

# Report on the Virtual Workshop: A Quest for Biowaiver, Including Next Generation Dissolution Characterization and Modeling

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## INTRODUCTION

The virtual workshop, “A Quest for Biowaiver, Including Next Generation Dissolution Characterization and Modelling,” was held on November 16–17<sup>th</sup>, 2022, via the MS Teams platform. The conference was co-sponsored by Jagiellonian University Medical College (JUMC) in Cracow, Poland and the American Association of Pharmaceutical Scientists (AAPS). The workshop was chaired by Vivian Gray (AAPS) and Prof Aleksander Mendyk (JUMC), with the support of the co-chairs Prof Nikoletta Fotaki (AAPS), Prof Jie Shen (AAPS), and Dr Jakub Szlęk (JUMC).

The main workshop themes included regulatory aspects, best practices on dissolution testing, and next-generation dissolution modeling. The objectives of the meetings were to provide participants with practical knowledge they can apply to their current work, as well as new concepts that will improve and broaden their experience. During the workshop, participants learned best practices for developing discriminative dissolution methods and expanded their knowledge of drug product characterization. In addition, they were introduced to new modeling concepts to support dissolution specifications. With a virtual format, the workshop attracted participants from all over the world.

The workshop included four sessions that were dedicated to specific questions related to dissolution studies. Each session was followed by a discussion between the panelists and participants. The topics of the various workshop sessions were as follows:

- Session 1: Regulatory Aspects and Expectations
- Session 2: Basics and Best Practices on Dissolution Testing
- Session 3: Next Generation Characterization for Dissolution Testing
- Session 4: Modeling and Artificial Intelligence Approaches

A total of 278 individuals registered for the virtual workshops. Most of the registered participants indicated industry (71%) and academia (24%) as their affiliation (Fig. 1). The largest number of participants signed up for the workshop from the United States, Poland, and India (Fig. 2).

On the first day of the conference, 198 participants joined the meeting. On the second day, 128 attendees joined the event, giving a total of 326 participants in the 2-day live workshop.

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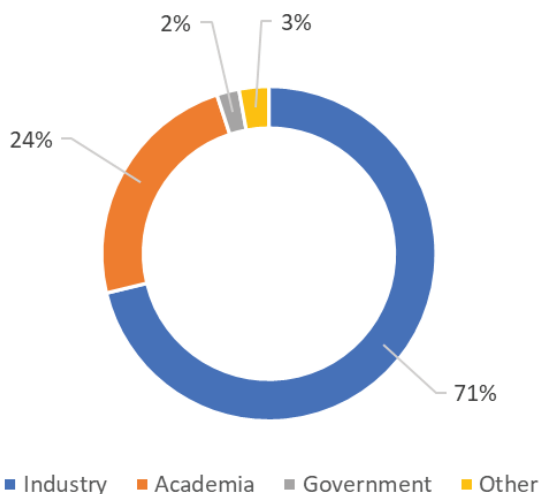


Figure 1. Number of registered workshop participants by institution type.

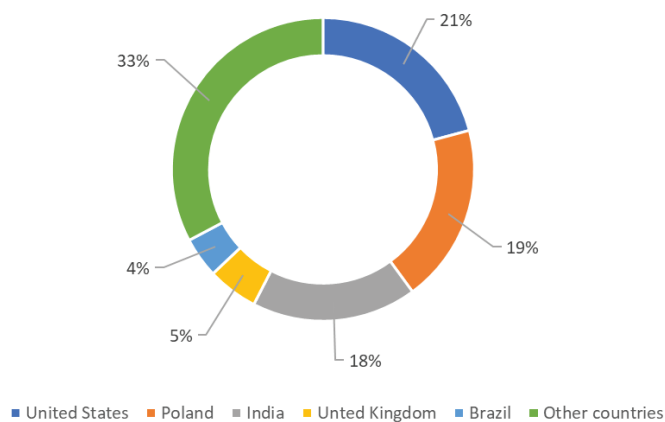


Figure 2. Number of registered workshop participants by country.

## SESSION 1: REGULATORY ASPECTS AND EXPECTATIONS

The virtual workshops opened with an introduction given by Vivian Gray and Prof Aleksander Mendyk, who outlined the agenda and goals of the meeting. The first session, “Regulatory Aspects and Expectations,” was moderated by Prof Aleksander Mendyk. The aim of the session was to review the biopharmaceutics classification system (BCS)-based biowaivers and to discuss the regulatory aspects of dissolution testing from both the US FDA and European perspectives. The first talk entitled, “Biopharmaceutics Classification System-Based Biowaivers ICH M9,” was given by Dr James Mann and Dr Xavier Pepin.

The BCS, which classifies molecules based on their solubility and permeability, was first published by Amidon et al. back in 1995 and led the US FDA to publish the first guidance on a BCS-based biowaiver in

2000 (1). The biowaiver concept was extended to other territories and adopted by the EU in 2010. The result of this staggered uptake of BCS-based biowaivers led to a lack of harmonization between territories, which proved challenging for pharmaceutical companies to navigate. There was lack of harmonization around whether BCS class 1 and 3 were both accepted or just BCS 1; dissolution apparatus, hydrodynamic conditions, and dissolution medium volume were some of the issues. In addition, some ICH countries like Japan did not formally recognize BCS-based guidelines. This was seen as an area ripe for ICH harmonisation and in 2019 after much discussion among member companies and the pharmaceutical industry, the harmonized guideline on BCS-based biowaivers was published in the form of ICH M9 (2).

The ICH M9 harmonization process focused on four main areas: solubility, permeability, excipients, and dissolution (2). For solubility, the main debate was around whether solubility should be classified based on highest strength or highest dose. The final guidance classifies based on highest single therapeutic dose but with some allowances to study strength if additional data are provided. The guidance also allows alternative methods for solubility classification based on the apparent full dissolution in 250 mL medium, which can be useful for amorphous drugs or salts of free moieties. Permeability classification is ideally based on human data using absolute bioavailability data. A high permeability would be granted if the bioavailability  $\geq 85\%$  or if the sum of urine parent, Phase 1 oxidative and Phase 2 conjugative metabolites, and faecal Phase 1 oxidative and Phase 2 conjugative metabolites exceeds 85% of the administered dose. In vitro assessment against approved high permeability references using Caco-2 cell lines can also help determine the drug high permeability. In addition, unless absolute bioavailability is used for determination of high permeability, the drug should be demonstrated to be stable in the gastrointestinal (GI) tract. For excipients, decision trees on allowed differences between test and reference were provided with more stringent criteria for BCS 3 drugs. For dissolution, the major discussion points were whether to include water in the medium and to allow 75 rpm paddle speed for apparatus 2. In the final guidance, water was not included, and 75 rpm is not specifically included, but scientifically justified approaches can be used if coning or high variability is observed. Overall, ICH M9 is welcomed by industry and is a great stride forward; however, the global acceptability needs to be achieved, particularly in the circumstances where flexibility and scientific justification are allowed.

The next talk was given by Dr Margareth R. C. Marques

(United States Pharmacopeia) concerning “Performance Tests in the U.S. Pharmacopeia.”

Dr Marques presented an overview of the USP general chapters related to drug product performance tests. The scope of the following chapters was discussed: <1092> The Dissolution Procedure – Development and Validation; <701> Disintegration, and <711> Dissolution, both harmonized with the *European Pharmacopoeia* and *Japanese Pharmacopoeia*; <1094> Capsules – Dissolution Testing and Related Quality Attributes; <1711> Oral Dosage Forms – Performance Tests. Also, she presented the general chapters related to products applied to the skin: <3> Topical and Transdermal Drug Products – Product Quality Tests; <724> Drug release; and the major revision made to <1724> Semisolid Drug Products – Performance Tests to align with the new FDA guidances related to products applied to the skin. The chapter <1236> Solubility Measurements was also discussed. This chapter contains the composition of some simulated biological fluids, both for human and veterinary applications, that can be used to assess product performance during formulation development. She summarized the activities of the USP Expert Panel on New Advancements on Product Performance Testing, which has already published several papers on the performance tests of dosage forms other than tablets and capsules (3–6). Note: The proposals for any revisions to the *USP–NF* are published in *Pharmacopeial Forum*, available free of charge at [www.uspnf.com](http://www.uspnf.com) for a period of 90 days for public comments.

The closing lecture of the first session was given by Prof Aleksander Mendyk, who spoke on “Dissolution Method Development from European perspective.”

Prof Mendyk focused on the comparisons of pathways of dissolution method development and synergies between US and Europe. He emphasized on the tendency to harmonize various regulations both in Pharmacopoeias (*USP* vs. *Ph.Eur*) and scientific guidelines. However, some discrepancies are still pending, i.e.,  $f_2$  calculation, yet ICH is another example of a successful consensus reached under the umbrella of the M9 guideline described by Dr James Mann and Dr Xavier Pepin.

The first part of the workshop ended with a question and answer session with attendees and speakers.

## SESSION 2: BASICS AND BEST PRACTICES ON DISSOLUTION TESTING

The second session of the workshop, “Basics and Best Practices on Dissolution Testing,” was moderated by Prof Jie Shen. The main themes were the challenges

of developing a discriminatory dissolution method, the influence of post-approval changes on dissolution testing, and the implementation of a statistical approach to generic development. The first speaker of the session was Vivian Gray (*Dissolution Technologies*), during which she gave a talk entitled, “Challenges When Developing a Discriminatory Dissolution Method.”

Vivian began with defining “discriminatory” method and why it is necessary, reiterating that discriminating methods can contribute to specifications that can distinguish between bioequivalent and bioinequivalent batches. She explored the necessary characteristics of a discriminatory method and gave resource material that provided regulatory and industry expectations. The primary references were the EMA Reflections paper and *USP* chapter <1092> The Dissolution Procedure: Development and Validation; she also provided two literature references of interest (7–9).

An outline was provided on how to develop a discriminatory method. The first step is to identify those critical quality attributes (CQA) related to the drug substance, drug formulation, and drug product manufacturing process. She gave examples in each category. The second step is to identify which of these attributes affect the in vivo release. The third step is to manufacture drug product that reflects the upper and lower limits ( $\pm 20\%$ ) of that variable, ideally about two or three variations for each category (drug, drug formulation, manufacturing process). Fourthly, run these variation products, preferably one variable at a time versus the target product. Lastly, compare the dissolution profiles and determine if there are significant differences among the variables and the target. Hopefully, there will be at least two or three variables that the method can pick up differences. If not, then go to a backup method that is possibly more complex and may not achieve sink conditions. She concluded with in addition to a discriminatory method there should be an in vivo linkage element to the in vitro method data.

Next, Dr Andreas Abend gave a talk on “Current Challenges of Dissolution Testing in Support of Postapproval Changes for Oral Drugs.”

Dissolution testing is widely used in the pharmaceutical industry to gain insight into bioperformance of drugs when in vivo drug substance release is a prerequisite of drug absorption and/or distribution of the drug to the site of action. Different in vitro methods aimed to mimic the physiological environment the drug may encounter after administration are usually applied

during drug product development to screen formulation candidates and in support of biopharmaceutics risk assessment. These methods are often performed under conditions that are not deemed appropriate for routine product quality assessment (10). Once formulation and manufacturing conditions relevant for late-stage clinical trials have been identified, the development of quantitative analytical methods and acceptance criteria (i.e., product specifications) begins (10). At this stage, a dissolution method that can be routinely operated in a quality control (QC) lab is validated according to applicable guidance (e.g., ICH Q2, USP, etc.) (11). One of the key challenges of late-stage drug development and product lifecycle management is the assessment of manufacturing changes on product quality. In general, health authorities classify deliberate manufacturing changes as minor, moderate, and major depending on their potential impact on in vivo performance of the drug. The US FDA issued several guidance documents for industry in the 1990s to clarify the expected dissolution tests required to support manufacturing changes for immediate and modified release solid oral products and on dissolution method development (12–14). In addition, for IR drugs, global harmonized guidance on how to apply for biowaivers based on the BCS is now implemented by health authorities that are members of ICH (1, 2). In the context of product lifecycle management ICH M9 can be applied to BCS 1 drugs under certain circumstances for major manufacturing changes which may otherwise require in vivo bioequivalence (BE) studies. BE studies may also be waived under certain conditions for over-encapsulated drugs used in blinded clinical trials or to demonstrate BE of lower strength in case BE was already demonstrated at a higher strength (15).

The assessment of moderate manufacturing changes on in vivo performance is typically based on comparisons of dissolution profiles of drug product made according to the new manufacturing process (the “test product”) and the existing, typically regulatory approved, process conditions (the “reference product”). For biowaiver applications following ICH M9, the test and reference products are usually a new formulation made under representative manufacturing conditions versus a reference listed drug (i.e., drug product already approved) (2). In some cases, dissolution profiles comparisons are made by using the approved QC dissolution method, whereas in other cases (e.g., level 2 formulation changes, BCS-based biowaivers, etc.) dissolution testing is performed in various aqueous media under conditions described in applicable pharmacopeias and guidance.

Although many superior mathematical models to test for dissolution profile similarity exist, the dissolution similarity factor ( $f_2$ ) proposed by Flanner and Moore is widely used in the industry and by regulatory agencies to assess similarity (16–18). Regardless of the mathematical approach that is either expected by regulators or – in case health authorities are open to alternative approaches – has been chosen by the applicant, a decision on similarity and thus in vivo impact can only be made with confidence if differences in the rate and extent of drug released in vitro measured by the applied dissolution method(s) are indicative of differences in the rate and extent of drug release in vivo, which subsequently indicate differences in systemic exposure (i.e., confirming BE) (19, 20).

Dissolution testing performed under multiple pH conditions or the approved QC method, which may or may not contain surfactants, is not a priori indicative of unacceptable in vivo performance unless these methods are clinically relevant (21). Once a clinically relevant dissolution method (CRDM) has been developed and validated, this method should be used to assess the impact of manufacturing changes as opposed to any dissolution methods with unknown clinical relevance (22). A clinically relevant dissolution specification (CRDS) can be established via traditional bracketing approaches or in silico. In addition, one can develop upper and lower ranges of dissolution profiles within which products exhibiting dissolution profiles falling inside these ranges (“safe space”) are deemed equivalent to the reference product (19, 23, 24). Therefore, companies should invest in the development of CRDS and safe spaces especially for IR drugs containing poorly soluble drug substances. To develop an appropriate dissolution method where rate and extent of drug release are limited by drug substance solubility, surfactants are required to achieve complete drug release within 60 minutes. However, justification of appropriate surfactant levels or agitation conditions are always challenging unless a link to in vivo data is available.

Scientists in industry are encouraged to define the dissolution similarity assessment test conditions, test materials, mathematical hypothesis, mathematical method, and acceptance criteria based on dissolution performance experience from reference material made under the approved conditions as well as pilot batches made under the anticipated new manufacturing conditions prior to any dissolution profile assessment, regardless of whether CRDS and safe space are in place or not. This is especially important to avoid unexpected results (failure to demonstrate similarity, unexpected variability) or “cherry picking” mathematical models that

may give more favorable results. Likewise, this should avoid the temptation to use readily available software and apply a variety of mathematical models until the desired result is obtained. When it comes to good science, understanding drug substance, formulation, and process variables that impact the in vitro rate and extent of drug dissolved are critical to relate to in vivo performance. This does not necessarily imply that all dissolution specifications or methods require developing CRDS and safe space – the decision not to link in vitro and in vivo data should be based on rigorous risk biopharmaceutics risk assessment and overall product lifecycle management considerations.

The last talk entitled, “A Statistical Approach on Generic Development” was given by Prof Aleksander Mendyk.

Prof Mendyk introduced regulatory framework of ICH Q6A and Q6B, detailing product specifications in qualitative manner and presenting an evolution of requirements for development towards quantitative inferences as per ICH Q8(R2). He presented an empirical approach using ANOVA for selection of crucial critical process parameters and more sophisticated computational tools, i.e., rule-based artificial intelligence systems (Cubist). As for the latter he highlighted flexibility, interpretability, and simplicity of this tool to be used for design space selection in a quantitative and multidimensional manner.

The meeting ended with a question and answer session, which also closed the first day of the workshop.

### **SESSION 3: NEXT GENERATION CHARACTERIZATION FOR DISSOLUTION TESTING**

The second day of the virtual workshop began with a third session moderated by Prof Nikoletta Fotaki entitled, “Next Generation Characterization for Dissolution Testing.” The session addressed concerns related to visualization of transport in pharmaceutical systems, biopredictive testing, and novel approaches on dissolution methods for microsystems. The first talk was given by Prof Przemysław Dorożyński and covered “Drug Dissolution in a Snapshot - Visualization of Mass Transport in Pharmaceutical Systems.”

Elucidation of drug dissolution mechanisms is a highly demanding task. Drug release mechanisms cannot be explained simply based on the drug release results. Only a comprehensive approach to the issues will help understand the drug release mechanism. Such an approach requires the coupling of drug release testing with other methods, e.g., with non-destructive imaging

methods, i.e., magnetic resonance imaging (MRI,) micro-computed tomography (micro-CT), and supporting techniques, such as nuclear magnetic resonance relaxometry (NMR) performed in situ during dosage form incubation in dissolution media.

In the presentation, the practical and scientific aspects of the application of imaging studies concomitantly with drug dissolution were discussed. Characterizing the internal structure of a drug delivery system via imaging may be a powerful tool in the development of a generic drug product. It enables identification of the optimal drug manufacturing methodology, but it could also be used to analyze the potential behavior of drug delivery systems in the GI tract, which could be a risk mitigation factor prior to BE studies (25, 26). MRI can also be applied as a tool for elucidating the dissolution profile features (i.e., kinetics, kinetics changes, and variability) (27). Imaging techniques, in conjunction with other methods, were recently used to investigate mass transport phenomena within polymeric matrix systems (28).

The next speaker, Dr. habil. Grzegorz Garbacz, spoke on “Biopredictive Testing as a Tool Supporting Rational Development of Oral Medicines.”

Bio-predictive studies have a significant role in the R&D cycle of oral drugs, from API studies through formulation, preparation, and initiation of clinical trials to product manufacturing. The three most important factors affecting release of API from a solid dosage form or drug delivery performance in the human GI tract are pH, temperature, and pressure (mechanical agitation). All these factors vary significantly depending on the particular section of the GI tract and the prandial state. Both fasted and fed conditions were recently investigated using a telemetric capsule Smartpill™ capable of continuous monitoring of pH, temperature, and motility forces (29).

Based on knowledge of the specific physiology of the digestive system, bio-predictive studies can be considered as an extension of pharmacopoeial dissolution tests. However, to conduct representative bio-predictive characterization of oral drugs, simple and straightforward tools are necessary. These devices should simulate dynamic fluctuations of pH, motility, temperature, and volume changes of the GI tract. In addition, they are intended to deliver data that are suitable for the simulation of absorption and pharmacokinetic (PK) modeling. One such tool is pHysio-grad® (Physiolution). The apparatus is a fully automated, dynamic system developed for the simulation of physiological pH gradients characteristic for the small intestine and colon. The system utilizes

a hydrogen carbonate buffer in which pH reduction is achieved by injecting carbon dioxide into the system. In contrast, to raise the pH of the medium, air or inert gas is introduced into the system, which displaces the carbon dioxide. The apparatus has several types of configurations allowing, among others, the use of liquid titrates and gases or measurements in small volumes. Another tool used for biopredictive studies is the Advanced Modular Platform (Physiolution). The multifunctional design of the apparatus allows the combination of USP apparatus type 1 and 2 functionalities with Stress Test Device, transfer models, and pH controller. The forces acting on the drug form in the GI tract are simulated by the device through a balloon placed in the drug chamber, which exerts pressure on the test product under pumping and deflating. Another apparatus, which can be used to test IR formulations is PhysioCell (Physiolution). This novel flow-through device is divided into three compartments, by which it reflects realistic pH, flow rate, and mechanical stresses impacting the drug formulation during GI tract transfer.

In summary, the cutting-edge biopredictive methods developed by Physiolution enable realistic simulation of the GI tract and support the rational, physiology-driven development of oral medicines. Moreover, applying biopredictive methods can shorten the time and decrease market development cost as well as reduce the risk of clinical trials and therapy failure.

The final talk of the session was given by Prof Nikoletta Fotaki on “Novel Approaches on Dissolution Methods for Microsystems; Case Study: Liposomes.”

First, Prof Fotaki discussed why there is a need for a discriminatory test for liposomes. FDA guidelines only state that a validated release test should be performed for liposomes with a suitable release medium and with suitable agitation. She described the current state of the in vitro release testing of liposomes. The release medium is selected according to the solubility, stability, and ease of drug assay. A surfactant or an organic solvent can be added to increase the drugs' solubility or to accelerate its release and should have a physiological pH (7.4) and osmolality (275-300 mOsm/L); currently, the most commonly used is PBS. Next, Prof Fotaki discussed points to consider for the release medium, emphasizing the importance of proteins, as they would have an effect on drug solubility/release from formulation. Regarding the dissolution testing apparatus and operational conditions, the current guidelines include sample dialysis as well as separate and continuous flow methods. She gave a perspective on the points to consider, including the need

to simulate the hydrodynamics in the bloodstream, the concurrent circulation of liposomes and released drug, and the need for an in vitro test to facilitate dispersion of moving particles. A detailed case study on the development of in vitro release studies for liposomal formulations was described, where the effect of buffer, synthetic surfactant, protein, and hydrodynamics were presented. Afterwards, she presented the development of clinically relevant in vitro test conditions. The final part of her presentation related to the use of PBPK modeling to identify in vivo predictive release tests for parenteral liposomal formulations. She concluded her presentation by noting the importance of understanding the factors affecting drug release from liposomes by composition of medium and simulation of hydrodynamics at the site where drug will be released from formulation.

The session ended with a series of questions and answers.

#### **SESSION 4: MODELING AND ARTIFICIAL INTELLIGENCE APPROACHES**

The fourth session of the workshop, “Modeling and Artificial Intelligence Approaches,” was moderated by Vivian Gray. Presentations included use of artificial intelligence in in vitro-in vivo correlation (IVIVC), physiologically based biopharmaceutics modelling (PBBK), and biopredictive dissolution. The first talk, “IVIVC Based on Artificial Intelligence,” was given by Prof Aleksander Mendyk.

Prof Mendyk began by reviewing a classic case of a level A IVIVC performed with direct implementation of the FDA guideline to be inefficient in this specific case. He then introduced an AI-based tool called a symbolic regression (SR), working under principles of genetic programming (GP). As an open source system, HeuristicLabs was challenged with the data from the case study and showed excellent improvement of both internal and external predictability of IVIVC. As the structure of the resulting IVIVC model is extremely complicated and the data setup positions it between level A and multiple level C models, this approach is still experimental and therefore not to be applied on a regular daily basis. At the end of his presentation, Prof Mendyk described his regression in vitro in vivo relationship (RIVIVR) package capable of handling the case study data in an automated manner with superior predictability, but under the heuristic principles of empirical model development and thus difficult to validate under the principles of regulated environment. His last remark emphasized data quality, which is crucial to empirical modeling like the one presented in his talk.

The following presentation was given by Dr Sandra Suarez-Sharp, entitled “The Application of PBBM in Support of Formulation, Manufacturing, and Controls Changes via Safe Space Biowaivers.”

Demonstration of BE of a drug product following major changes in the formulation, manufacturing, and controls (CMC changes) plays an important role in drug product development and lifecycle management. Regulatory agencies have published several guidance documents to decrease the regulatory burden (via biowaivers) following CMC changes (2, 30, 31). The safe space framework offers an integrated approach to biowaivers, encompassing both the conventional and mechanistic approaches in the construction of in vitro-in vivo relationships (IVIVRs) or IVIVCs (24). Recently, the US FDA published a guidance on the “Use of Physiologically Based Pharmacokinetic Analyses — Biopharmaceutics Applications for Oral Drug Product Development, Manufacturing Changes, and Controls” (also known as the PBBM guidance) for the purpose of waiving not only BE studies based on building a safe space but to also aid in biopharmaceutics risk assessment and setting clinically relevant drug product specifications (32).

Selection of the safe space approach depends on the type and amount of data available, and it is likely that a safe space built based on the mechanistic (PBBM) approach will result in wider manufacturing and regulatory flexibility than one based on conventional approaches. One advantage of the PBBM-safe space approach is that it is not confined to building IVIVCs, increasing the likelihood of gaining regulatory flexibility. Precisely, PBBM facilitates the establishment of the essential in vitro-in vivo link by delineating a mechanistic understanding of the in vivo drug release and its interaction with the physiology. This level of understanding results in the construction of IVIVRs, offering a simpler and feasible path to biowaivers, especially for immediate release drug products for which the rate of success of IVIVCs is rather low. Safe space pillars are the IVIVC and IVIVR, thus, the safe space approach is governed by IVIVC/IVIVR principles. As such, for regulatory decision making, at least two release rates with corresponding Cp-time profiles are needed for its establishment. However, to support high risk CMC changes, at least three formulation variants should be used in its construction. For generic drug products, in addition to building the safe space around the target formulation, the Reference Listed Drug (RLD) should also be included. It should be noted that from the regulatory perspective, extrapolation outside the knowledge space for high-risk dosage forms, e.g., extended-release formulations

and BCS class 2 or 4 compounds, is not recommended. During drug product development, however, the need for extrapolation is expected and constitutes a plausible and proven path for successful formulation selection.

In summary, safe space construction via the PBBM approach has the potential to expand the manufacturing and regulatory flexibility delineated under several regulatory frameworks such as BCS, IVIVC, and similarity testing.

The third and final lecture of the workshop was given by Prof Sebastian Polak, “3D Printing Combined with Biopredictive Dissolution and PBPK/PD Modeling for the Personalized Therapy Optimization - Are We There Yet?”

During his presentation, Prof Sebastian Polak discussed the potential of model-steered 3D printing combined with biopredictive dissolution and physiologically based pharmacokinetic/pharmacodynamic (PBPK/PD) modeling for the need of personalized therapy optimization. Model-informed precision dosing (MIPD) is a concept suggesting utilization of model-based prediction methods for optimizing treatment benefit-to-harm balance based on individual characteristics of the patient, disease, treatment, and other factors. Theoretical workflow consisting of several elements – PBPK/PD models, 3D printed tablets with the model-proposed dose, information range and flow, and the place of a real patient was presented. The discussed example was based on the Parkinson’s disease, which is a multisystem neurodegenerative condition that manifests itself through motor and non-motor symptoms including tremor, bradykinesia (slowing of motion and difficulty in initiating movement), and rigidity. This disease requires precise and variable therapy, which could potentially be supported by MIPD, but there are several obstacles inhibiting implementation. These include 3D printing method standardization, high throughput quality control dissolution testing, and others (33, 34).

This last presentation was followed by a question-and-answer session.

The workshop ended with the closing remarks given by Prof Aleksander Mendyk. He thanked the speakers for the time and effort they put into their presentations, as well as the audience for attending the meeting and participating actively in the question and answer sessions. He also stressed the importance of exchanging ideas between academia and industry, which can positively influence cooperation between the two communities. Finally, Prof Mendyk expressed hope for other virtual meetings in the

future, which proved to be a great tool for exchanging experiences among participants and experts from around the world.

The 2-day virtual workshop was well received by the participants, who addressed the organizers with positive feedback after the conference.

## CONFLICT OF INTERESTS

The authors have no disclosures related to this article.

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