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The *AAPS Journal* High Impact Article Award: Challenges and Strategies for Solubility Measurements and Dissolution Method Development for Amorphous Solid Dispersion Formulations

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At the American Association of Pharmaceutical Scientists (AAPS) 360 PharmSci meeting held in San Antonio in November 2025, the article titled "Challenges and Strategies for Solubility Measurements and Dissolution Method Development for Amorphous Solid Dispersion Formulations," received the *AAPS Journal* High Impact Article Award (*1*). The authors of this timely and useful white paper are Drs. Andre Hermans, Johanna Milsmann, Hanlin Li, Christian Jede, Andrea Moir, Bart Hens, James Morgado, Tian Wu, and Michael Cohen. All are members of the International Consortium for Innovation and Quality in Pharmaceutical Development. The lead author, Dr. Andre Hermans, received the award in the 2025 AAPS High Impact Manuscript Award Rapid Fire session on Tuesday, November 11, 2025. He presented a summary of the paper from the podium. Dr. Hermans is a long-standing member of the In Vitro Release and Dissolution Testing (IVRDT) Community of the AAPS.

This award-winning white paper is extremely timely for the dissolution scientist, providing guidance for developing meaningful and appropriate methods for amorphous solid dispersion (ASD) formulations, which are challenging dosage forms that are becoming more common. A summary of the publication is provided below.

ARTICLE SUMMARY

This manuscript represents the view of the Dissolution Working Group from the Innovation and Quality Consortium on the challenges of and recommendations on solubility measurements as well as the development of dissolution methods for immediate release (IR) solid oral dosage forms formulated with ASDs. Nowadays, numerous compounds populate the industrial pipeline as promising drug candidates, yet they suffer from low aqueous solubility. In the oral drug product development process, solubility along with permeability is a key determinant to assure sufficient drug absorption along the intestinal tract. Formulating the drug candidate as an ASD is one potential option to address this issue. These formulations demonstrate the rapid onset of drug dissolution and can achieve supersaturated concentrations, which poses significant challenges to appropriately characterize solubility and develop quality control (QC) dissolution methods. Because ASD formulations have evolved during the last few years, there is no standard practice within the industry on how to assess drug solubility that is representative of such formulations. To address this gap, the authors summarized various methodologies to determine drug concentration for the intended purpose. The authors characterized the challenges for ASDs associated with (i) definition of solubility and sink conditions for ASD dissolution, (ii) applications and development of non-sink dissolution (according to conventional definition) for ASD formulation screening and QC method development, and (iii) advantages and disadvantages of using dissolution in detecting crystallinity in ASD formulations. Related to these challenges, successful examples of dissolution experiments in the context of control strategies were shared. The authors conclude that classical sink considerations are based on crystalline (thermodynamic, i.e., ≥ 24 h) drug solubility. Thus, they are only partly adequate for QC dissolution testing of

supersaturating ASD formulations. Instead, assessing the supersaturation concentration of the amorphous form allows the identification of the kinetic sink factor for such formulations. Given the inherent instability of supersaturated systems, harmonization of in vitro protocols to determine amorphous apparent drug solubility in ASD formulations would substantially increase the reliability and reproducibility of such measurements.

REFERENCES

1. Hermans, A.; Milsmann, J.; Li, H.; Jede, C.; Moir, A.; Hens, B.; Morgado, J.; Wu, T.; Cohen, M. Challenges and strategies for solubility measurements and dissolution method development for amorphous solid dispersion formulations. *AAPS J.* **2023**, *25* (11). DOI: 10.1208/s12248-022-00760-8.N