394f Using Fbrm Measurements, Fines Destruction and Varying Cooling Rates to Control Paracetamol Csd in a Batch Cooling Crystallizer

Ronald W. Rousseau and Stephanie Barthe

Controlling crystal size distribution is important to downstream processing and to product quality. It is well-recognized that selective removal of segments of the crystal population can be used to influence CSD, for example by manufacturing a product with a larger dominant size or narrower distribution. Early work on the use of feedback control to manipulate the residence time distribution functions of fines in a continuous crystallizer demonstrated the utility of such an approach in handling process upsets or in reducing cycling that resulted from system instabilities. These efforts were extended to batch crystallization, although there remained significant difficulty associated with on-line analysis of the size distribution.

The development of new technologies, such as Focused Beam Reflectance Measurement (FBRM), provides a methodology for on-line monitoring of a representation of the crystal size distribution in either batch or continuous systems. Properly installed, the FBRM allows on-line determination of the chord length distribution (CLD), which is statistically related to the crystal size distribution and depends on the geometry of the crystal.

In the present work, we develop a formal relationship between chord-length measurements and crystal size distributions. The approach has been implemented on an experimental system in which paracetamol was crystallized from solutions in ethanol and an FBRM was used to monitor the evolution of CLDs. These data then formed the basis of estimates of the paracetamol crystal size distributions being formed in a batch cooling crystallizer. Different runs on the system have examined operations with and without fines destruction and at various cooling rates. The results demonstrate how selective fines destruction influences the size distribution of the crystalline products, and they lay the foundation for implementation of control schemes that move the CSD in preferred directions.