

New Developments in Screening for Pharmaceutical Salts and Polymorphs: High Throughput versus Conventional Laboratory Scale Experimentation

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The selection of the solid form for a new active pharmaceutical ingredient (API) is a decision of paramount importance, that usually has to be made at an early stage, i.e., at a time when the clinical research results and the success of the future drug product are yet unknown. Therefore, it is crucial to evaluate the best suitable solid-state form of a drug substance in a timely and cost effective manner.

High throughput screening (HTS) strategies for solid-state forms have emerged as new tools to enhance the possibilities, and to support the selection most suitable solid-state form.

For a new drug substance with acidic or basic functional groups a screening for crystalline salts is generally followed by a screening for polymorphs, hydrates and solvates of one or several salt candidates which have been identified during the initial salt selection process. In some cases a screening for suitable co-crystals or even optimal formulations may turn out to be decisive on whether a substance will become successful drug product or not.

Solvias AG has developed new proprietary HTS technologies [1-3] tailored to the needs of chemical and pharmaceutical development of new drug substances. These technologies are particularly useful for the discovery and preparation of new crystalline salts, polymorphs, solvates and hydrates. One important advantage is that generally fewer HTS experiments, i.e., less than 300 to 400 experiments are needed to establish a complete survey on crystalline forms.

However, it is important to understand that current HTS technologies do not replace profound experience in solid-state chemistry. This is particularly true for the polymorphism of molecular crystals when the situation in terms of solid-state forms reaches a certain complexity and when the different solid-state forms have to be scaled-up to laboratory or even to production scale. In order to understand the entire situation for a complex system with several polymorphs, hydrates and solvates, the best procedure is an interactive strategy with two or three series of HTS experiments, that are paralleled with laboratory experiments on a 100 to 300 mg scale.

The “*Solvias Profile Study*” reflects this strategy and is designed to resolve even most complex cases in a reasonably short time frame.

References

[1] R. Hilfiker et. al.; *J. Thermal Analysis & Calorimetry*, Vol. 73 (2003) 429-440.

[2] F. Blatter et. al.; *PCT Publication*, WO 2003/026797.

[3] M. Szlagiewicz et. al.; *PCT Publication*, WO 2004/045769.