Quantification of amorphous content in a Drug Substance

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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.

Microcalorimetry has been shown to be a powerful tool for the quantification of small amounts of amorphous in solid compound based on the measurement of the energy of crystallization.[1] Generally, the corresponding sample is subjected to various relative humidities, but any organic vapour can also be used and should have a similar effect on the crystallisation behaviour of the amorphous part.[2, 3]

This communication will discuss the applications of different organic vapours in microcalorimetry to induce recrystallization of amorphous part in drug substances. The selection of the atmosphere used to induce recrystallization according to the amorphous content in the sample will be emphasized by using a selected example. Data including validation for a robust analysis method will be presented.

[1] M. ANGBERG ; *Thermochim. Acta*; **248**; pp. 161-176, 1995
[2] H. AHMED, G. BUCKTON, D: A: RAWLINS; *Int. J. of Pharma.*, **130**, pp. 195-201, 1996
[3] K. KAWAKAMI, T. NUMA, Y. IDA; *J. of Pharma. Sci*., **91**, pp.417-423, 2002