446c Drying of a Monohydrate Api under Thermodynamically Safe Conditions

G. Scott Jones, Raymond Scaringe, and Shawn Yin

Crystallization of an active pharmaceutical ingredient (API) as a monohydrate is common in the pharmaceutical industry. Removal of lattice-bound water in crystalline hydrates to give an undesired crystal form, or polymorph, presents a potential pitfall while drying these materials. The current study discusses laboratory investigations of the conversion of a monohydrate to its anhydrous form. These studies demonstrate batch-to-batch variation in the kinetics for dehydration of the desired monohydrate. In order to avoid concerns over these kinetic differences, relative humidity conditions were established under which the desired monohydrate is the thermodynamically preferred crystal form. These conditions and a dew-point hygrometer were utilized to devise and test several approaches to drying the monohydrate API on multiple pilot-scale batches. The laboratory investigations and successful pilot plant scale-up of the drying protocols will be discussed.