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# Highlights from the 2023 AAPS 360 Annual Meeting – In Vitro Release and Dissolution

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## INTRODUCTION

The American Association of Pharmaceutical Scientists (AAPS) successfully held its PharmSci 360 Annual Meeting and Exposition event on October 22–25, 2023, at the Orange County Convention Center in Orlando, FL. This year's meeting was held entirely in-person and did not include a hybrid element, allowing pharmaceutical scientists from around the world to convene in a physical setting. This was the first complete return to in-person annual meeting event post-pandemic among the pharmaceutical scientists of AAPS.

The fully in-person event facilitated a productive In-Vitro Release and Dissolution Testing (IVRDT) Community meeting, which was successfully led by Jie Shen, the community Chair, and Sanjaykumar Patel, the Chair-Elect. During the meeting, they highlighted the accomplishments of 2023 and outlined potential plans for 2024. The interactive nature of the session made it appealing to participants and aided in generating ideas and possible topics for community events in 2024.

In 2023, the IVRDT community within the AAPS achieved several notable accomplishments and collaborations. The community organized two AAPS-hosted webinars, namely "New USP Dissolution Performance Verification Standard: What, Where, and When" and "Titanium Dioxide Free Drug Products: Challenges During Drug Product Development." Both webinars attracted a substantial audience and featured highly interactive question and answer sessions, enhancing participant engagement.

The IVRDT community collaborated with the Society of Pharmaceutical Dissolution Sciences (SPDS) - US Chapter to organize two additional webinars. These webinars focused on the Dissolution of Complex Formulations and Dissolution for an Inhaled Product. These collaborative efforts fostered knowledge sharing and exchange within the dissolution sciences field, both within and outside of the AAPS organization.

In February 2023, the IVRDT community cooperated with the University of Philippines Manila to organize an outreach workshop on dissolution testing-related topics. The workshop received a positive response, indicating its value in disseminating knowledge and promoting engagement in the field.

During the AAPS 360 annual event, the IVRDT community proposed and presented the need for harmonization and the value of small-volume vessels. Ishai Nir led a rapid-fire presentation advocating for the use of small-volume vessels. This initiative aimed to address a pertinent issue in the field and stimulate discussions around the topic.

These accomplishments and collaborations signify the active involvement and contribution of the IVRDT community within the AAPS organization and the broader pharmaceutical science community.

One of the IVRDT community's most significant accomplishments was the nomination of Ms. Vivian A. Gray for the AAPS Distinguished Service Award. Her nomination was widely regarded as "ideal recipient," with unanimous agreement that she perfectly exemplified the award's description of an individual who has "contributed significantly and consistently over a long period to benefit AAPS in achieving its mission." Ms. Gray's notable contributions to AAPS and the field at large include her involvement in

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organizing programs, participating in expert panels at USP, and publishing and presenting extensively. Vivian helped organize and participate in many overseas workshops that included many speakers from the AAPS IVRDT Community. Her expertise and stature in the field were highlighted by her numerous invited talks, such as the recent invitation from the USP to provide an overview of the field to their Expert Panel. The IVRDT community took great pride in witnessing her well-deserved reception of the award.

*Patrick J. Sinko (2023 AAPS President) and Doodipala Samba Reddy (2023 AAPS Awards Committee Chair) presented the Distinguished Service Award to Vivian A. Gray.*

During the community meeting at the AAPS 360 annual event, the IVRDT community leadership team actively collected and compiled feedback to determine the focus areas for future events and proposals for the 2024 AAPS 360 annual meeting. The selected topics put forth for consideration included biorelevant/biopredictive dissolution, release and dissolution methods for nanomedicines, the current regulatory expectations of the quality control method, and the dissolution of complex formulations, including long-acting injectables. The meeting proved to be highly successful, fostering scientific engagement within AAPS and reinforcing the commitment to advancing dissolution science with the aim of achieving another fruitful year in 2024.

Below is a summary of the key presentations that were deemed vital during the community meeting at AAPS 360.

## SYMPOSIUM: ACCELERATING THE DRUG DEVELOPMENT PROCESS THROUGH FORMULATION AND DELIVERY STRATEGIES

In the symposium, Dr. Shawn Zhang from DigiM delivered an informative presentation entitled “Novel Analytical Imaging and Dissolution Modeling.” This talk centered around novel methodologies that employing imaging, artificial intelligence (AI), and in silico modeling to accelerate the formulation development of complex formulations. The presentation pointed out the need and importance of understanding the internal microstructures to maintain the quality and performance of drug products. The presentation highlighted a wide range of significant microstructural attributes, from API size distribution to the spatial arrangement of excipients, which can be quantified and contribute to a quality-by-design approach. The use of imaging techniques was particularly emphasized, which can facilitate the vast array of formulation techniques and the library of parameters ideally suited for studies.

The presentation included the capability of DigiM, which consists of a suite of high-resolution imaging techniques, AI analysis, and in silico dissolution models to transform drug products and intermediates into a library of reusable digital twins. The quantified critical quality attributes (CQAs) and verified in silico models can be developed into mechanistic and predictive formulation via microstructure digital twins, which are integral to drug product understanding. This presentation showcased examples of AI-powered transformation applied in the formulation development of complex oral solid dosage forms, controlled release products, and nanocarriers. Additionally, Dr. Zhang discussed dissolution results on long-acting, diffusion-controlled dissolution results with polymer degradation modifications, and a new particle intrinsic dissolution model. The application of an image data management and microstructure engineering platform powered by generative AI was discussed in contexts of drug development and regulatory support.

Dr. Zhang's presentation provided valuable insights into the innovative application of analytical imaging and dissolution modeling, showcasing their potential to significantly enhance formulation development processes for complex drug products.

## SUB-SCIENTIFIC TRACK: ADVANCED MODELLING AND PREDICTIVE APPROACHES IN DRUG DEVELOPMENT, MANUFACTURING, AND ANALYSIS

In this session, three in vitro release and dissolution-related presentations were provided by Mr. Ishai Nir, Dr. Hyunho Kang, and Dr. Devin Janai Swiner, respectively.

Firstly, Ishai Nir, representing the Instrumentation Subgroup of the In Vitro Release and Dissolution Testing Community, presented the Rapid Fire “Non-compendial

small volume dissolution for early-stage formulation model development."

This Rapid Fire talk began by outlining the unique challenges of optimizing more varied and complex new formulations in early-stage development. This work increasingly relies on modeling and other indirect techniques. The need for reference data to support these becomes a more pressing challenge. However, with limited material at these early stages, tests such as dissolution at standard compendial volumes are often impractical.

Nir introduced the array of commercially available non-compendial small-volume dissolution testing solutions. He pointed out that these, along with a desire to harmonize with the Chinese Pharmacopeia, which explicitly defines one such setup, has led the USP to launch a program to review some of these solutions for what they dubbed "Reduced Volume Dissolution" for possible inclusion in the General Chapters.

Nir then addressed one of the principal questions regarding this approach: the ability to correlate results derived from these non-compendial methods to future conventional dissolution studies. He presented data published by Prof. Piero Armenante's group at the New Jersey Institute of Technology, including CFD modeling and experimentally measured results. These demonstrated that scaling of only one setup parameter - agitation speed - generated data exhibiting a very high correlation of dissolution rate predictions between full scale and these small or reduced volume setups. The latter's advantage is the ability to run more studies with the same amount of material as conventional dissolution.

To conclude the talk, Nir proffered that the use of these small/reduced volume surrogate testing in early-stage development offers a solution to testing limitations due to the lack of availability of suitable amounts of test material and minimizes the cost and complexity for some of these studies that require "exotic" biorelevant media. Small/reduced volume dissolution testing can also continue to play a role in final dissolution methods in cases where the analytical method may have an issue with sensitivity due to a very low API dose or the desire to develop more discriminatory methods.

Finally, he summarized the talk with the critical observations that small/reduced volume dissolution is already an essential part of the modern performance testing portfolio because it is easily and reproducibly accomplished using existing baths and commercially available accessories while offering very similar dissolution profiles to complete scale testing with only a slight adjustment of agitation rate. Hopefully, these advantages will lead to the USP and other pharmacopeias, including harmonizing the *ChP* 250-mL option and other commercially available small/reduced volume dissolution setups.

Secondly, Dr. Hyunho Kang presented "Evaluation of Predicting Long-Term Release Rate of the Islatravir Implant." The talk began with information on long-acting implantable formulation with Islatravir, the product's general release dissolution behavior, and the strategy for collecting in-vitro release profiles using apparatus 7. It was emphasized during his presentation that due to the implant's targeted long-term release behavior, a significant amount of effort and duration is required to collect the real-time release profiles of the product. To overcome this limitation, an accelerated dissolution method can be critical to developing the formulation and predicting its release profile in the long term so that a proper evaluation can be performed on the materials before introducing the products to clinical trials and commercial areas.

He discussed that developing an accelerated in vitro release (Acc-IVR) method needs to consider many factors. The polymeric implant is sensitive to environmental conditions both in chemical and physical ways, which can quickly impact the dissolution, and a slight change in formulation composition can either accelerate or slow down the release. Furthermore, as the drug is released from the implant, a gradual depletion could cause a deviation from the previous release behavior of the implant. He highlighted that when the method is developed, it is critical to ensure that the correlation between the real-time in-vitro release (RT-IVR) and Acc-IVR can be acquired by accelerating the release but have very minimal or no effect on other characteristics of the materials being tested during in-vitro release.

The presentation introduced the Acc-IVR method for the product. Several case studies were also provided, where the RT-IVR data from multiple batches with varied potencies, which was acquired for more than a year, was compared to Acc-IVR data to evaluate the prediction capacity. Further, the driving force of this accelerated method and its relationship to the prediction modeling equation was investigated for better understanding, further development of the technique, and expanding its potential to apply to other implant drug products with varied formulations and other characteristics.

Finally, Dr. Devin Janai Swiner presented "Using Surface Dissolution Imaging to Understand the Mechanism of Weakly Basic Drug Solubility in Enabled Conventional Oral Formulations." The talk centered around the current challenges in formulation development of weak base pharmaceutical compounds, emphasizing additional risks for compounds with pH-dependent solubility. Drug performance of traditional strategies, such as amorphous solid dispersions (ASDs), were compared to an "enhanced conventional formulation," which incorporates small organic acid and polymer in the tablet blend, with the observation that high levels of acids can increase weak base solubility with the polymer sustaining supersaturation in two-stage biorelevant dissolution. Surface dissolution imaging technology was used to probe the solid-liquid interface and intrinsic dissolution rates of these formulations, showing how drug releases enhance conventional compacts and, in turn, increase the solubility.

*Pictures of IVRDT community meeting.*