

# Crystallization Development

From Screening to Kilogram Supply



Polymorphism Investigation

Form Selection & Process Design

Crystallization Process Optimization

Multigram to Kilogram Supply (GMP/non-GMP)

*A crystallization process for a non-specified pharmaceutical drug substance*

As the bulk properties of a drug substance can have enormous impact on the downstream processing properties (filterability, dryability, flowability) or formulation (bulk density, impurities), the development of a robust and scalable crystallization process is an essential step in drug development.

A crystallization process is also the most frequently used technique for purifying solid drug substances. Irrespective of whether the chemical or chiral purity needs to be enhanced, a specially designed crystallization process is the best choice for processing.

Solvias offers a seamless approach to design and optimize a robust and scalable crystallization process together with kilogram supply of API under GMP, if required.

### Polymorphism Investigation

- Determination of relevant polymorphic forms
- Evaluation of polymorphic transformations
- Identification of thermodynamic most stable form
- Identification of hydrates and solvates

### Form Selection & Process Design

- Determination of temperature-dependent solubility of relevant polymorphs
- Identification of metastable zone width
- Evaluation of different crystallization techniques (cooling, seeding, addition of antisolvent, pH shift, salt formation, azeotropic distillation)
- Variation of solvent systems (solvent quality, solvent class)
- Determination of proper stirring time and speed
- Assessment of changes in substrate concentration
- Process development in terms of crystal design (size, shape)
- Comprehensive analytical testing (HPLC, headspace GC, X-ray powder diffraction, particle size distribution, microscopy, etc.)

### Crystallization Process Optimization

- Systematic variation of relevant process parameters (cooling profile, stirring profile, seeding process, spiking with impurities, water activity)
- Optimization of process and bulk properties (space volume yield, batch cycle time, compression of final product, filterability)

### Multigram to Kilogram Supply

- Proof of concept on 250g scale
- Delivery of seeding crystals from gram to kilogram scale
- Crystallization on kilogram scale under GMP or non-GMP
- GMP release testing
- Shipment of final product to customer
- Technical transfer of crystallization process

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### Our Contribution

The unique combination of Solvias expertise in solid-state chemistry, crystallization process development and kilolab production under GMP and non-GMP, supplemented with state-of-the-art instrumentation, enables us to tackle the majority of all drug development candidates.

### Your Process

- Faster
- More efficient
- Safer
- More cost-effective

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