lactose is available in several grades, including anhydrous direct tableting grade, a free-flowing spray-dried form (Fast-Flo), and several particle size grades of lactose monohydrate. While lactose monohydrate is useful both for dry mix and wet granulation, the anhydrous type should be avoided in aqueous granulation processes. The conversion of the anhydrous form to the monohydrate during aqueous granulation may contribute to approximately 5.3% weight gain, resulting in final batch yield discrepancies.

API and excipient material attributes and other considerations critical to the manufacturing process and scale-up of solid dosage forms are identified below:

1. Impact of excipient variability on product quality
2. Particle shape, size, and surface area (flow properties)
3. Solubility in water and granulating fluid
4. Crystallinity and polymorphism
5. Moisture sensitivity and equilibrium moisture content (EMC)
6. Bulk and tapped densities of major components
7. Granulation and drying properties
8. Compaction behavior
9. Potential changes during storage

Impact of Excipient Variability on Product Quality

Solid dosage formulations and processes are significantly impacted by material properties of the API and excipients. The sources of variation in product quality are attributable to complex interplay between CMAs of API and excipients and the manufacturing process as shown below:

$$\text{Product Variability} = f(\text{API Variability, Excipient Variability, Process Variability})$$

Usually, API properties and their impact on finished product quality are better understood compared with variability in excipients. There are several reasons for this, including naturally derived raw materials used as excipients, adaptation of food-grade materials for pharmaceutical uses, and their inherent lot-to-lot variability [4–6]. For example, many functional excipients used in the design of controlled release formulations are polymers. These polymers are rarely well characterized and controlled for their functional properties such as viscosity, particle size, and powder flowability. Even for excipients with existing pharmacopoeia monographs, the specifications listed are usually related to their chemical properties, whereas specifications corresponding to physical properties important for a formulation and process may not be identified. Recently, attempts are being made by the industry consortium—International Pharmaceutical Excipient Council, working with regulatory agencies, and the manufacturers and users, in addressing excipient variability and the role of performance testing, test methodology, and harmonization [7]. A draft United States Pharmacopeia Chapter <1059> Excipient Performance addresses this issue by identifying the CMAs of functionally categorized excipients and the performance tests that may be useful to characterize them [8]. There are numerous examples in the literature studying the effect of excipient variability on finished