

## **101a Application of Raman and Fbrm Techniques in the Development of Pharmaceutical Crystallization Processes**

*Lifen Shen, Dimuthu Jayawickrama, Robert Wethman, and Victor Hung*

Control of polymorphism and powder properties are often the most important issues in the crystallization process development of active pharmaceutical ingredients (API). In-line analytical methods have been proven to be useful in providing real-time information on polymorphism and particle size distribution of crystals. This presentation will focus on the application of in-line Raman and FBRM measurement in the development of two BMS APIs. The first example describes the development of a polymorph transformation process that converts a monohydrate to a neat form of an API. In this work, an integrated crystallizer equipped with FBRM, Raman, and temperature probes was used to allow real-time monitoring of the crystal size and form, which offers great advantage of quantitative analysis and in-depth understanding of the transformation process. The second example illustrates the application of in situ analytical methods to generate data on the effective metastable zone width (MSZW) and the use of such information in the development of a robust process.