**Complex Chemistry, Simply Delivered: Cocrystals Design, Development and Scale-Up**

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**Introduction**

Pharmaceutical compounds frequently encounter problems during development. Salt formation is one widely used approach to improve such properties, however cocrystals, using non-ionic interactions, offer an alternative route.

Cocrystals offer various physicochemical properties modifications, which can include: solubility, dissolution rate, stability, melting point, hygroscopicity and crystallinity.

Pyrimethanil has been used as a model compound to investigate cocrystal formation with the aim of modifying its properties to produce a material with superior characteristics.

**Development Process**

Cocrystal Screening ➔ Characterisation ➔ Single Crystal Structures ➔ Scale Up ➔ CrystDev Modelling

**Discussion & Summary**

The benefits of cocrystals were demonstrated in the pyrimethanil system in which 50 salts/cocrystals were identified. SCXRD indicated the materials’ nature, and basic characterisation showed their relative stability.

The most promising candidates were scaled up (grams) to evaluate their solubility and dissolution profiles. Crystallisation development, including the use of DynoChem modelling software, was then performed on one system to improve the particle properties.

**Regulatory Aspects**

Cocrystals are classified in a similar way to polymorphs.

*FDA Requirements [1]*

Evidence that both API and coformer are present in the unit cell

Co-existence with non-ionic interactions between the components

Substantial dissociation occurs before the site of pharmacological activity is reached

Pharmorphix® Solutions

SCXRD

SSNMR

Spectroscopic Techniques

pKa Determination

SCXRD, SSNMR

Intrinsic Dissolution Rate Solubility Studies

**References**