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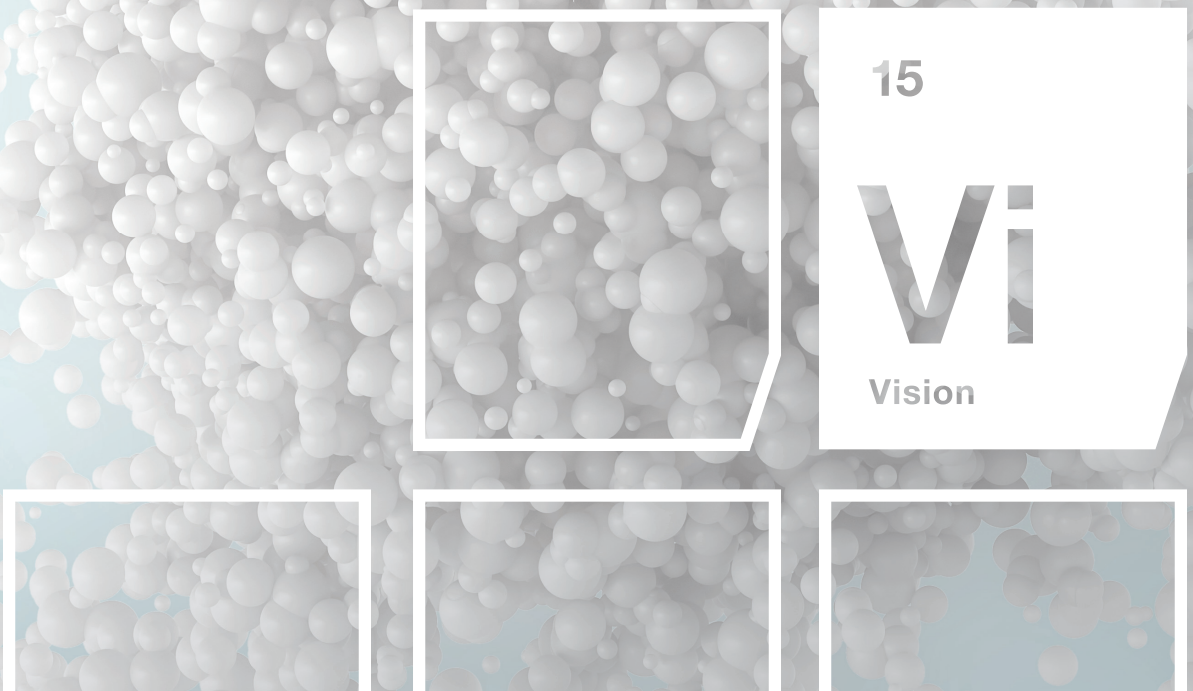
Our experts answering your questions

Solid-state characterization and crystallization process development



You asked, we answered. The subject matter experts of Thermo Fisher Scientific answer your most frequently asked questions on solid-state characterization and the crystallization process.

Q1: When should one start with solid-state characterization and crystallization process development?

A1: Starting as early as possible is recommended, typically around the stage of toxicity campaign planning. Early initiation of solid-state characterization allows for identification of crystallization properties and potential manufacturing developability issues. However, the investment should be balanced against the risk of failure in early-phase compounds. Engaging in a dialogue with manufacturing partners to understand the cost-benefit analysis of different stages of crystallization is crucial.

Q2: What is the best timing for a solid form screen?

A2: There is no one-size-fits-all answer. Historically, solid form screening was conducted late in development due to the risk of compound failure. However, trends are shifting towards conducting these screenings earlier, such as during preclinical development or the first clinical trial stage. Although this increases the risk, conducting a limited early screen with a more comprehensive follow-up later can prevent significant downstream issues.

Q3: How long does crystallization process development take?

A3: The duration depends on the development stage and the specific requirements of the molecule. Initial process development might take around four weeks, but for later stages, such as clinical trial phase two, you might need 3 to 6 months. Complex projects close to commercialization can require extensive, multi-year efforts to fully optimize the processes.

Q4: What are the timelines for different solid-state chemistry activities?

A4: Screening activities typically require up to six weeks from the receipt of material to the delivery of a report. This timeline applies to both crystallization process development and solid form screening. However, solid form characterization can often be completed within two weeks.

Q5: How much time could be saved or lost depending on when crystallization and solid-state chemistry activities are initiated?

A5: Early initiation can prevent significant delays, particularly if unforeseen issues such as the discovery of new polymorphs occur. Late discoveries can lead to months of redevelopment for both crystallization processes and formulations. Poor planning or late starts in solid-state activities can also result in the loss of clinical trial slots, potentially delaying a project by years.

Q6: What are the advantages of having API development and subsequent formulation development services within one service provider?

A6: Integrating API and formulation development can significantly streamline the process, ensuring that changes in the API production (like particle size or shape for better filterability) are well-coordinated with formulation requirements. This synergy can prevent delays and additional costs associated with redoing formulation studies and can overall accelerate development timelines.

Q7: What's the difference between a polymorph and a salt screen?

A7: A polymorph screen looks for different solid forms of an API where the chemical content remains the same, but the crystal structure varies. A salt screen, on the other hand, aims to generate salts of the API, requiring the presence of an ionizable functional group in the API and the identification of suitable counter ions. Both screens are similar in method but differ in objectives.

Q8: What are the benefits of a solid form screen?

A8: A solid form screen provides extensive information that can guide both crystallization process development and formulation design. It evaluates solubility, identifies stable and meta-stable forms, and helps in understanding how different solid forms might behave under various manufacturing and storage conditions. This information is crucial for optimizing product stability and efficacy.

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