

XRPD CHARACTERISATION OF PHARMACEUTICAL SOLIDS - QUANTITATIVE PHASE ANALYSIS AND LOWER LIMITS OF DETECTION

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X-ray powder diffraction (XRPD) is a well-established technique in many areas of drug discovery, development, and manufacture. For well crystalline samples, detection, identification and quantification of crystalline phases down to 0.05% is possible when sample preparation and presentation is appropriate.

Although the physical nature of a specimen from which the X-ray powder-diffraction data are collected is seemingly simple, sample preparation is generally the source of most of the serious problems with accurate quantitative phase analysis. Frequent issues are:

- Preferred orientation
- Spotiness effect (too small sample amount and / or crystallite size \gg 5 microns)
- Inhomogenities / sample not representative for the bulk

Preferred orientation can be dealt with preferably by suited sample preparation and presentation or - to some degree - by software corrections. The same is not true for spotiness effects leading to random intensity errors which cannot be corrected for due to their random nature. For too large crystallites grinding is the only option, but this is frequently impossible for pharmaceutical solids as grinding may introduce phase transformations or prevents analysis of the final dosage form such as tablets. Experience tells, that more than 50% of all pharmaceutical samples submitted to our labs suffer from too large grain size, making reliable quantitative phases analysis and lower limit of detection analysis impossible.

The emphasis of this presentation is on the basics of sample preparation requirements, quantitative phase analysis and lower limits of detection for pharmaceutical solids. Basics as well as possibilities and limits will be discussed using several selected examples, with the focus on recognizing sample preparation related issues and how to avoid them.