PolyCrystalLine

experts in crystal forms

Analytical Services

- cGMP Quality Control Testing
- Analytical Characterisation
- Structure Determination

www.polycrystalline.it

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COMPLETE LIST OF INSTRUMENTATION
AT YOUR SERVICE

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- FT-RAMAN (Fourier Transform RAMAN Spectroscopy)
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- PSD (Particle Size Distribution)
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- Solid-state NMR
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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 m^2

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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experts in crystal forms

Analytical Services

A modular approach allows PolyCrystalLine to customise analysis methods in accordance to client's requirements, thus providing specific and effective solutions in compliance with Good Manufacturing Practice (GMP).

We can acquire existing methods and validate them in our laboratories.

Alternatively, PolyCrystalLine can provide method development and validation following ICH and GMP guidelines, then a complete method transfer will include exhaustive protocols and reports.

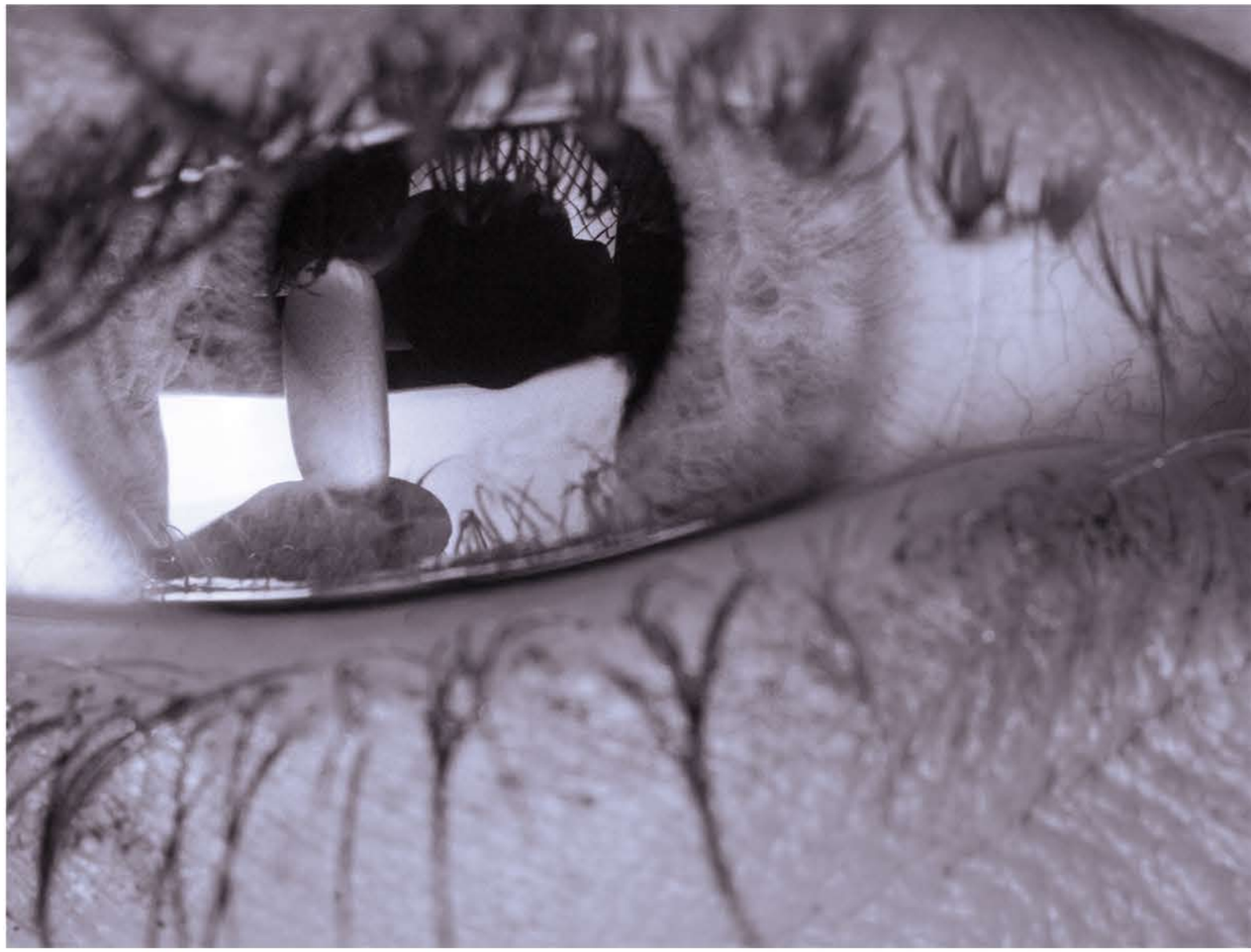
cGMP Quality Control Testing

PolyCrystalLine has been inspected and approved by AIFA (Agenzia Italiana del Farmaco), obtaining the Good Manufacturing Practice (GMP) certification for the following analytical techniques:

- XRPD
  The XRD pattern is the fingerprint of each polymorphic form. It is used to distinguish between amorphous and crystalline material and quantify the percent crystallinity of a sample
- FT-IR (Fourier Transform Infrared Spectroscopy)
  Detects functional groups and characterises covalent bonding information
- FT-RAMAN (Fourier Transform RAMAN Spectroscopy)
  Provides information on the physical form of the material

We can acquire existing analytical methods and validate them in our laboratories. Alternatively, PolyCrystalLine can provide method development and validation following GMP guidelines, then a complete method transfer will include exhaustive protocols and reports.

Quality assessment results are produced within 24/48 hours of receipt of the sample.



Analytical Characterisation

An in-depth knowledge of the API molecular and crystal structure is of great importance in order to understand its properties. Our well-equipped, state-of-the-art laboratories offer comprehensive testing services according to the pharmacopoeia and to client's specifications.

We can acquire existing analytical methods and validate them in our laboratories. Alternatively, PolyCrystalLine can provide method development and validation following ICH and GMP guidelines, then a complete method transfer will include exhaustive protocols and reports.

SPECTROSCOPY

Optical spectroscopy is used to identify the chemical composition of matter and to determine its physical structure. Also, one can use the unique collection of absorption bands to confirm the identity of a pure compound or to detect the presence of specific impurities.

- FT-IR (Fourier Transform Infrared Spectroscopy)
  Detects functional groups and characterises covalent bonding information
- FT-RAMAN (Fourier Transform RAMAN Spectroscopy)
  Provides information on the physical form of the material
- ICP-MS (Inductively Coupled Plasma Mass Spectrometry)
  Elemental determination
- PSD (Particle Size Distribution)
  Determines information about the size and range of a set of particles representative of a material
- SEM (Scanning Electron Microscopy)
  External morphology, chemical composition, and crystalline structure and orientation of materials
- Solid-state NMR
  Physico-chemical characterisation of materials
- UV-Vis Spectrophotometer
  Measures absorption in the ultraviolet-visible spectral region

POWDER DIFFRACTION

X-Ray Powder Diffraction (XRPD) is a rapid analytical technique primarily used for phase identification of a crystalline material and can provide information on unit cell dimensions. Once all the peaks in the diffraction pattern generated by a pure active ingredient have been indexed, a drug can be uniquely fingerprinted. The characteristics of the unit cell, together with its chemical composition, can also be used to predict the morphology and physical properties of a drug. Structural analysis using XRPD is particularly valuable for characterizing alternative forms of registered drugs when patents are about to expire.

- XRPD
  The XRD pattern is the fingerprint of each polymorphic form. It is used to distinguish between amorphous and crystalline material and quantify the percent crystallinity of a sample
- VT-XRPD (Variable Temperature XRPD)
  Permits the direct identification of crystalline phase as a function of temperature
- XRPD Single Crystal
  Provides detailed information about the internal lattice of crystalline substances, including unit cell dimensions, bond-lengths, bond-angles, and details of site-ordering

PolyCrystalLine provides and follows the transfer of the method developed where it is needed to perform the analyses within our company.

THERMAL ANALYSIS

Thermal methods measure the physical or chemical properties of a substance or a mixture as a function of the temperature or time whilst the sample is subjected to a controlled temperature program. Thermal data serve as an indicator of conformational stability, reaction-rates and composition of the sample. They are also useful for determining sample purity and water, carbonate and organic contents and for studying decomposition reactions.

- Differential Scanning Calorimetry (DSC)
  Measures how physical properties of a sample change, along with temperature against time
- Evolved Gas Analysis (EGA)
  The nature and amount of volatile products released by a substance are measured as a function of temperature whilst the substance is subjected to a controlled temperature programme
- Hot Stage Microscopy (HSM)
  Characterises materials as a function of temperature showing their transitions during heating
- Melting Point
  First impression of the purity of a substance
- Thermogravimetric Analysis (TGA)
  Determines a material's thermal stability and its fraction of volatile components by monitoring the weight change that occurs as a specimen is heated

MOISTURE CONTENT CHARACTERIZATION

In the pharmaceutical industry, it is essential to know the amount of water contained in the individual active ingredients and excipients of a drug in order to correctly predict its lifetime, stability and effectiveness.

- EasyH2O
  Selectively determines the water content in a sample by means of thermo-coulometric determination
- Karl Fischer
  Moisture determination based on the amount of reagent used to convert the water
- Dynamic Vapour Sorption (DVS)
  Provides detailed information about the uptake and loss of moisture of the material

LIQUID CHROMATOGRAPHY

Liquid chromatography is an analytical chromatographic technique that is useful for separating ions or molecules that are dissolved in a solvent.

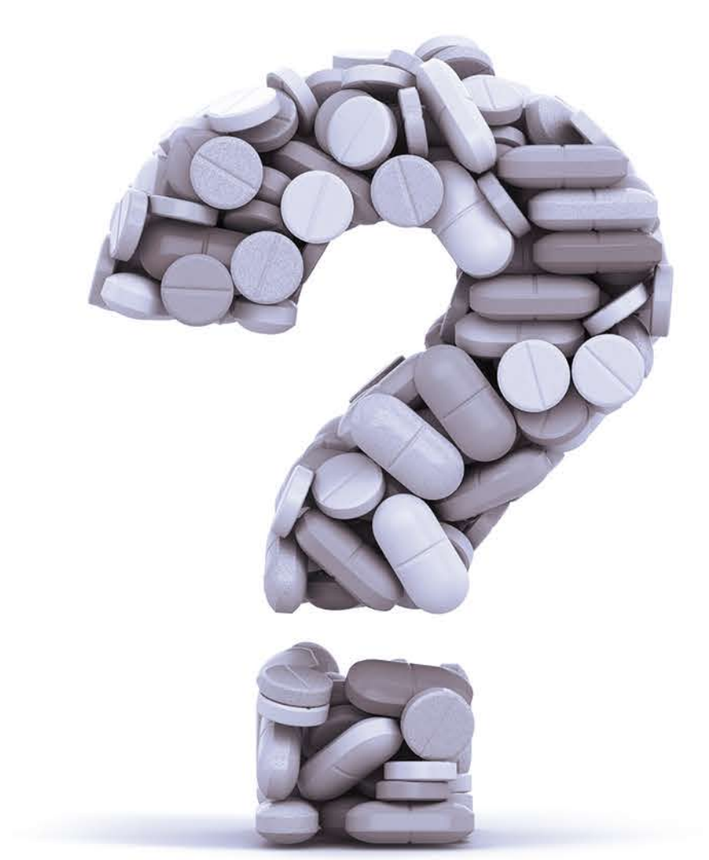
- HPLC (High-Performance Liquid Chromatography)

Crystalline Form Quantitation

Quantitation methods are validated in order to quantify specific crystal forms or amorphous content in API mixtures and tablets (formulated compounds). Percent crystallinity is an important parameter as it can influence the processing behaviour of a drug as well as its pharmacological performance.

Depending on the physical-chemical API characteristics the following analytical techniques are used to obtain high accuracy, specificity and sensitivity:

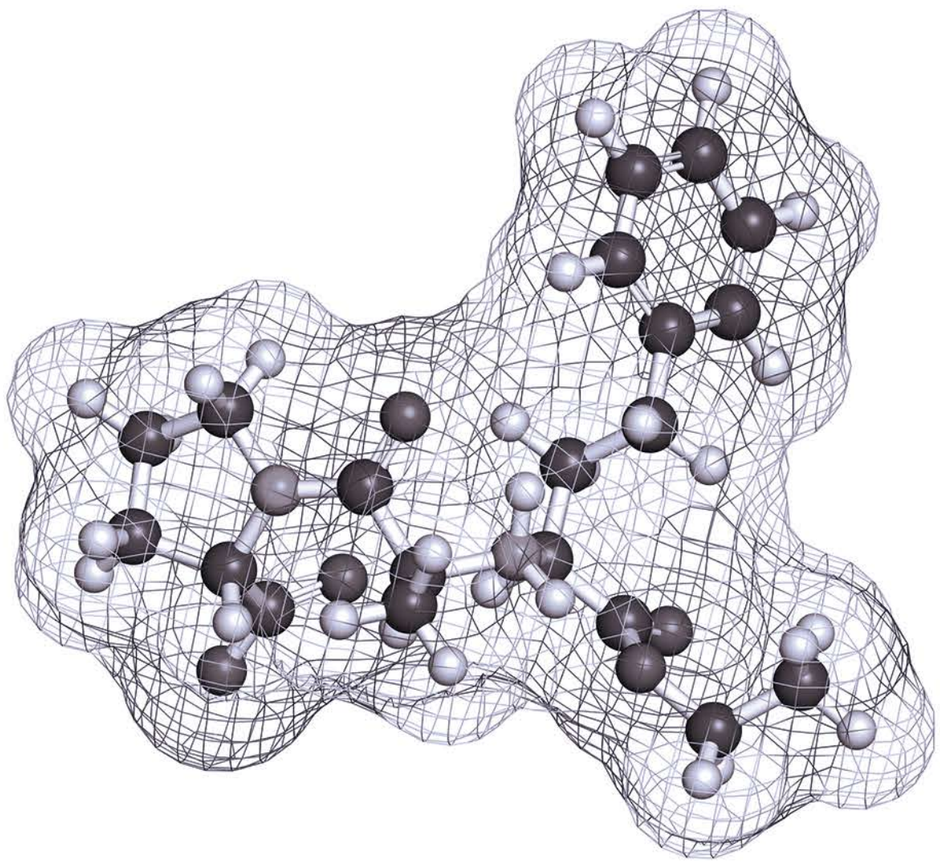
- XRPD
  The XRD pattern is the fingerprint of each polymorphic form. It is used to distinguish between amorphous and crystalline material and quantify the percent crystallinity of a sample
- XRPD Single Crystal
  Provides detailed information about the internal lattice of crystalline substances, including unit cell dimensions, bond-lengths, bond-angles, and details of site-ordering
- FT-IR (Fourier Transform Infrared Spectroscopy)
  Detects functional groups and characterises covalent bonding information
- FT-RAMAN (Fourier Transform RAMAN Spectroscopy)
  Provides information on the physical form of the material
- Differential Scanning Calorimetry (DSC)
  Measures how physical properties of a sample change, along with temperature against time



Structure Determination

An in-depth knowledge of the API molecular and crystal structure is of great importance in order to understand crystal properties (i.e. density, molecular packing, surface, etc.). Our crystallographic know-how allows us to determine API structure from single crystal analysis using Single Crystal XRPD to compute "error free" powder diffraction patterns for comparison with those measured on bulk materials thus assessing amorphous content. The calculated XRD pattern is also free from preferred orientation phenomenon and it is the best data to patent a new crystalline form.

A crystal structure can be determined from a powder diffraction pattern using the Rietveld method, but in most cases identifying the lattice type and dimensions of the unit cell is sufficient. Once all the peaks in the diffraction pattern generated by a pure active ingredient have been indexed, a drug can be uniquely fingerprinted. The characteristics of the unit cell, together with its chemical composition, can also be used to predict the morphology and physical properties of a drug. Structural analysis using XRPD is particularly valuable for characterizing alternative forms of registered drugs when patents are about to expire.



Dissolution & Solubility Testing

Dissolution tests are used to determine the dissolution rate of the active ingredients of solid dosage forms allowing the selection of the most suitable crystal form.

The thermodynamic solubility and dissolution rates of APIs are performed at different pH values, using a dissolution tester and methods as described in the "European Pharmacopoeia (2.9.3)".

In Vitro Bioequivalence Testing (BE)

In Vitro Bioequivalence studies are requested to determine rate/extent of absorption of each therapeutic moiety for potential generic products for which there is a Reference Listed Drug (RLD) approved for marketing, potential new drug products for which adequate clinical studies have already been conducted and reformulated drug products.

We provide in vitro bioequivalence studies of solid oral dosage forms following ICH guidelines and European Pharmacopoeia.

Dynamic Vapour Sorption (DVS)

The moisture sorption properties of drug formulations are recognised as critical factors in determining their storage, stability, processing and application performance. DVS can rapidly measures uptake and loss of moisture by flowing a carrier gas at a specified relative humidity over a sample, suspended within an ultra-sensitive digital microbalance.

DVS gives information about the solid-state changes occurring within the sample. The various mechanisms by which solids interact with water, and the important role played by the crystalline or amorphous form of the solid could also get analysed by using sorption method.

Method Development and Validation

PolyCrystalLine can be entrusted with your most sensitive projects for method development and validation of API's intermediates, raw materials and finished products. Our experience covers the full spectrum of pharmaceutical development phase I, II and III.

We can acquire existing analytical methods and validate them in our laboratories. Alternatively, PolyCrystalLine can provide method development and validation following ICH and GMP guidelines, then a complete method transfer will include exhaustive protocols and reports.

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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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