

Determination of amorphous content.

Development of analytical methods and their limitations

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The final steps of chemical syntheses of solid drug substances are generally crystallisation followed by milling or sieving. A change of the crystalline form and/or the presence of an amorphous part may induce important changes concerning the physical properties (dissolution rate, bioavailability, stability, processability...) of the corresponding drug product. Therefore, it is mandatory for the development of robust processes to determine the influence of significant parameters, such as temperature, solvents of crystallization, drying, milling, storage conditions, on the crystalline form and on its crystallinity. For this purpose robust quantitative methods have to be develop and validate.

During the presentation we will go through the different analytical techniques available to detect and quantify amorphous part in drug substance. The benefits as well as the limitation of each analytical technique will be discussed.

A special focus will be done on thermal analytical techniques such as hyper-DSC or isothermal microcalorimetry which is the most commonly used to quantify low amount of amorphous content in drug substance.