MS32-01 **Solid Form Deisgn of Pharmaceutical Products.**
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The solid form of the Active Pharmaceutical Ingredient (API) in medicines can often take one of several forms. Identifying the most appropriate solid form is a crucial aspect of drug design and development due to the direct influence form has on the quality and performance of the drug product. Salts, co-crystals, polymorphs and hydrates of the API itself may be required to achieve the desired properties and to enable the robust manufacture of the drug product. The use of databases, informatics based tools and computational models can be used to assess solid form suitability and ultimately to design the optimum solid form in order to achieve these goals. Here the role of knowledge derived from databases and computational modelling in the development of pharmaceutical drug candidates will be illustrated using examples with a focus on designing desired traits into the drug product.

Keywords: design; pharmaceutical; informatics

MS32-02 **Improving the quality of protein-ligand complex structures.**
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The determination of protein-ligand complex structures is a complicated and involved process. The ligand position in the resulting structural model is the outcome of the interplay between many factors. The most critical step is the collection and processing of good experimental diffraction data. This must be followed by a careful refinement of the protein model and production of difference density to assess whether the ligand has bound sufficiently to give rise to interpretable electron density. Use must then be made of prior knowledge of ligand stereochemistry [1], for instance based on CSD structural information [2], to fit the ligand into its density and then refine a final structural model for the complex. The fitting process can be accomplished either manually or by means of an automated tool. Sub-optimalities or errors in any of these steps can lead to poor ligand structures in the complexes, and indeed Liebeschuetz and co-workers have estimated [3] that more than 20% of ligand structures in the PDB have questionable stereochemistry when assessed against the CSD. Examples from the PDB that demonstrate problems at each of the stages will be shown. The possibility of correcting errors in the PDB archive by submission of "re-refinement" results from BUSTER will be discussed [4].

[1] Grade webserver (http://grade.globalphasing.org)
[2] Bruno, I.J., Cole, J.C., Kessler, M., Luo, J., Motherwell, W.D., Purkis, L.H., Smith, B.R., Taylor, R., Cooper, R.I., Harris, S.E., Orpen, A.G. (2004) *J. Chem. Inf. Comput. Sci.* **44**, 2133-2144.
[3] Liebeschuetz, J., Hennemann, J., Olsson, T., Groom, C.R. (2012) *J. Comput. Aided. Mol. Des.* **26**, 169-183.
[4] Smart, O.S., Womack, T.O., Flensburg, C., Keller, P., Paciorek, W., Sharff, A., Vonrhein, C. Bricogne, G. (2012). Acta Cryst D68, 368-380.

Keywords: refinement methods; protein ligands; structural accuracy.