## MS36-P7 Solid form control and design through structural informatics

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Uncontrolled crystal form polymorphism can have a critical impact on pharmaceutical drug product robustness, exemplified by Norvir™ [1] and Neupro™ [2]. The Norvir™ example illustrates how such polymorphism can be driven by a stronger set of hydrogen bonds in the stable form. At the CCDC we are developing structural informatics approaches to solid form design, including the Hydrogen-Bonding Propensity method which would have predicted the likely existence of the more stable polymorph of ritonavir (Norvir™)[3].

Software including such methodologies is being developed under the guidance of the Crystal Form Consortium (CFC); a partnership between the CCDC and eleven global pharmaceutical companies. Here we will describe the potential application of these methodologies to minimise risk in solid form design.

**Keywords:** Polymorphism, Interaction, Pharmaceutical, Solid Form

## MS36-P8 Cocrystallization out of the blue: DL-mandelic acid/ethyl-DL-mandelate cocrystal

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We present exceptional behavior of racemic mandelic acid in an ethanol solution. Dissolution of racemic mandelic acid in ethanol followed by evaporation to dryness results in a DL-mandelic acid/ethyl-DL-mandelate cocrystal. This behavior indicates that racemic mandelic acid tends not only to transform into an ester in ethanol, but also to immediately cocrystallize with untransformed acid molecules, thereby preventing a complete conversion of the acid into the ester. Cocrystal formation in ethanol was found to be reproducible under various conditions. DL-tropic acid and DL-phenyllactic acid that contain similar functional groups were tested as well, but no cocrystal formation was detected. The DL-mandelic acid/ethyl-DL-mandelate system has four chiral centers and presents a crystalline system with one of the co-formers being an ester, which is quite a rare phenomenon for cocrystals. Moreover, such an unexpected behavior of DL-mandelic acid should warn us that cocrystallization should be taken into account not only in the field of crystal engineering, but may even emerge as a byproduct in organic synthesis.

**Keywords:** cocrystallization, cocrystals, DL-mandelic acid