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The Trouble with Hydrates - A Pharmaceutical Industry Perspective. Norbert Nagel. *Analytical Sciences Department, R&D, sanofi-aventis Germany.*
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Most active pharmaceutical ingredients (APIs) are prone to the formation of different solid forms which may include anhydrous as well as well as hydrated or solvated crystalline forms. The presentation outlines, why it is of high relevance for the pharmaceutical industry to characterize the different crystalline solid forms and to identify the most suitable one for the use in the drug. Thermodynamic stability is usually the decisive criterion for phase selection and can vary with the environmental variables temperature and pressure. For hydrates, also the relative humidity / water activity plays a role.
Hydrates can therefore be more prone to phase transformations than anhydrous and solvent-free solid forms, which can be critical during manufacturing and storage of a drug. The different manufacturing steps of a drug product (tablet) are briefly presented and it is discussed, which solid phase transformations are to be expected depending on the nature of the hydrate.
The different approaches to characterize hydrous and anhydrous phases, especially with respect to thermodynamic stability are outlined and different classification schemes for hydrates are presented. Different ways to monitor, whether a phase transition has taken place during manufacturing or storage of a drug product (tablet) are shown.

Keywords: hydrates; polymorphism; pharmaceuticals

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New Strategies in EXPO2009: Applications to Pharmaceutical Compounds. Rosanna Rizzi[a], Angela Altomare[a], Corrado Cuocci[a], Carmelo Giacovazzo[a], Anna Moliterni[a]. [a]*CNR-Istituto di Cristallografia, via G. Amendola 122/o, 70126 Bari, Italy.*
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The steps necessary to perform a crystal structure solution from powder data are the following: a) unit cell indexation; b) space group determination; c) crystal structure determination; d) crystal structure refinement. In the last years the development of new and powerful strategies has allowed to solve crystal structures of size and complexity forbidden for old techniques. In the EXPO2009 program new approaches have been introduced, aiming at making easier and straightforward the *ab initio* crystal structure solution from powder diffraction data. They concern:
1) The unit cell indexation. A new indexing procedure has been introduced, particularly optimized for the triclinic system with a new global figure of merit for recognizing the correct unit cell. The procedure is also able to automatically estimate the most probable extinction group.
2) Space group determination. The use of the joint probability distribution method has been used in combination with the automatic control of the experimental pattern.
3) Crystal structure determination. A recent theory aiming at reducing the effects of the limited resolution in the electron density maps has been implemented in EXPO2009.
5) MAD technique. The method of joint probability distribution function, has been applied to powder data to find the anomalous scatterer substructure.
To manage organic crystal structures new strategy in direct space, combining Direct Methods and Simulated Annealing approaches, has been implemented. Over the past few years, a growing number of crystal structures of organic and particularly pharmaceutical compounds have been solved using these real space techniques. Knowledge of crystal structure is crucial for fully understanding and optimizing the pharmaceutical properties and in last years the characterization of all accessible polymorphs of molecules is important for pharmaceutical company for patenting motivation etc.
Some interesting results, obtained with EXPO2009 on pharmaceutical compounds, will be shown.

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Keywords: powder; pharmaceutical compounds; structure solution

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Multicomponent Crystals in the Development of New Solid Forms of Pharmaceuticals. William Jones. *University of Cambridge/Chemistry/Cambridge-UK.*
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Recent interest has centered on the use of multicomponent crystals (cocrystals) as a valuable alternative strategy in the development of new solid forms of pharmaceutical molecules. The use of these multicomponent crystals is particularly useful when standard methods such as salt formation is not possible or does not provide appropriate benefit. In this lecture I will summarize the strategies that are available for preparing cocrystals and in particular I will discuss the role of hydrogen bonding as a reliable means for choosing appropriate cocrystal formers since screening amongst all the possible combinations will be important. In our work we use a variety of techniques including dry and liquid assisted grinding. I will also give examples that have now become available that demonstrate that these multicomponent solids do in fact offer attraction in the development of new solid form pharmaceuticals.

Keywords: cocrystal; crystal engineering; crystalline pharmaceuticals

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Modeling Single Crystal Diffuse Scattering on Polymorphs of the Drug Benzocaine. Eric J. Chan[a], T. Richard Welberry[a], Aidane P. Heerdegen[a], Darren J. Goossens[a]. [a]*Research School of Chemistry, Australian*