

characterization measurements such as angle of repose, angle of spatula, floodability, and flow through a hopper should be evaluated for the blend. Typically, a material with high angles of repose, low floodability, and low bulk density contributes to manufacturing problems if not processed using wet granulation, slugging, or roller compaction.

### Granulation Properties

The granulation properties of the drug and excipients are important for products manufactured using wet granulation. The ability of formulation components to hold the granulating fluid (kg fluid per kg material) can be measured alone or in combination. This information can be utilized in estimating the granulating fluid requirements for a scale-up using the following equation:

$$W = (A_1B_1 + A_2B_2 + A_3B_3 + \dots) \times f, \quad (5.2)$$

where  $A_1, A_2, A_3, \dots$  are the weights (kg) of components 1, 2, 3, ... in the batch;  $B_1, B_2, B_3, \dots$  are fluid holding capacities (kg fluid per kg material) of components 1, 2, 3, ...; and  $f$  is a scale-up factor typically between 0.5 and 0.9. The amount of fluid required for the scale-up batch depends on other factors such as type of equipment, atomization, and rate of addition.

### Drying Properties

The drying performance of a material is contingent on its ability to dry from a wet mass formed during the granulation process. Although various processing conditions such as drying temperature, relative humidity of the drying air, air velocity, and exposed granule surface area affect drying, the material affinity for the solvent dictates the drying rate. Small to medium molecular weight materials with low to medium water solubility lose water quickly and dry rapidly (e.g., lactose, calcium sulfate, and dicalcium phosphate). Some materials such as high molecular weight Povidone, hydroxypropylmethylcellulose, starch, hydrophilic gums, and polyethylene glycol are difficult to dry, especially if present in relatively high proportions in the formulation. However, an efficient drying technique such as use of the fluid bed dryer is useful to overcome drying problems for an otherwise difficult to dry material.

### Compaction Behavior

The compaction behavior of tablet components plays a key role in the tableting process. The compaction property of the final blend is dictated by the individual components. Manufacturing processes such as wet granulation, roller compaction, and slugging can significantly alter compaction characteristics. In early preformulation, compaction behavior can be conveniently studied using an instrumented single station press (Carver or Korsch).

### Potential Changes during Storage

Absorption and desorption of moisture and associated hardening and polymorphic conversion should be considered. Changes in physical characteristics of excipients