

# Drug Substance in Drug Product: Solid State Identification and Particle Size Determination in Tablets

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The solid state form (polymorphs, pseudopolymorphs) as well as the particle size have a huge impact on properties and behaviour of an active substance. Because differences in the crystal structure may influence the efficacy and safety of a medicament authorities demand recently information not only on the polymorphic form of the pure drug substance but also in the drug product [1]. A second important issue is patent protection or the prolongation of such protection by process patents describing special solid state properties as polymorphic forms or particle size. For both, it is necessary to have analytical methods which are able to determine the polymorphic form as well as particle size of a drug substance in a drug product.

The applicability and limitations of several methods (X-ray powder diffraction, DSC and Raman microscopy) for the identification and quantification of solid state forms in solid or a semi-solid pharmaceutical dosage forms will be shown on the basis of several examples.

Several methods exist which are able to determine the particle sizes in a matrix, like Raman microscopy, Time of Flight Secondary Ion Mass Spectroscopy (TOF-SIMS), FTIR and NIR microscopy and microthermal analysis ( $\mu$ TA) or to separate the substance of interest from the matrix and determine the distribution by conventional methods of particle size determination. Results of a feasibility studies using Raman microscopy and TOF-SIMS for the differentiation of non-micronized and micronized drug substance in tablets as well as the determination of the particle size distribution of the drug substance in these tablets will be presented.

## References

- [1] ICH Topic Q6A, Specifications: Test Procedures and Acceptance Criteria for New Drug Substances and Drug Products: Chemical Substance