Poster Presentation

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24 hours – High-Throughput Crystal Structure Production

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In the pharmaceutical industry crystal structures of low molecular weight compounds are analyzed for a variety of reasons: absolute structure determination, proof of constitution, characterization of different polymorphic forms, obtaining three-dimensional models as starting points for the study of structure-activity relationships, etc. Not for all purposes highly redundant, high-resolution data sets are needed; this thought, together with the purchase of a new hybrid pixel detector which can be operated in a very fast shutterless mode, initiated the idea to test how many useable crystal structures we can produce within 24 hours. Our goal was to invest as little effort as possible and to set up an automated process with minimal human intervention but a maximum chance of success which we defined as getting to a correct final result providing useful information, e.g., is it the correct compound? Is the sample chiral or racemic? Which crystal would be the best one for a full data collection? Is it a new polymorph? We selected a data collection protocol which yields an interpretable data set up to 1 Å resolution in less than 10 minutes, the diffraction images are indexed and processed using an in-house script arching over the necessary individual XDS steps, followed by space group determination (XPREP) and structure solution/refinement (SHELX). First results and findings of our experiment series will be presented and the adjustable parameters will be discussed. Ideas to adapt and improve the process will be offered.

Keywords: high-throughput crystal structure analysis, pharmaceutical crystallography, data collection and processing