PharmaBlock

Crystal Engineering

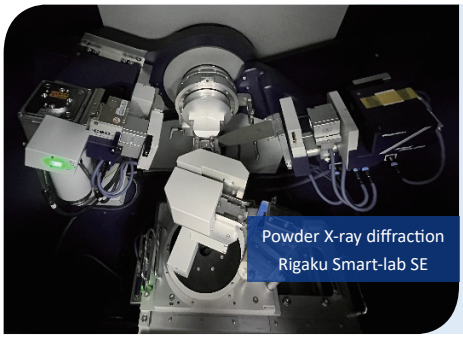
At PharmaBlock, we have a team of 30+ scientists dedicated to crystal engineering. Our work covers the entire pharmaceutical life cycle, ranging from studying the properties of PCC compounds to quickly selecting the best candidate drugs, and optimizing the process and quality of drug substance and drug product.

Phase	Development Objectives	Studies
Discovery (Lead to Candidate)	• A crystalline form of API with purification • A suitable form for PK and tox studies	• API characterization • Rapid form screen and selection include crystalline/salt/cocrystal • Rapid formulation screen
Early Development (DRF, GLP tox, Ph I & II)	• A suitable form and formulation to support GLP tox • Assess and select the most stable form and risk identification	• Crystal-form screening of the selected free form or salt • Solubilization and compatibility study
Late Development (Ph III, launch)	• The final form to support the pivotal study through product launch • Final API and DP manufacturing processes	• Comprehensive crystal-form screening • Form control in API and drug product manufacturing
IP/Life-Cycle Management	• Patent all important solid forms • Select the optimal form for new API manufacturing, new indications and formulations • Generics	• Comprehensive salt and co-crystal screening • Solid-form screening of reaction intermediates

What we can do?

Solid State Study and Pre-formulation Study

The discovery of API polymorphs and salt/cocrystal forms at all stages is an important consideration in the Pharmaceutical Life Cycle. Our routine screening, which utilizes high-throughput technologies, requires a minimum amount to provide quick identification of lead candidates. These candidates are then prepared for complete characterization.
We also provide a fast screen of solubilization formulation to support the Tox/DMPK study at an early stage of API development, especially for BCS II/IV.


Powder X-ray diffraction
Rigaku Smart-lab SE

Screen techniques

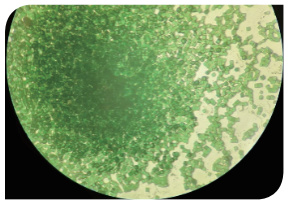
- Temperature cycling
- Slurry
- Cooling
- Anti-solvent
- Evaporation
- Grinding
- Compression

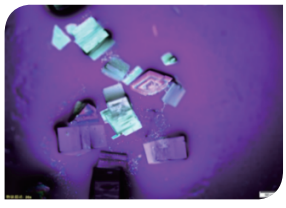
Complete physicochemical characterization of APIs

- Powder X-ray Diffraction (PXRD)
- Thermogravimetric Analysis (TGA)
- Differential Scanning Calorimetry (DSC)
- Dynamic Vapor Sorption (DVS)
- Scanning Electron Microscopy (SEM)
- Particle Size Distribution (PSD)
- Nuclear Magnetic Resonance (NMR)
- Polarized Light Microscopy (PLM)
- Solubility and bulk stability

Single Crystal Growth and Structure Identification

In addition to common methods for single crystal growth (e.g. vapor diffusion, liquid-liquid face diffusion, and evaporation), molecular chaperone technologies such as cocrystal agents, templates, and inducers, as well as MOF-based crystal sponge, are used for oil/gel-like compounds. These methods significantly improve the efficiency of single crystal growth, supporting the determination of chiral structure and analysis of crystal structure.





Crystallization Process Development

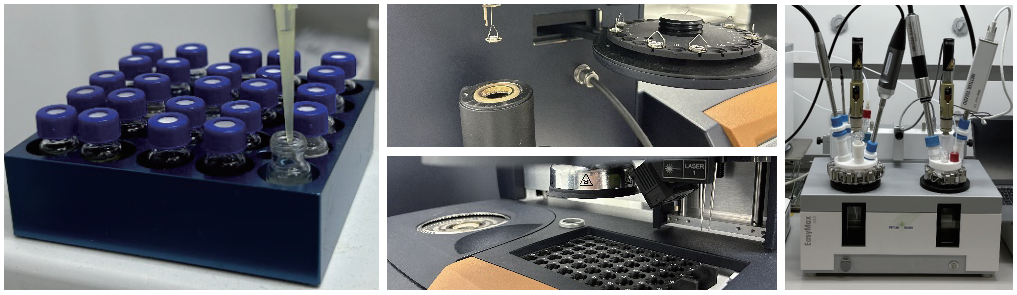
Crystallization is both science and art. By taking a quality-by-design approach, we offer crystallization process development to achieve reproducible, scalable, and robust high-quality solid. Our state-of-the-art instrumentation and experienced scientists provide this service from the lab to manufacturing.

Crystallization process considerations

- Solid form control
- Chemical purity and residual solvents
- Particle size distribution control
- Efficiency and yield
- Solubility and metastable zone width

PAT tool

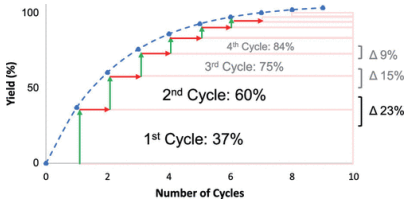
- FBRM-particle trace
- Raman-solid form
- Easy viewer-crystal habit and PSD

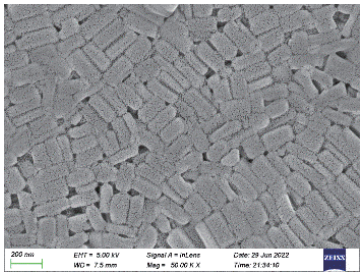


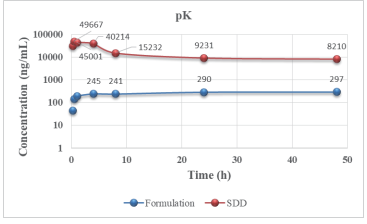
In addition to the classic batch-to-batch solvent-based crystallization process, we also focused on the development of new technologies, including sublimation, melting, and continuous processes.

Chiral Resolution

By combining high-throughput screening with our library of chiral reagents (comprising more than 100 types), we can identify and select the best solvent and chiral reagent to develop diastereomeric crystallization.
We developed a dynamic kinetic resolution (DKR) method that achieves a 85% total yield and 96% ee value for 10 kg in GMP manufacturing. This makes the process more efficient, environmentally friendly, and lowers PMI.







Supersaturation Drug Delivery System (SDDS)

For drugs with poor solubility, we provide a strategy for drug delivery called SDDS, which is typically based on Amorphous Solid Dispersion (ASD) and nano-suspension systems.
We first perform a fast screening of excipients and solvents to develop a formulation of SDDS, which is then scaled up for further evaluation of stability (bulk and chemical), solubility, and dissolution behavior. This ensures that the SDDS system performs optimally in PK studies.
Through thorough study of the SDDS, we have the ability to prepare samples from the laboratory to manufacturing scale.

SDDS method

ASD

- Spray drying
- Freeze drying
- Hot melt extrusion

Nano-suspension

- Ball milling
- High pressure homogenization(HPH)
- Microprecipitation method

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