

## X-RAY POWDER DIFFRACTION AT THE HEART OF PHYSICAL FORM DISCOVERY IN CPOSS

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The multi-centred, collaborative RCUK Basic Technology project entitled “Control and Prediction of the Organic Solid-State” (CPOSS)<sup>1</sup> is studying physical form diversity in organic molecular solids through the combined application of theoretical and experimental investigations. The vision is to provide a complete picture of predicted and observed crystalline forms and enable improved methodologies for crystal structure prediction.<sup>2</sup> The experimental approach uses an automated parallel crystallisation methodology in which molecules are recrystallised under a wide range of conditions (including ca. 70 solvents and a range of supersaturation, temperature and agitation values) typically yielding ca. 30 polycrystalline samples per day.<sup>3</sup> Powder diffraction is at the heart of the analytical strategy for both identification and discovery of novel crystalline forms. Examples will be presented that demonstrate: (1) the use of multi-sample transmission foil X-ray powder diffraction to identify novel forms produced from the crystallisation search;<sup>4</sup> (2) that whilst single-crystal diffraction remains the principal method for crystal structure determination, capillary X-ray diffraction data combined with accurate temperature control, variable count time data collection and efficient, flexible software tools for global optimisation<sup>5</sup> and Rietveld refinement<sup>6</sup> enable ‘routine’ crystal structure determination in the absence of suitable single crystal samples;<sup>7</sup> (3) the potential for both standard 2kW sealed tube and rotating anode X-ray sources (12kW) combined with capillary geometry, primary monochromation, position sensitive detectors and sample temperature control for effective *in situ* studies of crystallisation, desolvation and phase transformations as part of a systematic and efficient approach to physical form discovery at non-ambient temperatures.<sup>8</sup> The examples will be described with an emphasis on instrumental, sample (preparation and presentation), data collection and data analysis considerations.

1. [www.cposs.org.uk](http://www.cposs.org.uk); 2. Florence *et al.*, *J. Pharm. Sci.*, 95, 1918-1930, 2006; 3. Florence *et al.*, *J. Appl Cryst.*, 39, 922-924, 2006; 4. Florence *et al.*, *J. Pharm. Sci.*, 92, 1930-1938, 2003; 5. David *et al.*, *ChemComm*, 931-932, 1998; 6. Coelho, A. A. Topas User Manual. Version 3.1. Bruker AXS GmbH, Karlsruhe, Germany, 2003; 7. Hulme *et al.*, *Acta Cryst.* E62, o3046-o3048, 2006; 8. Fernandes *et al.*, *Acta Cryst.* E63, o202-o204, 2007.