Crystal Structure Analysis and Solid Form Selection in the Pharmaceutical Industry

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The selection of the solid form is an important milestone in the development of new drug product. The aim of the process is to select the solid form with the most desirable properties including aqueous solubility, chemical and physical stability and suitable drug product processing attributes for formulation e.g. mechanical properties. The selected form may be either the free base or acid of the active pharmaceutical ingredient (API) or a salt.

It is vital to ensure the most thermodynamically stable polymorphic form has been selected. Different polymorphs have unique physical properties resulting in different solubilities, chemical and physical stabilities and different bioavailabilities. Metastable polymorphs may convert to more stable forms on processing and examples of this have been reported [1]. The characterization of all solid forms is important and can provide many intellectual property opportunities [2].

Crystal structure analysis, taking a molecular perspective of the crystalline state, can be combined with both manual analytical techniques (e.g. PXRD, thermal analysis, microscopy) and automated high throughput solid form screening techniques to ensure the optimum solid form is selected.

[1] Bauer J.F., Spanton S., Henry R., Quick J., Dziki W., Porter W., Morris J., *Pharm. Res.,* 2001, **18(6)**, 859. [2] Bernstein J.*, Polymorphism in Molecular Crystals*, OUP, New York, 2002.

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