ThermoFisher SCIENTIFIC

# Accelerating speed to market through solid-state and crystallization development

# Solid-state chemistry plays a pivotal role in pharmaceutical manufacturing, offering distinct advantages that significantly enhance drug development processes.

By harnessing the power of solid-state characterization and crystallization development from the early stages, pharmaceutical companies can accelerate their product development timelines, achieving market readiness more swiftly while avoiding costly errors. Understanding the solid form landscape is crucial for developing a scalable and efficient crystallization process that ensures the desired purity and optimizes bioavailability for drug formulation. This proactive approach in defining solid-state parameters early in the process allows for greater control over the drug substance and drug product processes, ultimately leading to more effective pharmaceutical drug development.

Thermo Fisher Scientific experts Stephen Boppart, Director of Business Management API, and Matthew Jones, Senior Manager of Crystallization discussed the Thermo Fisher approach for accelerating speed to market through solid-state and crystallization.

In this discussion, they highlighted the importance of a global network and integration with drug product formulation development to accelerate speed to market. Early investment in synthetic route finding and a better understanding of solid-state properties and crystallization of the drug candidate can help avoid the trial-and-error cycle and streamline the progression of pharmaceutical products from development phases to commercialization. By focusing on these advanced methodologies, pharmaceutical manufacturers can unlock new opportunities to refine their production strategies and improve the overall outcome.

## The power of global network

Thermo Fisher leverages its global network to facilitate smooth API development and manufacturing from grams to tons. These facilities are capable of handling complex processes such as high-pressure manufacturing, advanced catalysis, continuous flow chemistry, and spray drying, which are integrated with formulation development to ensure seamless transitions from API to product development. This integration highlights the role Thermo Fisher plays as a global small molecules solutions provider within the end-to-end CDMO framework. Each site is equipped with state-of-the-art technologies and is operated by teams with extensive experience, underscoring the commitment to deliver efficient and scalable solutions for small molecules, pharmaceutical development, and production. This broad capability not only supports rapid scale-up but also enhances flexibility in meeting the needs of clients globally.

## Importance of crystallization and solid-state chemistry

Crystallization processes play a pivotal role in enhancing efficiency, reducing costs, and establishing robust control strategies in drug manufacturing. Effective crystallization not only ensures the stability and bioavailability of the active pharmaceutical ingredient (API), but it also optimizes its fit to the formulation, which is crucial for the seamless integration of the API into final drug products.

Finding the most appropriate physical form for your API is critical, as this has an impact on the downstream performance of your product. Optimizing characteristics such as size and shape, particle size distribution, flow, powder density, bioavailability, and melting point enables more efficient formulation and manufacturing process development at the drug product stage. Our extensive capabilities and experience in solid-state chemistry ensure that you receive the best solid form for your drug product development and eventual scale-up.

Thermo Fisher has a dedicated Solid-State Chemistry center at its production site in Linz, Austria. The expert team provides services with the goal of ensuring the optimal fit of your small molecule's API to the formulation requirements, including improved solubility.

# Process development and scale-up

Process development is often undervalued at the early development phases due to the time or budget constraints. When inefficient research processes often get moved into ADME TOX or early clinical studies, it can lead to negative implications such as:

- Higher costs and longer production times for initial clinical supply
- Bridging studies may be required if alternative routes are developed
- Risk of failed batches if the process is not robust
- Inefficient processes are not moved into commercialization
- Raw materials or reagents require special handling or are not readily available

During the scale-up process, any changes in synthetic routes, reagents, or catalysts require careful consideration of their impacts on crystallization. A deep understanding of API solid-state properties is essential to ensure consistent and economical manufacturing. This knowledge helps in making informed decisions that align with the desired quality and regulatory standards.

## Purging impurities

Crystallization is frequently employed to replace chromatography for purging impurities because it generally yields a higher efficiency and output. The choice of solvents and the specific conditions used during the crystallization process significantly impact the purity levels achieved. This makes it a critical step in ensuring the quality and safety of the pharmaceutical products.

## Regulatory considerations and polymorph screening

Regulatory authorities demand a detailed polymorph screening to ensure the robustness of the process and to mitigate risks associated with polymorph stability. Such screenings are crucial to prevent problems experienced by companies in the past, for example, where an unexpected stable polymorph appeared post-launch, leading to significant financial losses due to stability issues.

## Integration of API and drug product development

Solid-state knowledge is integral to developing efficient crystallization processes tailored to meet both clinical and commercial supply demands. This detailed understanding facilitates the design of APIs with specific physical characteristics—such as particle size, shape, and polymorphic form—that are optimized for seamless integration into drug formulations. Effective crystallization ensures that these API properties align well with the manufacturing requirements and enhance the performance of the final drug product. By rigorously controlling these properties, we ensure that the API not only supports robust manufacturing processes but also contributes positively to the drug's stability, bioavailability, and therapeutic efficacy.

## In summary

Thermo Fisher enhances pharmaceutical manufacturing through advanced solid-state chemistry and crystallization techniques. These methods improve market readiness, drug stability, and bioavailability, essential for effective drug formulation. As a global API development and formulation development provider, Thermo Fisher integrates complex processes like high-pressure manufacturing and continuous flow chemistry across its global network of sites. This ensures efficient API development from grams to tons and seamless transition between development phases in the CDMO framework. With its deep solid-state knowledge and advanced crystallization capabilities, Thermo Fisher aligns API characteristics with manufacturing needs and drug product formulation development needs, boosting the drug development process. This strategic approach positions Thermo Fisher as a leading partner in the pharmaceutical industry, driving innovation and meeting customer needs with precision, quality and expertise.

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Published 2024