Comparison of quantitative methods for analysis of polyphasic pharmaceutical

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The chemical industrial development in pharmaceutical industry is faced with the acceleration of the development time of new medicines and with harmonization guidelines which are required by health authorities for worldwide registration.

In development the choice of the solid phase to be developed as drug substance and as drug product is done very early in order to avoid delays due to new development, bioequivalence studies and upscale has to be taken into consideration since synthetic processes will be optimized from the first mg material to the production amount in tons range.

Adequate very sensitive quantification methods are needed for the development and are also now required for the monitoring of undesirable solid form (s) as routine tests. Limit of detection methods are often not sufficient.

The pre-requisite for quantitation are selectivity, sensitivity and most important the proper definition of standards, what is a challenge for metastable forms.

Several methods are available, thermal analysis and calorimetry, spectroscopy (e.g. FT-IR ad Raman), X-ray diffraction. The different steps and problems to be solved are discussed.

Examples illustrate the different techniques and compare their possible use.