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PREFACE

Editorial: *Improving Product Quality through Process and Materials Understanding*

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Since their invention by William Brockedon in 1843, tablets have remained the most popular perorally administered dosage form in the world, and are generally the pharmaceutical industry's first choice for development programs [1]. Despite more than 150 years of production history, incorporating drug molecules into a mass reproduced solid platform capable of precision drug delivery remains challenging, and is typically informed by traditional, empirical formulation experience. Both primary processing (raw materials generation) and secondary processing (raw materials manipulation) rely on the interplay between solid internal structure, the resulting properties, and the eventual material performance as a result of those properties [2, 3]. During the multiple steps needed for tablet manufacturing, the successful marriage of materials properties and process parameters is key; however, a complete understanding of how relationships between components and manufacturing result in desirable dosage form attributes is yet to be achieved. Facilitation of the research needed to enable rationally designed dosage forms underlies the creation of the FDA's *Quality by Design (QbD)* initiative [4], aligned with the Process Analytical Technology (PAT) Guidance for Industry [5] and the *Final Report of the Pharmaceutical cGMPs for the 21st Century — A Risk-Based Approach* [6].

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To make the next leap forward in modern dosage form formulation and manufacturing, a deeper and mechanistic understanding of pharmaceutical materials is needed. The type and number of tests incorporated into every phase of a pharmaceutical development program is driven by time, money, and the amount of material available. To that end, the scarcity of powder materials comprised of lead active molecules is known to be a rate-limiting step for generating meaningful pre-formulation data capable of providing the confidence needed for successfully pushing dosage form development programs in the right direction towards successful completion.

Computational modeling and *in silico* prediction of properties extracted from the crystal structures of lead API can enable better understanding of how solid materials will behave as they are combined with various excipients and manipulated during high-speed manufacturing. Most importantly, however, materials-sparing development approaches minimize the use of limited initial supplies of drug substance, while holding the potential to yield important insights into aspects that can potentially affect product quality. In combination with traditional macroscopic testing, harnessing data from models centered on materials understanding could act as predictors of the macroscopic performance of solid drug substance in a variety of formulations, and help direct successful early development. Moreover, deeper probes of the nuanced information "hidden" in crystal structures could also be used to engineer 'smart pharmaceutical materials' having enhanced performance relative to their parent compounds. Such a strategy could be used for enabling the design of elegant drug delivery platforms, or potentially for repurposing existing API molecules for different therapies.

As pharmaceutical materials science continues to grow, knowledge management will be imperative to the translation of these data into meaningful information, and the ultimate success of QbD. The breadth of research from academia, industry, and worldwide regulatory bodies, which

encompasses computational models, engineering advancements, and analytical methodologies essential to advanced formulation and drug product manufacturing presents the additional challenge of how to harness the potential and share results to help guide product development for the future [7].

In assembling this special issue dedicated to Professor Kenneth R. Morris, we, the guest co-editors attempted to span the numerous research areas to which he has dedicated himself throughout his scientific career. These include: powder mechanics and flow, the impacts of solid-state structure on solubility and permeability, crystal engineering, process-induced transformations of crystalline and amorphous materials, PAT, solid-state computational modeling, drug product risk assessment, and New Prior Knowledge. After much discussion, we felt that the broad theme *Improving Product Quality through Process and Materials Understanding* would capture Ken's passion for pharmaceutical materials science, and are proud to showcase articles covering these areas. We are all thankful for all the contributions to this Special Issue, and the help in celebrating the outstanding research career of a wonderful scientist, teacher, mentor, and friend.

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