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Micro-scale solubility measurement to guide early decision making

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Key physicochemical properties of a drug molecule typically include solubility, pKa, and lipophilicity, which, in turn, greatly influence the biopharmaceutical and ADMET properties of the molecule. When combined with the consideration of achieving a pharmacological effect while minimizing the potential for any safety issues, these physicochemical properties are crucial for designing drug product composition and manufacturing processes, and ultimately, are directly or indirectly connected to developability as well as NME attrition.

As early-stage drug development works with limited amounts of synthesized compound, the crucial parameter of equilibrium solubility is often sacrificed for more urgent in vitro activity and toxicity screening tests. The reason for this is the discrepancy between throughput, substance consumption and accuracy of available methods. With most pipeline molecules having issues with poor solubility, 'blind' development regarding solubility may lead to significant downstream challenges in the development process.

The Solubility Company's proprietary image-based Single Particle Analysis (SPA™) Method brings a solution to this issue. The SPA™ Method uses machine vision, optical shape recognition and intelligent algorithms to determine the solubility from powder samples of less than 100 µg per measurement. As an image-based technology the SPA™ Method does not require chemical structure information or chemistry specific method development for accurate measurement. Most importantly, the SPA™ Method produces values equivalent to gold standard "shake-flask" equilibrium solubility values within minutes, instead of hours or days.

The SPA™ Method has been applied in measuring the solubility of drugs and excipients, in aqueous media, organic solvents, lipids and vehicles. In addition, the SPA™ Method has enabled small-scale measurement of the apparent solubility of salts, polymorphs, cocrystals and amorphous drug forms. Examples from our work using the SPA™ Method will be given in this presentation.