These dosage forms rely on a larger carrier particle, such as *a*-lactose monohydrate, to which the drug is attached. The lactose is usually fractionated, such that it lies in the size range of 63–90 μm. On delivery, the drug detaches from the lactose, and because the drug is micronized, it is delivered to the lung, while the lactose is eventually swallowed. It should be realized that the polymorphic form of the lactose used could affect the aerosolization properties of the formulation. The β-forms were easily entrained but held onto the drug particles most strongly when the flow properties were studied. The anhydrous α-form shows an opposite behavior, and the monohydrate α-form demonstrates an intermediate behavior. Interactions with packaging materials can also alter the powder characteristics; for example, long contact times with polyvinyl chloride, polyethylene, or aluminum should be avoided, because the adhesion force between the drug and these surfaces is much higher than that between it and the lactose carrier. Thus, detachment and loss of drug in the formulation could occur. As lactose is widely used as a carrier, its compatibility with the new drugs should be studied in detail, especially if there are any amino groups in the structure. The surface property of lactose is also important. With increasing specific surface area and roughness, the effective index of inhalation decreases as a result of the drug being held more tightly in the inhaled airstreams. Therefore, characterization of the carrier particles by, for example, surface area measurements, SEM, and other solid-state techniques, is a recommended preformulation activity.

The recent approval of Exubera, an inhalation form of insulin, by the U.S. FDA is a classical example where the dosage form is an integral part of drug action. Using the Nektar company's delivery system to create a fine powder mist, insulin in Exubera is absorbed, as the mist of fine powder reaches into the deep portions of the lung structure, without getting impacted. Although reduction in particle size is pivotal to the pulmonary delivery of drugs, micronization makes powders difficult to flow, and these changes should be studied using techniques such as DVS, microcalorimetry, and IGC. The high energy at the surface of micronized powders can often be relieved by exposing it to air of higher humidity, which can crystallize the amorphous high-energy regions. As a result, the common preformulate stage evaluations include the measurements of the micromeritic, RH, and electrostatic properties of the powder. Different salt forms show variant flow properties; for example, stearate salts are generally better for aerosol formulation.

Nebulizer formulations are normally solutions, but suspensions (particle size of <2 μm) are also used. Important preformulation considerations include stability, solubility, viscosity, and surface tension of the solution of suspension.

7.9 General Compatibility

Some excipients are universal to specific dosage forms. General compatibility testing with components such as lactose and other fillers, lubricants such as magnesium stearate, and suspending agents such as PVP and the like can be done at the preformulation level if a sufficient quantity of drug is available. In cases where a specific dosage form, such as a pulmonary delivery aerosol, is definitely desired, this testing becomes more important. Generally, chemical reactivity known between prominent function groups can be put to test in projecting the likely excipients. The testing involves