529g Control of Api Powder Properties Via Agitated Drying

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The bulk powder properties of a pharmaceutically active ingredient significantly impact the solid dosage formulation as well as drug product performance. Typically, powder properties can be influenced by the crystallization conditions. However, we observed that in the case of BMS-ABC, crystallization with different solvents and subsequent temperature cycling did not change the particle size or morphology of the needle-like crystals. That prompted studies to determine the influence that post-crystallization operations had on the powder properties. Our initial experiments showed that agitated drying significantly changed the particle size and bulk density depending on the solvent content in the cake when agitation was started. Needle agglomeration dominated above a critical moisture content of 8%; while below this moisture content needle attrition dominated. To determine the onset of agitation, the solvent content in the dryer headspace was monitored in-line with mass spectrometry and a hygrometer. We also studied the effect that different types of dryers (filter, conical and fluidized bed dryers) and delumping techniques (cone-mill, air jet mill) had on the powder properties. The lab observations were then implemented successfully on 3 and 25 kg scale. The impact of these powder property changes on drug product performance showed good correlation between bulk density, particle size and tablet dissolution rate.