Drug Development

CASE STUDY

Pushing the detection limits of drug characterisation

Drug products are manufactured to an extremely high standard to maintain product safety when taken by patients. Specifications used throughout the manufacturing process cover not only the drug itself, but also the level of potential impurities (chemical, solvent, or polymorph), which are set to limits that are monitored by regulatory bodies to uphold safety and product quality requirements.

X-ray powder diffraction is a key analytical technique in the pharmaceutical industry for characterising drug compounds. This is used for throughout the development process to fingerprint compounds and quantify impurities.

GlaxoSmithKline

The Challenge

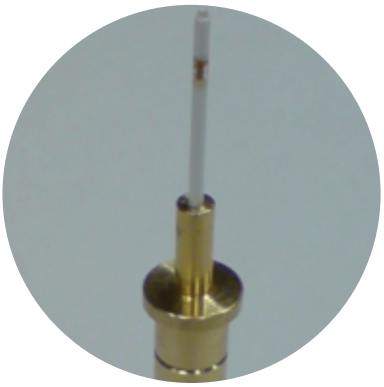
GSK development scientists were working on the detection limit for the presence of a solvate within a manufactured drug batch. This limit was necessary to develop confidence that solvent in the process was kept to a minimum.

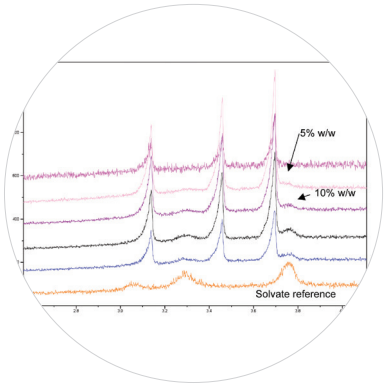
The crystalline development form was produced by desolvation, but residual traces of a disordered/poorly crystalline solvate remained, which required monitoring to maintain the regulatory specification. The poor crystallinity of the solvate broadens the diffraction peaks making it very difficult to quantify in low amounts. Using laboratory based diffractometers, the detection limit of this form in the mixture was 15% w/w and it was difficult to obtain improved

The Solution

Diamond beamline I11 is designed to provide high resolution X-ray powder diffraction data (both spatial and temporal) with rapid data collection and the brighter source delivers exceptional count statistics. The experiment required careful setup as this sample was susceptible to degradation in the X-ray beam.

The sample was flash cooled to 90K and the data collected for 1 minute with the capillary continuously stepped along its rotation axis to collect repeat scans free of degradation. Using the high spatial resolution mode, the diffraction peaks measured were sharper and therefore better defined than those obtained using the laboratory source. The new diffraction pattern allowed for better discrimination of the two drug versions in the mixture lowering the detection limit to around 10%, with the potential to achieve 5%. Typical manufactured batches were found to contain less than 10% w/w solvate.





The Benefits

This experiment has shown that the manufactured batches contain a limited amount of the solvate material and that the current limit of detection is suitable for specification. The use of this national facility demonstrates GSK's commitment to using the best science to answer important structural questions.

"Without the use of I11, we would not have been able to reach these detection limits that have led to greater understanding and control over the solvate material, thereby allowing us to have confidence in the reproducibility of our manufacturing process."

Dr Matthew Johnson, GlaxoSmithKline

For further information

Diamond Industrial Liaison Team

+44 1235 778797

industry@diamond.ac.uk

diamond.ac.uk/industry

@DiamondILO