

437i Developing and Implementing High-Throughput Screening of Pharmaceutical Salts and Polymorphs

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The major challenges for automated high-throughput (HT) screening in pharmaceutical development of API is to synthesize salts and then characterize them without breaking the HT workflow.

As an innovative solution to the above challenge, a 96-well crystallization block was developed with Zinsser Analytic and implemented in HT screening. The block was designed to fulfill a dual function: to create a multi-well reaction system and to facilitate sample presentation for the subsequent X-ray powder diffraction (XRPD) and Raman analyses. It consists of an aluminum body with 96 bores and Teflon inserts that tightly fit into the bores. The inserts accommodate movable syringe plungers made of Teflon-coated aluminum pistons and topped with a thin circular glass. For reaction and crystallization operations, the vertical position of the plungers is fixed to create wells of the desired reaction volume. After the successive filtration and drying operations, the plungers are pushed up to bring the solids above the surface of the block, so that the block itself becomes a multi-sample holder for automated collection of XRPD patterns and Raman spectra.

The automated commercial CRISSY liquid and powder distribution system (Zinsser Analytic) coupled with the crystallization block, enabled automated screening for salts and (pseudo)polymorphs in a HT mode and allowed for the seamless extension of the HT workflow into XRPD and Raman measurements.