

# Polymorphism, Salts & Crystallization



*An Integrated Approach to Solid-State Development*

# Introduction: Solid-State Development



The majority of drugs are administered as solids. This means that apart from the molecular structure of the active ingredient, solid-state properties significantly influence the performance of the final product.

Often new substances with pharmaceutical activity are weak acids or bases or may have sub-optimal solid-state properties. In such cases it may be preferable to develop the drug as a salt or co-crystal form.

When only amorphous forms are known, specially designed crystallization screenings can help to find crystalline candidates, often improving the chemical purity and stability.

Selection of the best available crystalline candidate should be based on the following physical and chemical parameters:

- Stability (chemical and physical)
- Solubility/dissolution/bioavailability
- Hygroscopicity
- Melting point
- Polymorph landscape complexity and polymorphic transformations
- Number of polymorphs
- Processability
- Ease of preparation

In addition to its impact on chemical and physical properties, salt and co-crystal formation is also relevant for intellectual property considerations because solids with superior properties can be patent protected.

# At Solvias...

...we support you every step of the way

Solvias provides comprehensive physical chemistry services for the identification and selection of polymorphs, salts, and co-crystals, including method development for polymorphic purity and the optimization of crystallization processes. With years of drug development experience as a former research group of a major pharmaceutical company, we can help you crystallize your ideas.

## **Solid Form Selection**

In a well-designed salt/co-crystal screening process, the optimal salt/co-crystal will be chosen quickly, based on parameters such as solubility, hygroscopicity, crystallinity, stability, and ease of production.

Solvias solid-state development programs provide you...

## **Polymorph Screening and Characterization**

Optimizing the experimental effort in polymorphism screening requires using the appropriate number of precisely designed experiments to address the specific questions and stage of development of the drug substance under study. Our polymorphism screening strategy has been optimized through decades of experience and is readily tailored to our customers' needs. Characterization of relevant polymorph properties provides the understanding needed for subsequent substance development, including crystallization process scale-up.

...with time and money saving solutions...

## **Crystallization Screening**

Together, experience and technology work to provide effective screening for the crystallization of amorphous and hard-to-crystallize substances.

## **High-Throughput Screening**

Our robust technology provides the maximum information with the minimum amount of your valuable drug substance.

## **Polymorphic Purity/Amorphous Content**

Accurate and sensitive determination of polymorphic purity in both the drug substance and the drug product as well as the amorphous content in the drug substance assures product quality and reliability.

...adapted to your substance...

## **Crystallization Development**

Proper solid-state characterization combined with a proven crystallization development program leads to robust, reproducible, and scalable crystallization processes that generate the desired crystalline form, size, and shape.

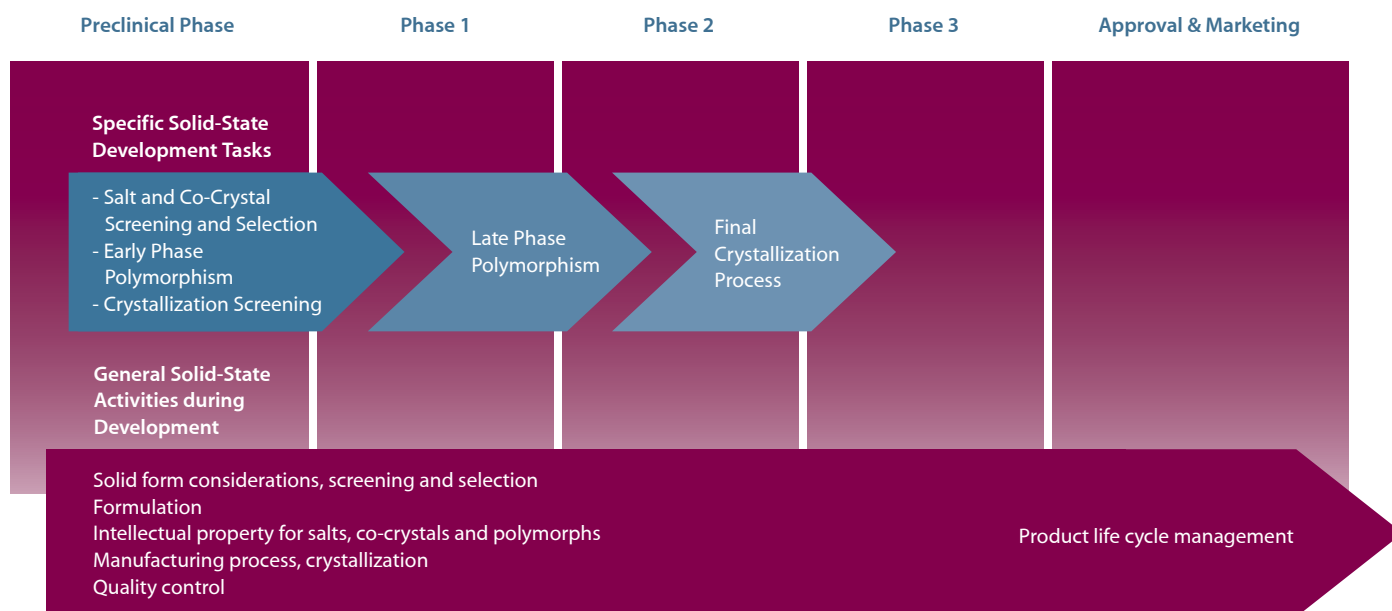
...and development stage.

## **Consulting and Patent Support**

Our experts can provide evaluation of studies or individual data, along with comprehensive reports and testimonials. Our patent and search teams provide an effective resource for protecting your valuable intellectual property and maintaining a competitive advantage.

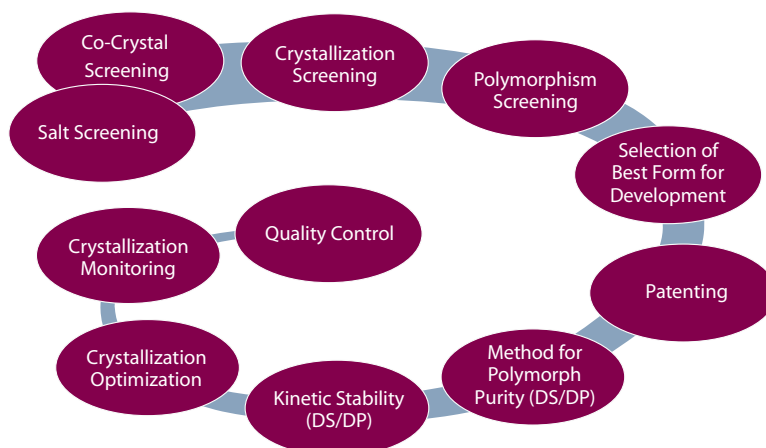
# Polymorphism, Salts & Crystallization

An Integrated Approach to Solid-State Development



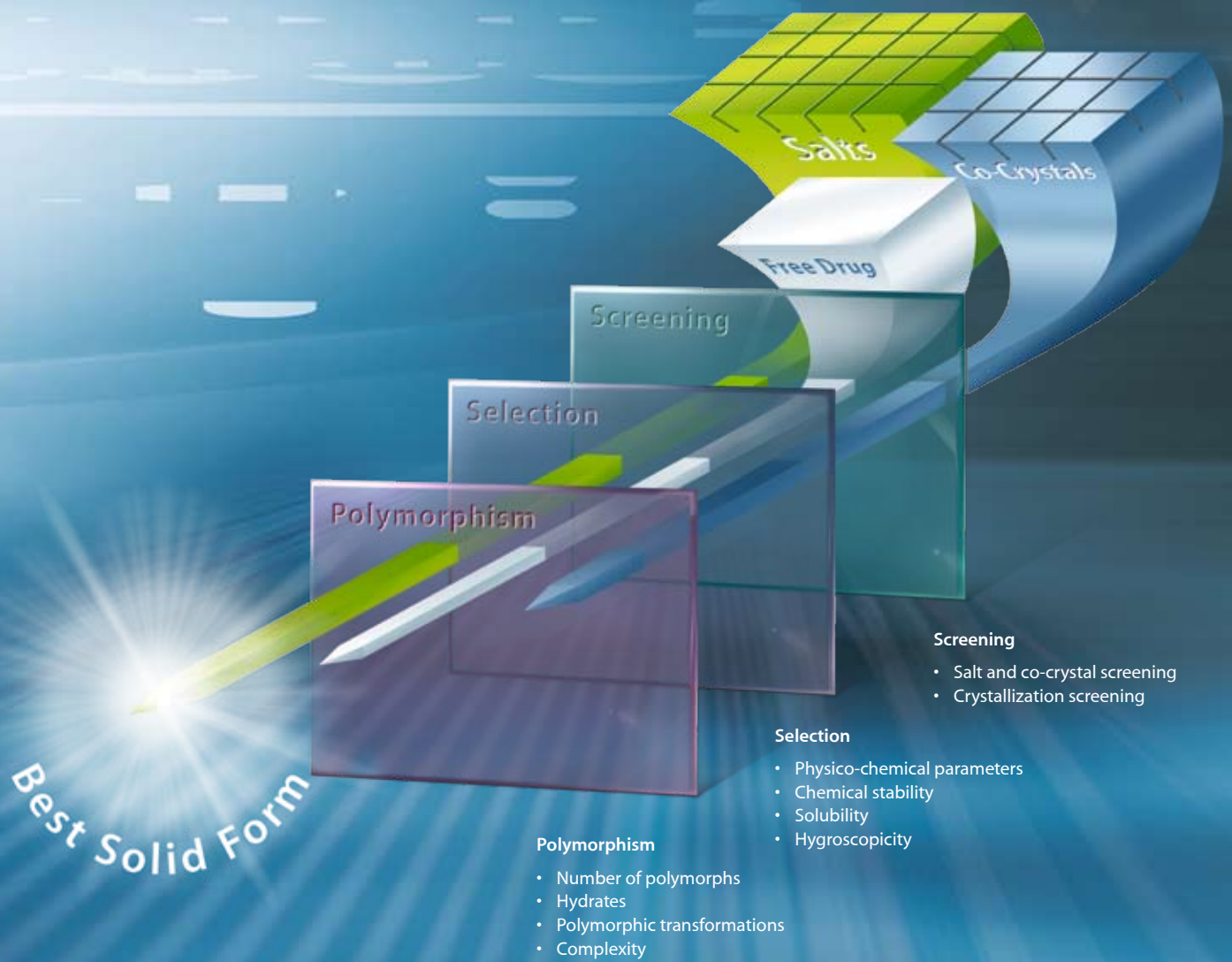
*Schematic and abbreviated diagram of the developmental phases of a drug with highlighted specific solid form tasks. Solvias specifically adapts its services to the developmental stage of your drug and provides you with the most valuable information precisely when you need it.*

From preclinical development through manufacture of the final drug product, the identification, selection, and understanding of the solid forms will have an enormous practical and commercial impact. At Solvias we follow specifically designed strategies to best fit the development process of drugs.



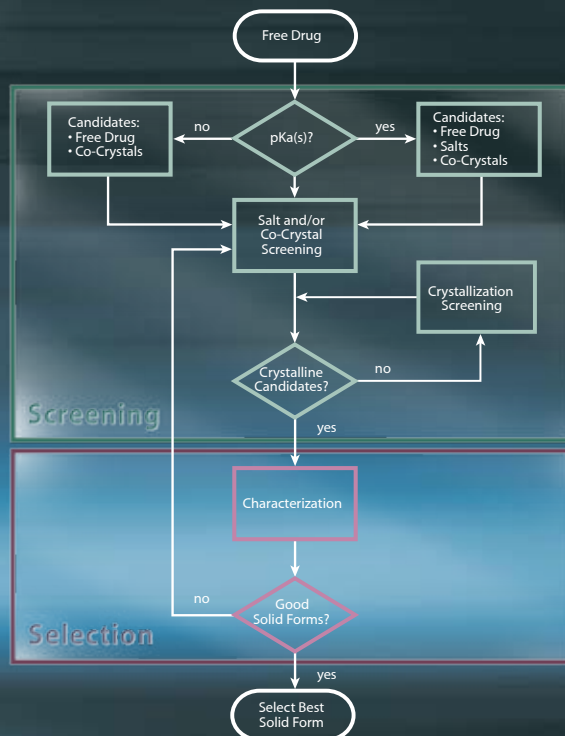
For the best overall results, Solvias provides an integrated and comprehensive approach to solid-state development – from systematic salt, co-crystal, and polymorph screening to controlled scale-up of the crystallization process, all complemented with the full range of physico-chemical studies performed in our laboratories.

# Selection of the Best Solid Form



## Important Physical and Chemical Parameters for Selection of the Best Crystalline Solid Form

- Stability (chemical and physical)
- Solubility/dissolution
- Hygroscopicity
- Melting point
- Polymorph landscape complexity and polymorphic transformations
- Number of polymorphs
- Processability
- Ease of preparation



Solvias Salt and Co-Crystal Screening Programs

Solvias Crystallization Screening Programs

Solvias Characterization Programs for Free Drug, Salts, and Co-Crystals

- Physico-chemical parameters
- Stability programs
- Bulk properties

Solvias Polymorphism Programs

- Early phase
- Late phase
- HTS

# Services

Solvias Solid-State Development Programs Designed to Meet Your Needs

## **Solid Form Screening and Selection**

- Polymorphs, salts, and co-crystals
- Selection of the best solid form
- High-throughput screening as well as conventional approach
- Understanding of polymorphic transformations
- Preformulation characterization
- From mg to kg scale
- Menu-style programs, tiered approach

## **Crystallization**

- Crystallization screening to crystallize amorphous and difficult to crystallize compounds
- Crystallization optimization to improve polymorphic purity, chemical purity, yield, rate, size, and morphology
- Scale-up development

## **Method Development and Validation**

- Polymorphic purity
- Amorphous content
- Polymorphic form in drug product

## **Support**

- Troubleshooting
- Consulting
- Patent support
- Expert reports and testimonials

## **Quality Control**

- Drug substance
- Drug product

## **Quality Management**

- ISO-9001-certified QM system SQS
- cGMP inspected and approved contract laboratory
- GLP on request

## **Features & Key Success Factors**

- Efficient integrated approach, proven study strategies
- Flexibility: modular approach, with decision points throughout the programs
- Large solid-state group with an outstanding track record
- Generation of intellectual property for the customer
- Ability to handle highly potent and cytotoxic compounds
- Complete project management
- State-of-the-art technology and hyphenated techniques to explore the polymorph landscape and understand the polymorphic transformations

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