

## **PARTICLE SIZE ANALYSIS BY TWO-DIMENSIONAL XRD**

Bob B. He, Bruker AXS, Madison, Wisconsin, USA

The particle size is an important factor affecting the properties of solid materials. The particle size can affect the behavior of pharmaceuticals in many ways, such as dissolubility, flow properties and stability. The measurement of the particle size by the conventional x-ray diffraction is based on the measurement of diffraction peak broadening or diffraction profile analysis. Although line broadening appears when the particle size is smaller than 100 nm, in practice, the Scherrer equation can adequately determine the average size of crystallites smaller than 30 nm when the broadening is significant enough to be resolved from instrumental broadening. The particle sizes pharmaceutical systems are typically in the range of a few micrometers to millimeters. The term “grain size” is usually used in this size range. Therefore, the conventional method of particle size analysis by x-ray diffraction is not always suitable for pharmaceuticals.

This presentation introduces a new grain size measurement method based on the  $\gamma$ -profile analysis on two-dimensional diffraction patterns. The availability of an area detector makes it possible to measure the spotty diffraction rings due to large grain size or poor sampling statistics. Line profile analysis is suitable for measuring crystallite size smaller than 100 nm (1000Å), while  $\gamma$ -profile analysis is more suitable for larger crystallites from 0.1  $\mu\text{m}$  to a few millimeters depending on the x-ray incident beam size, divergence, sample shape and size, instrument geometry and detector resolution. The  $\gamma$ -profile analysis is based on the sampling statistics. Sampling statistics believed to be “poor” for other applications are actually preferred for crystallite size determination. The sampling statistics are determined by both the sample structure and instrumentation. For a given instrument window, the number of grains contributing to a selected diffraction ring is determined by the effective diffraction volume, grain size and the multiplicity of the diffracting crystal planes. A two-dimensional diffraction system can be calibrated by a sample with known crystal size, crystal structure and x-ray absorption coefficient. The grain size of an unknown sample can then be determined by quantitative analysis of the spotty diffraction ring. The mathematic modeling for  $\gamma$ -profile analysis and experimental examples are also given in this presentation.