in Phase II are suggestive of customized repetitive batches with often slight modifications in batch sizes. The dosing amount and solubility ratio are important factors for deciding the formulation strategy. Combination of the first two approaches given earlier would determine the optimal path for dosage forms.

For this phase of development, Huang (2005) has recommended a standardized approach to developing a tablet and capsule formulation. This approach standardizes the formulation where few compositions are available for scientists to *plug and play* their API and quickly develop a clinical image dosage form. Huang recommends formulation composition with soluble and insoluble types of inert diluents and commonly used disintegrants such as crospovidone, sodium croscarmellose, sodium starch glycolate, and calcium carbonate. For lubrication, Huang recommends magnesium stearate at 0.5% or separate screening studies for other lubricants such as stearic acid (1%), hydrogenated vegetable oil (lubritab, 2%), and sodium stearyl fumerate (1%). Finally, glidant use is recommended as optional with colloidal silicon dioxide as the ingredient of choice. Understanding of API material characteristics (e.g., ductility, brittleness, etc.) also aids in selecting appropriate standardized formulation. The use of these formulations certainly has some distinct advantages at this stage of development. Standard manufacturing process also can be applied to these standardized formulations. These formulations can be evaluated for the two standard processing approaches, namely, dry granulation and wet granulation (Figures 23.3 and 23.4). Process understanding of how a standardized placebo behaves with the two processing techniques provides indications to an optimum processing technique for a formulation. The development time required for further process understanding is relatively low.

Once the standardized formulation composition and preferred processing technology are well understood, plugging in the API and manufacturing the clinical dosage is a relatively low-risk proposition. The impact of API drug load on the standardized formulation is the only risk that one has to manage to successfully manufacture a clinical drug product. If the drug loading in the formulation is high (i.e., >10%), there is higher potential for it to impact the manufacturing process. Understanding of API properties (i.e., morphology, density, flow, particle size, compressibility, cohesivity, etc.) can

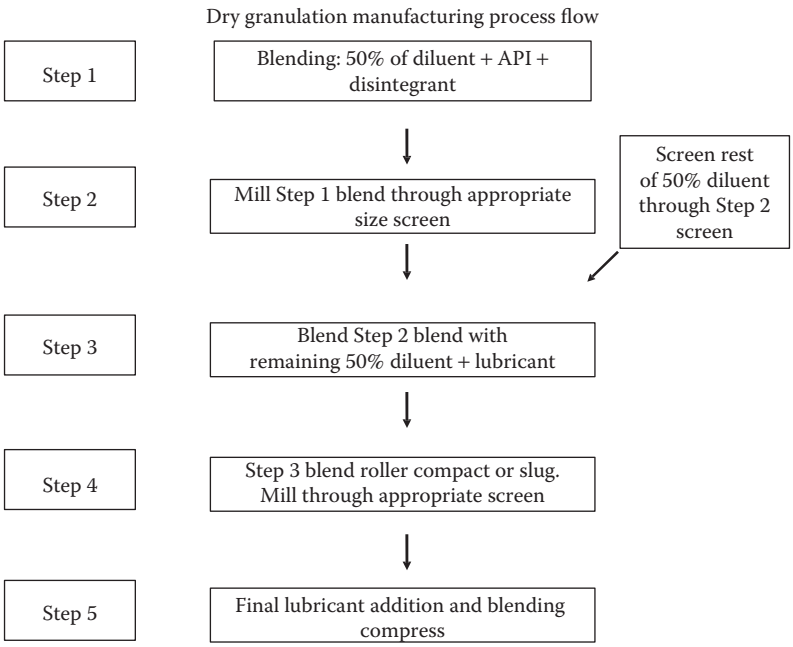

FIGURE 23.3 Example process flow for the dry granulation process.