

**PHARMACEUTICAL POWDER X-RAY DIFFRACTION :  
FROM DESIGN TO FINAL SELECTION OF A DEVELOPABLE MATERIAL**

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During the development of a drug compound, the material selection process can't be missed. This is mostly due to the potential impact of the material on *in vivo* absorption and its variability, crystallization process and formulation : Drugs are materials ! To save time and increase chances of success into the selection and characterization process of relevant material candidates, XRPD can play a major role.

The first part of the talk will focus on the use of XRPD during the material selection strategy of the drug substance from early phase until freezing of the isolation steps of the process. Several examples will stress how XRPD can help select the right material, from crystallinity evaluation until in-depth structural and physical characterizations. We will see that *ab initio* powder pattern indexing (a good compromise between time, amount of substance used and relevance of results) is often the cornerstone of this strategy. Moreover, the objective being the knowledge of the most thermodynamically stable phase under ambient conditions, XRPD can play another major role in the elaboration of the phase diagram: volume changes can be evaluated from precise anisotropic thermal expansion XRPD studies and can then be combined with calorimetric data to determine the stability domain (according to Gibbs) for each identified phase through application of fundamental thermodynamics rules.

The second part of the talk will be exemplified with challenging case studies, among which Zopiclone and Fananserine. Zopiclone will stress the role of chirality during solid state study and influence of water vapour pressure, while Fananserine will point out the conformational polymorphism case with 4 known forms. The synergy of crystallography and thermodynamics will demonstrate its efficiency to help in the design and the selection of the right and fast developable candidate as well as to provide state-of-the-art data for patents and towards regulatory authorities.