



	PARTICULAR EQUIPMENT	TEAM WORK	QUALITY DATA	FLEXIBILITY	TRANSFER AND DEVELOPMENT
XRD	XRD		X <ul style="list-style-type: none"> <li>Quantitative method</li> <li>Critical importance to the product</li> <li>Subject to separate review</li> </ul>		X <ul style="list-style-type: none"> <li>Method supplied</li> <li>Repeated with multiple technicians</li> <li>Requirement to match sophisticated blending technique</li> </ul>

## TRANSFER AND VALIDATION OF A QUANTITATIVE POWDER X-RAY DIFFRACTION METHOD

### BACKGROUND

The client needed to transfer and validate a method to quantify the level of crystallinity in both an API starting material and the related finished drug product, which comprised a mixture of the API with both crystalline and amorphous excipients. Both the starting material and the drug product had the potential to contain a proportion of amorphous API as an impurity; this was highly undesirable in terms of product safety and efficacy. A very tight specification for acceptable levels of crystallinity was set by the client; hence, method precision and accuracy were crucial. Methods transfer and data sets were subject to client review and approval.

### EXECUTIVE SUMMARY

The client asked us to work with them because collaboration with a local company in the US had resulted in an overly-complicated and non-cost effective method for quantitative crystallinity determination. In addition, they were wary of becoming too reliant on a single supplier using a single type of diffractometer, and wished to establish a methodology for readily transferring analysis between instruments and laboratories.

### OUR APPROACH IN MORE DETAIL

Our support was based around the use of our cGMP-compliant Bruker-AXS D8 Advance X-Ray Diffractometer, and our previous experience in developing XRD methods for quantitative crystallinity determination.

#### Method Transfer

The client supplied a range of standard materials including a nominally 100% API standard, a 100% amorphous API standard and samples of the inactive excipients. In addition, X-Ray peak intensity and position standards were sourced from NIST (National Institute of Standards and Technology) and Bruker-AXS respectively. An



internal standard was also supplied (lithium fluoride) for incorporation into all test and calibration samples.

Initially, method development focussed on transferring the existing method from the client's instrument to our instrument. In addition to ensuring that our instrument was configured to generate comparable results in terms of relative peak intensity and position, it was necessary for our team to understand and successfully transfer the sophisticated powder blending technique required to generate test and calibration samples. The success of our method transfer – both the analytical and the blending methods – was demonstrated by analysis of multiple samples and sample replicates. A second analyst was also fully trained against the analytical and blending procedures and generated successful data.

The work carried out at Agenda1, particularly with reference to instrument configuration and relative peak intensities (e.g., with NIST standards), will allow this method to be more readily transferred between instruments in the future.