

Services within Solid State Development of Pharmaceuticals

Introduction

The solid state properties of your active pharmaceutical ingredient / drug substance (API / DS) may impact several critical drug parameters such as solubility, bioavailability and stability. In particular, if your API / DS is a class II (or class IV) compound according to the Biopharmaceutics Classification System (BCS, ref 1), bioavailability can not only be improved by optimized solid form selection but also by, for example, reducing particle size. Using a combined approach, XSpray Microparticles offers its extensive knowledge in solid state development of pharmaceuticals to improve the performance of your final product.

Depending on your particular needs and requirements we provide salt and/or polymorph screens, optimization of particle size and physical form, characterization of your API / DS, or consultation in a specific question.

Our extensive experience in solid state science from the pharmaceutical industry guarantees that the produced results meet regulatory requirements as well as your project-specific needs and timelines.

Screening services

XSpray can perform screening services to optimize solid form selection. The different solid forms that can be selected include:

- Salts
- Hydrates
- Polymorphs (same chemical composition but different solid state arrangement of molecules)
- Cocrystals (incorporates a pharmaceutically acceptable guest molecule into a crystal lattice along with the API / DS)
- Amorphous form(s)

Both the screening and following evaluation are carried out in a tear-based systematic approach. The result is, in most cases, a trade-off between different important properties, such as; solubility, dissolution rate, bioavailability, hygroscopicity, stability, purity, yield, crystallinity and mechanical properties.

The outcome of such a screen can have further advantages in terms of intellectual property.

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XSpray's RightSize™ Technology for enhancing bioavailability

Beside solid form selection, other methods to improve bioavailability for class II (or class IV) compounds include particle size reduction and the use of solid dispersions. RightSize™ Technology produces high quality particles in the nm or low µm size range. Furthermore, it is also well suited for co-precipitation of drug substance with a variety of excipients including solid dispersions. For further details about RightSize Technology, see separate documentation.

Services to increase solid state stability

Stability is of particular concern during the development of solid biopharmaceutical and other amorphous products. The shelf life of an amorphous product can be substantially increased if solid state properties are optimized during formulation development.

Small molecules

Pharmaceutical solids frequently have several polymorphs and hydrates. The presence of multiple solid forms of your API / DS may give rise to unexpected instability issues if it is not addressed early on during development. XSpray can address this issue in different ways:

- Conversion to the thermodynamic stable polymorph at room temperature
- Determination of the relative stability between polymorphs and/or hydrates at different temperatures and determining if polymorphs are monotropic or enantiotropic related
- Perform non-GMP solid state stability studies at +4°C, 25°C/60% RH and 40°C/75% RH, respectively

Biopharmaceuticals

XSpray can provide support during solid state development of biopharmaceuticals and other amorphous products:

- Support during optimization of the freeze-drying cycle and determination of glass transition temperature of the freeze-concentrated phase (T_g)
- Support during selection of excipients and their concentrations and determination of the glass transition temperature (T_g)
- Characterization and quantification of the different solid state forms (crystalline and amorphous) which constitute the freeze-dried product
- Assessment of critical water content in freeze-dried samples
- Assist in the material selection and handling of container stoppers
- In certain cases, determination of the transition temperature, T_m. for thermal denaturation of proteins in aqueous formulations

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Characterization

XSpray Microparticles has the required expertise and solid state instrumentation to characterize your API / DS and deal with most aspects of pharmaceutical solid state development. Analyses that can be carried out by XSpray Microparticles include:

- X-ray Powder Diffraction (XPRD)
- Dynamic Vapor Sorption (DVS)
- Scanning Electron Microscope (SEM)
- Differential Scanning Calorimetry (DSC)
- Thermogravimetric analysis (TGA)

Services within regulatory aspects of solid state development

Regulatory authorities have attended to polymorphism in the International Conference on Harmonization (ICH) Guideline Q6A (ref 2) and in background information from the FDA's advisory committee for pharmaceutical science meeting, October 2002 (ref 3).

XSpray can address polymorphism in pharmaceutical solids in a regulatory context and can perform and write the solid state part of your Investigational New Drug Applications (INDs) and Investigational Medicinal Product documentations (IMPDs).

Contact

In addition to the services outlined above, Xspray Microparticles can also perform specific services according to your particular needs. For example, analysis of a specific sample, characterization of a particular batch or providing consultation with regard to a specific question.

For further inquiries, please contact:

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