

Challenging analytical development for polyphasic new entities. Case studies

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The relevance of proper selection and monitoring of the polymorphic form of new entities has an impact on the strategy and on the expertise in the analytical development of new entities including salt selection(1-3). Since a great number of compounds have acid or basic properties even several salts with the same ion may co-exist. Therefore the characterization of polymorphs and solvates of all salt forms have to consider polyphasic systems for the salt selection, the manufacture and the storage of the drug substance and the drug product.

The analytical laboratory needs several techniques which should deliver proper information and allow to develop quantitative methods for process development. Batch monitoring as well as technical support for registration require validated methods in a GMP environment.

The analytical methods should be able to detect phase mixtures and in particular high sensitivity is required to detect seeds which may act differently from sample to sample in case of kinetic transformation.

X-ray diffraction with crystal modelling and thermal analysis and microcalorimetry as well as combined techniques with robotic are the most efficient techniques. Spectroscopic and microscopic techniques find also their applicability in specific cases.

Some examples will focus on the use and development of proper analytical methods depending on the project needs.

Salt selection in polyphasic systems

Development and monitoring solvate/hydrate polyphasic substances

Development of polyphasic hydrates

Rational selection criteria for two “iso-energetic” drug substances and quantitation

Quantitation of amorphous phase produced by milling/processing

Detection of crystalline content in a drug product

References

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