PolyCrystalLine

experts in crystal forms

R&D Services

- Polymorphs, Salts, & Co-Crystals
- Solid Form Selection
- Stability & Formulation Studies

www.polycrystalline.it

Contents

Equipment

COMPLETE LIST OF INSTRUMENTATION
AT YOUR SERVICE

SPECTROSCOPY
- FT-IR (Fourier Transform Infrared Spectroscopy)
- FT-RAMAN (Fourier Transform RAMAN Spectroscopy)
- ICP-MS (Inductively Coupled Plasma Mass Spectrometry)
- PSD (Particle Size Distribution)
- SEM (Scanning Electron Microscopy)
- Solid-state NMR
- UV-Vis Spectrophotometer

POWDER DIFFRACTION
- XRPD
- VT-XRPD (Variable Temperature XRPD)
- XRPD Single Crystal

THERMAL ANALYSIS
- Differential Scanning Calorimetry (DSC)
- Evolved Gas Analysis (EGA)
- Hot Stage Microscopy (HSM)
- Melting Point
- Thermogravimetric Analysis (TGA)

MOISTURE CONTENT CHARACTERIZATION
- EasyH2O
- Karl Fischer
- Dynamic Vapour Sorption (DVS)

LIQUID CHROMATOGRAPHY
- HPLC (High-Performance Liquid Chromatography)

Quality

CRYSTALLISATION DEVELOPMENT
AND SCALE-UP

CHEMICAL SYNTHESIS REACTORS EQUIPPED WITH pH, TEMPERATURE, FBRM AND TURBIDITY SENSORS
- EasyMax 102
- Atlas Syrris
- Glass reactors equipped with remote control box

CRYSTALLISATION SYSTEM FOR
MEDIUM-THROUGHPUT SOLID-STATE RESEARCH
- CrystalBreeder

750 m²

OF LABORATORIES
AND OFFICES

GMP

COMPLIANT ANALYTICAL
LABORATORY

What makes us different?

PolyCrystalLine has more than 10 years of experience in solid state design and control. Our comprehensive range of solid state services and know-how will help strengthen the success of your product.

EFFICIENCY
- Working closely with our clients allows us to optimize time and results

RELIABILITY
- We are committed to continual improvement based on sound science and the use of modern technologies

EXPERTISE
- Highly trained team of chemists and analysts with more than 10 years of experience in the development and optimization of APIs crystallisation

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R&D Services

Our extensive experience has led our researchers to develop specific and flexible protocols for the study of crystalline forms. These can be adapted to meet the needs of the pharmaceutical industry and solve any kind of issues related to APIs. We are able to satisfy the most various research needs and budget requirements, ranging from elementary to in-depth screening of APIs.

Every experiment is carried out manually by highly-trained researchers, thus avoiding the inaccuracies of mechanised High-Throughput Screening (HTS).

All protocols can also be carried out on highly potent and cytotoxic products.

Polymorph Screening

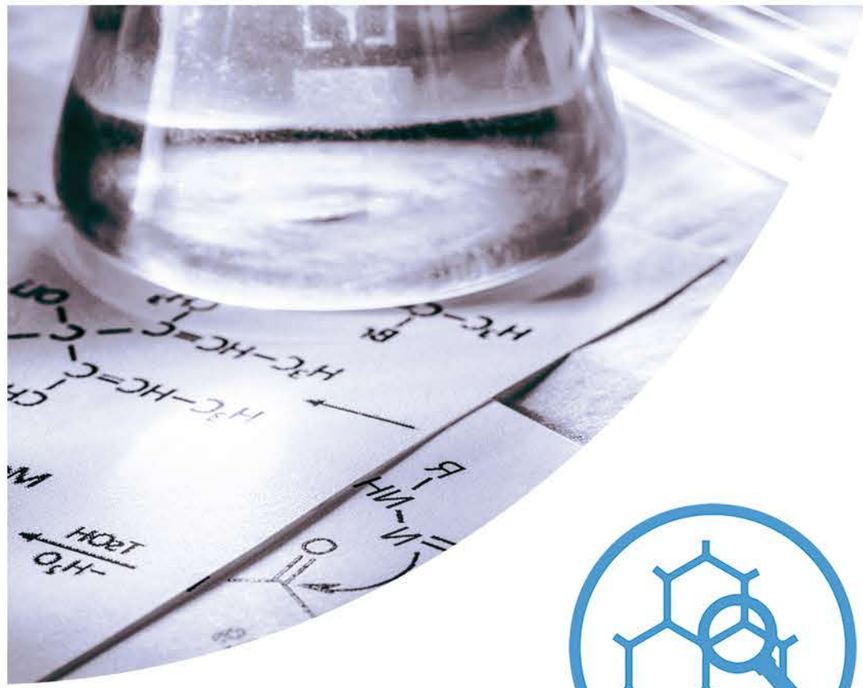
Polymorphism is very common among pharmaceutical substances and the regulations require, when appropriate, specifications characterising the drug substance so as to assure its bioavailability.

Polymorphic form may profoundly affect the pharmaceutical stability, dissolution rate, solubility, bioavailability, and manufacturability from solid dosage forms or suspension drug products.

We have developed a reliable workflow based on our experience on crystallisation, which have been proven to produce new polymorphs with the following key steps:

"By the time of an NDA submission, the applicant should have established whether (or not) the drug substance exists in multiple solid-state forms."

FDA drug substance guideline



Step 1. Patent and literature search

Step 2. Starting material characterisation

Step 3. Solvent screening

Step 4. Polymorph screening

Step 5. Characterization of new forms

Salts and Co-Crystals Screening

The development of a salt or a co-crystal can be a strategic choice to optimize the solid state properties of an API, because their formation can deeply influence its properties, having impact on:

- Bioavaibility (i.e. dissolution rate and solubility)
- Manufacturability (i.e. chemical and physical stability or mechanical properties)
- Shelf life (i.e. hygroscopicity and stability)
- Taste (i.e. to mask unpleasant taste of API instead of coating or inclusion complexes)

We can explore the formation of API salts and co-crystals with combined programs targeted to quickly identify the solid form with optimum properties.

Step 1. Patent and literature search

Step 2. Characterisation of sample as received

Step 3. Salts and co-crystals screening

Step 4. Characterization of new forms

Solid Form Selection

For the selection of the optimal API, several solid forms may be available from one molecule.

PolyCrystalLine provides an effective form selection programme that will lead to a better orientation and targeted selection of the optimum solid form of a certain pharmaceutical molecule with requested technological and functional properties.

We focus on the selection of the best form of your compound for development and manufacture.

Step 1. Process scale-up to 2g

Step 2. Characterisation of all forms after scale-up

Step 3. Comparative dissolution test

Step 4. ICH stability test of all forms

Step 5. Selection of the optimal crystal form

Amorphous Studies

In some cases, the amorphous form is the preferred one due to inherent advantages like increased solubility and potential higher bioavailability, making the amorphous form a promising approach for delivering poorly soluble drugs.

However, its physical and chemical instabilities, and to date the prediction of physical and chemical stability of drugs in the amorphous state still proves challenging.

PolyCrystalLine has extensive experience to produce and characterise amorphous materials using several techniques, also evaluating the conditions of conversion into the crystalline form with adaptable and flexible protocols.

Hydrates Screening

Crystalline materials are well known to be capable of forming crystal hydrates, arrangements in which one or more molecules of water are incorporated into the crystal lattice.

Having the knowledge of the hydrates behaviour in the polymorph system of an API is the first step in avoiding issues during the formulation or the production process.

With over 10 year of experience PolyCrystalLine is able to study and optimise hydrate crystalline forms, using dedicated protocols and methodologies aimed to identify various degrees of hydration and to characterise the possible interconversion through the different forms identified and their stability.

Formulation Studies

It is important to understand that a drug contains many other substances additional to the API itself (excipients), and studies must be carried out to ensure that the API is fully compatible with them.

Preformulation involves the characterization of a drug's physical, chemical, and mechanical properties in order to choose what excipients should be used in the preparation of the final product.

Formulation studies then consider different factors (i.e. particle size and polymorphism) because all of these can influence the bioavailability and hence the activity of a drug. Finally, the drug must be combined with inactive additives ensuring that its quantity is consistent in each dosage unit.

PolyCrystalLine offers tailor-made formulation studies to identify and select excipients with optimal solid state properties.

Stability Studies

The thermodynamic relationships between polymorphic forms is crucial and must be established carefully, because as drug crystallises from different conditions the kinetically favoured metastable polymorph appears first.

However, this metastable polymorph may undergo environmental induced transformation (most importantly temperature, pressure, light, mechanical stress and humidity) to produce thermodynamically stable form at its own expense, affecting important properties such as the ability to process and/or manufacture the drug substance and the drug product, as well as on drug product stability, dissolution, and bioavailability.

Therefore, a precise knowledge of the stability of crystal forms and their interrelationship is critical for formulation development.

Polycrystalline has developed an innovative strategy using tailor-made experiments to obtain information on the stability of drug substances.

Project Consulting and IP Protection

Before starting a R&D project an effective study of the state of the art is useful and advisable. This is possible thanks to our multiple electronic databases (i.e. crystallographic, journal publications, patent applications, and granted patents).

PolyCrystalLine advises and assists clients to determine the patentability of their inventions, avoid infringing other inventors' patents, avoid duplicating research and development effort, and gain intelligence on the innovative activities improving planning for business decisions.

Also, we help our clients to navigate through complex experimental design, parameter choosing, data interpretation and correlation addressing potential changes, which may occur during physical transformation. If an undesirable polymorph is uncovered in both scale-up or process transfer to other production sites, our experts will determine the root-cause and will suggest appropriate corrective actions.

We can optimize the characterization research focusing on a specific crystalline form, with the most desirable physical properties, guiding clients in choosing the optimal drug form.

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R&D Services

- Polymorph Screening
- Salts & Co-Crystals Screening
- Solid Form Selection
- Amorphous Studies
- Hydrates Screening
- Formulation Studies
- Stability Studies
- Project Consulting and IP Protection

Analytical Services

- cGMP Quality Control Testing
- Analytical Characterisation
- Crystalline Form Quantitation
- Structure Determination
- In Vitro Bioequivalence Testing (BE)
- Dissolution & Solubility Testing
- Dynamic Vapour Sorption (DVS)
- Method Development and Validation

Production Services

- APIs Synthesis
- Quality by Design (QbD)
- Process Scale-Up

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