

Bruker / MIT Symposium 2015

CRYSTAL POLYMORPHISM IN THE PHARMACEUTICAL INDUSTRY: PRACTICE, PROBLEMS, PROGRESS AND PREDICTION

Susan M Reutzel-Edens, Small Molecule Design & Development Eli Lilly and Company;
e-mail: reutzel@lilly.com

Engineering crystal forms of small molecule drugs to desired specifications is an essential first step in drug product design, relying heavily on the effectiveness of salt and polymorph screening programs. Whether the goal is to crystallize a compound for the first time for purification purposes, to thoroughly investigate the solid form landscape en route to designing the commercial dosage form or to mitigate the risk of late appearing, more stable forms, polymorph screens are designed to find as many crystal forms as possible. However, with new forms continuing to appear all too frequently well after compounds have been thoroughly screened, we are reminded that the problem of polymorph appearance remains unsolved, despite millions of dollars invested in novel tools and technologies for crystallization screening. In this presentation, challenges in defining experimental solid form landscapes, ensuring that viable forms are not missed, and transferring knowledge about form landscapes from those of structurally-related molecules, are discussed. The use of computed crystal energy landscapes for enhancing the effectiveness of experimental solid form screens is also explored for molecules of pharmaceutical complexity.