cial stage. This makes lyophilized formulations an excellent commercial candidate for products with minimum competition and/or a strong intellectual property (IP) position.

Considering that even relatively unstable proteins such as interferon or hemophilia factors were introduced as room temperature stable lyophilized formulations, it is safe to assume that properly developed lyophilized formulations can allow room temperature storage of most protein therapeutics. This would not only make the storage, distribution, and handling of the product more convenient but also allow the distribution of biopharmaceuticals, including vaccines, to developing countries or regions where a cold chain has not or cannot be established.

Furthermore, the possibility of using various types and volumes of diluent allows flexibility in lyophilized formulation applications. Lyophilized formulations can be reconstituted with smaller volumes of diluent to overcome stability issues at higher concentrations or achieve smaller injection volumes. Preservatives can often compromise longer-term stability of proteins in a liquid state, but can be added in diluents to produce shorter-term multidose formulations. For instance, lyophilized formulations can be reconstituted with commercially available bacteriostatic diluents containing benzyl alcohol or custom diluents containing preservatives specifically selected for the product.

Delivery Devices

As previously stated, the main disadvantage of a lyophilized formulation is the inconvenience of reconstitution prior to administration. In order to take advantage of the improved stability of lyophilized formulations without compromising ease of use, various devices have been introduced to the market to aid the reconstitution process. These include vial adapters, vial-to-vial systems, needless transfer systems, or direct connection to vial systems. Other advanced container/closure systems, such as dual chamber syringes, e.g., Lyoject® or Lyotip™, are also available. For multidose formulations, cartridges designed to be reconstituted with bacteriostatic diluents followed by injections with pen injectors are available.

As device technology evolves, it is feasible that a lyophilized formulations could be manufactured as easily and cost-effectively as current container/closure systems, and delivered as conveniently as a prefilled syringe. The most ideal attributes of a product could be achieved with this technology, with the stability of a lyophilized formulation and the convenience of a liquid formulation.

Strategy to Switch Formulations

The best time to switch from an initial formulation to a commercial formulation is before phase III clinical trials. This is the time when all development activities, including manufacturing of drug substance, process to formulate and fill/finish, final container-closure and delivery options, stability study programs, and clinical dosing