Sweden) that produces laboratory (LS-2), pilot (LS-6), and production scale (PS-20) spray-freeze-drying equipment [29].

Spray-Drying Process Optimization for Biopharmaceuticals

Whether conventional spray-drying, spray-congealing, or spray-freeze-drying, optimization of a spray-drying technique for a biopharmaceutical formulation depends on many factors. Some of the factors affecting the final spray-dried formulation properties are determined by the material to be sprayed, by the spraying conditions, by the type of equipment, and by the specific spray-drying technique itself. Optimization is determined by the specific properties that are prioritized by the researcher. For biopharmaceuticals, these properties typically include yield, morphology (i.e., shape, size, and porosity), flow characteristics, and product condition (i.e., chemical degradation, protein denaturation, and other physicochemical properties). The prioritization of one or more of these properties is specific to the biologic and its application—what is desirable for one product may be undesirable or irrelevant for another. For instance, spherical, dense particles are usually desired for most spray-dried pharmaceutics; however, for spray-dried, inhalable insulin the target morphology is a light, nanoporous particle [30]. While size, morphology, and flow properties may vary depending on the product and its application, other properties, such as yield and final product condition, are always maximized. For a conventional spray-dryer, the factors that affect the quality of the final product are excipients in the formulation, instrument design, feed solids concentration, inlet temperature, outlet temperature, liquid feed rate, and airflow rate. All of these parameters are interrelated, and adjustment of one parameter may require an adjustment of another. Because the parameters are interrelated and because of the sheer number of parameters, the spray-drying process is usually viewed as an empirical process requiring many trial runs to obtain the desired product [31]. Researchers have attempted to develop models to describe the spray-drying process [32]. All of these approaches are goal-oriented and have a particular formulation target in mind when optimizing the spray-drying process. In addition, because of the interrelation between the parameters, a strict model describing the overall process is difficult at best. However, modeling the spray-dry process is useful in making some generalizations about the overall process.

Two main factors affect the yield in conventional spray-drying—loss of material due to instrument design and loss due to material properties. Loss of material due to instrument design may be minimized by selecting an appropriate spray-dryer design for maximal recovery such as a wide drying chamber for a spinning disk atomizer, a high efficiency cyclone for fine particles, or an electrostatic collector for submicron particles. Other loss due to instrumentation is generally finite and independent of batch size and, therefore, can be minimized by increasing the overall batch size when possible. Suboptimal material properties are the other major hindrances to maximum product yield. When a spray-dried material is “sticky,” it will tend to collect on the walls of the spray-dryer [33]. This problem may be minimized by decreasing the outlet temperature below the glass transition point (T_g) of the