

AN OVERVIEW OF METHODS AND STRATEGIES FOR HIGH-THROUGHPUT POLYMORPH SCREENING: CRYSTALLISATION, DIFFRACTOMETRY AND DATA ANALYSIS

Christian W. Lehmann
Max-Planck-Institut fuer Kohlenforschung
Muelheim an der Ruhr, Germany

Enormous progress has been achieved over the last five years in the field of high-throughput polymorph screening. Previously a manual and labour intensive task, limited to few crystallisations, it has developed into fully automated workflows with hundreds of parallel crystallisations and analyses. Driven by economic, regulatory and intellectual property issues, the pharmaceutical industry employs increasing means for polymorph research, which is reflected by a growing choice of commercial instruments and workstations for crystallisation and diffraction analysis. This scenario is completed by the presence of several companies offering polymorph screens.

Since computational and predictive methods are presently unable to substitute for experimental screening, while parameter space is vast, high-throughput methods are of particular interest. A key challenge is however, matching the crystallisation environment with the requirements for diffraction analysis. This challenge has been met by developing a multi-well plate with detachable cavity walls, thus presenting the crystalline sample to the X-ray beam on a flat surface. The resulting design and related solutions have found entry into commercial products as well as applications driven by further miniaturisation.

Of equal importance is the automated analysis of the diffraction patterns in terms of phase identification and quantification. Recently tools have been devised to achieve this and in combination with the experimental details of the crystallisation the complex picture of a polymorphic system can be drawn.