Exploring high-throughput synchrotron X-Ray powder diffraction for the characterization of pharmaceuticals

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X-Ray Powder Diffraction (XRPD) is a popular method in pharmaceutical industries to characterize drug substances and drug products during their development [1, 2, 3]. While most of XRPD measurements are still performed on laboratory instruments, the use of Synchrotron-XRPD is an alternative which offers distinct advantages such as higher brightness, tunable photon energy, and a structured time profile. Nevertheless, due to the operational complexity, limited accessibility, and higher costs associated with conventional synchrotron measurements compared to laboratory instrumentation, synchrotron XRPD (S-XRPD) is at present primarily used for advanced troubleshooting purposes only.

In recent years, High-Throughput (HT) systems have emerged as a viable alternative bridging the gap between traditional laboratory instrumentation and the aforementioned conventional synchrotron measurements utilizing capillary setups. This advancement became feasible thanks to recent progress in beamline instrumentation, detectors, and data processing strategies. HT systems benefit from the advantages of synchrotron sources, while accelerating data collection, streamlining sample preparation and data processing, thereby reducing costs. A notable example of such a system has been recently developed at the Material Science beamline of the Swiss Light Source [4]. This system can produce high-quality patterns that rival or surpass the best laboratory-XRPD results, all within an acquisition time of less than 5 seconds, i.e. orders of magnitude faster than laboratory-XRPD. Such advancements hold the potential to shift perceptions of S-XRPD, expanding its practicality for routine screening purposes.

In this presentation, we will provide an overview of the HT system and guide the audience through various case studies involving organic compounds. We will compare XRPD patterns obtained from both laboratory equipment and from the HT system. In addition to qualitative analysis, we will also discuss applications of the HT system for structural analysis of several pharmaceutical compounds. Finally, we will present first results of our investigations of the use of the system for quantitative analysis and discuss performances and limitations to quantify small traces based on *ad-hoc* calibration curves, examining factors such as the achievable levels of detection and quantification, as well as the reproducibility and reliability of quantification.

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[4] Reinle-Schmitt, M., Šišak Jung, D., Morin, M., Costa, F. N., Casati, N. and Gozzo, F., (2023). *International Journal of Pharmaceutics: X*, *Rev.* **6**, 100221.