Structure Indexing and Solution from Non-Ambient XRPD Data

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Despite excellent recent progress, crystal structure determination from powder data remains a challenge.[1] This is especially so for flexible and weakly diffracting organic (inc. pharmaceutical) compounds.[2] Of particular interest to the pharmaceutical industry is the full structural characterisation of crystalline forms under both ambient and non-ambient conditions. This arises from a desire to understand the behaviour of solids, and how the materials respond to a range of humidities and temperatures.

The necessary diffractometer hardware to conduct non-ambient experiments (*e.g*. an Anton Parr humidity stage or a TTK temperature stage) is well established,[3] but the application of such experiments to pharmaceutical compounds is less so.[4] Here we present the methodology required to obtain high resolution non-ambient data for crystalline forms that correspond to phase changes observed in other solid state analytical techniques (*e.g*. DSC or GVS). We have indexed and subsequently solved the structures of observed forms from this non-ambient data to give full structural information across the phase diagrams. In addition, the thermal expansion coefficient for the material can be determined by indexing over a range of temperatures. This value is key for the construction of a pressure *vs*. temperature thermodynamic phase diagram.

[1] a) see, for example, David W. I. F., Shankland K., McCusker L.B., Baerlocher Ch., *IUCr Monogr. Crystallogr*., 2002, **13**, 337; b) Harris K.D.M., Cheung E.Y*., Chem. Soc. Rev.*, 2004, 33. [2] Shankland K., Markvardsen A.J., David W.I.F., *Zeit. Krist*., 2004, **219**, 857-865. [3]see, for example, Anton-Parr-Str, Graz, Austria: website www.anton-parr.com . [4] Brittain H.G., *Spectroscopy*, 2001, **16**, 14-16.

Keywords: powder diffraction under non-ambientconditions, pharmaceutical structuredetermination, hydrates