

Applications of X-ray Powder Diffraction to High throughput Discovery of Crystalline Forms of Pharmaceuticals

Greg Stephenson
Eli Lilly and Company

X-ray diffraction is viewed as the definitive method for crystal form discovery, oftentimes referred to as the “gold standard” for crystal form identification. As the world of combinatorial chemistry and high throughput screening has progressed from compound discovery to pharmaceutical development, a need for rapid assessment of crystallization outcome has posed new challenges for powder diffraction. Since parallel crystal form screening crystallizations are conducted on the small scale, the method need not only be fast, but also highly sensitive. The inherent challenges of obtaining sufficient quality patterns to distinguish crystal forms with confidence using small amounts of sample, due primarily to problems of poor particle statistics and preferred orientation, have led to application of other perhaps less definitive techniques such as Raman or infrared microscopy. This presentation will elaborate on some of the developments we have made in our laboratory to obtain high quality patterns on small amounts of material.