation. This can be a significant asset in the vaccine market, where vaccine access can be limited to vaccines which are stable at ambient temperatures. Additional investments in stabilized formulations and easy-to-use drug delivery systems could improve the reach and effectiveness of these international efforts.

## Business Issues by Development Phase

### *Discovery*

Early in development, a formulation team should prepare a survey of formulation technologies and delivery devices available for consideration. This activity should be updated on a regular basis so these considerations can be shared with members of various product teams. Not all innovations result from in-house activities, so the team should be open to licensing or purchasing access to technology platforms which allow their products to have meaningful differentiation in the market.

Pre-formulation activities may start during this time period, during which the potential for a liquid or a lyophilized formulation may become evident.

Manufacturability issues may also arise at this time. Flagging these issues to process development will allow ample time for preparation for pre-Investigational New Drug (IND) product supply.

### *Pre-IND*

Once a team commences preparations for registration, an ideal formulation becomes an item on the critical path and thoroughness is often at risk of being compromised for development speed. Formulation professionals need to properly advise the team on the trade-offs between formulation risk and overall program risk. If a rational