

Meeting Report: AAPS Workshop on “Dissolution Testing, Biowaivers and Bioequivalence” in Moscow, Russia

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The workshop in Moscow, Russia, was held at the Sechenov First Moscow State Medical University (MSMU) on October 6 and 7, 2011. All presentations were given in Russian translated from English. All sessions were followed by Q and A panel discussions with written questions for the speakers.

The first day consisted of the English presentations using simultaneous translation. After the opening remarks by **First MSMU Vice-Chancellor, Prof. A. A. Svistunov**, **Vivian Gray** from **V. A. Gray Consulting** gave the first talk, titled “General Concepts—Design of Dissolution Method Development, including Quality by Design (QBD).” Her talk gave the principles needed to develop a meaningful dissolution test, one that followed the concepts of QbD. The emphasis is on understanding the product-release mechanism and knowing the critical quality attributes, leading to clinically relevant dissolution specifications. Next, **Nikoletta Fotaki** of the **University of Bath**, UK, gave a presentation on “Predictive Dissolution Testing and Development of IVIVCs.” Her presentation discussed how predictive dissolution can be useful through all stages of product development, especially early stages, and how accurate in vitro simulation of the GI tract (through media and hydrodynamics) can lead to successful IVIVC–IVIVR. The methods should be designed with the critical drug substance and formulation properties in mind. The last presentation of the session was by **Prof. Dr. Eric Beyssac**, **University of Auvergne**, Clermont-Ferrand, France, on the subject “Dissolution of Sustained Release Dosage Forms and In Vivo Predictability.” Prof. Beyssac showed examples of equipment that was appropriate for sustained-release products and discussed developing IVIVC using these types of equipment.

In the afternoon, **Vivian Gray** spoke about GMPs in the Dissolution Lab and **Terry Way**, **USP** (European office), discussed “The Role of Dissolution Testing: USP Perspective.” The third speaker was **Allan Little**, from **Agilent**, whose talk was titled “Dissolution Apparatus Qualification: Performance Verification Standard (PVT) versus Mechanical Qualification (MQ), What’s Right for Your Laboratory.” He stated that proper qualification of the dissolution apparatus is critical and compared the merits of qualification performed with the USP PVT and MQ. **Johannes Krämer** of **PHAST**, Homburg, Germany, spoke on “Disintegration Instead of Dissolution: A Case Study.” His talk illustrated how a disintegration test could be used as the regulatory test instead of the dissolution test. He

gave a case study that employed the use of Statistical Moment Theory: Mean Time to justify the regulatory disintegration test with regulatory authorities. **Hans Jürgen Knitter**, **Bayer/Erweka**, Germany, spoke on “Automation in Dissolution.” He discussed the pros and cons of automation and described different types of automation that are applied to dissolution testing. Validation of the transfer of a manual method to an automated method was described.

The second day was serial translation in Russian for the remaining three talks that were in English. The first speaker was **Igor Shohin** (senior lecturer in **First MSMU**; Head of lab in Chemrar, Russia), who spoke on “Biowaiver Procedures—Practical Aspects.” The lecture was devoted to some practical aspects of the biowaiver procedure, solubility and permeability determinations, and comparative dissolution kinetic studies with some examples. Biowaivers are not accepted in Russia by the regulatory authorities, but workshop attendees realized the importance of BCS-based biowaiver procedures. In addition, results of some First MSMU team studies were provided, and a presentation from the pharmacokinetic and dissolution laboratory was shown. **Nikoletta Fotaki** returned to discuss “From Dissolution to BA/BE Studies.” She gave case studies where modeling and appropriate in vivo data led to successful development of IVIVCs. Then **Johannes Krämer** spoke on “Examination of Level B Correlations with a BCS Class 2 Immediate-Release Formulation.” He presented a case study using multisource propafenon film-coated tablets where the use of level B correlation of mean times provided an IVIVC. After lunch, **Olga Baula** (**National Expert in Quality of Medicines, WHO Expert**, Ukraine) gave a talk on the regulatory aspects of biowaiver procedures in Ukraine. Baula spoke about the practical use of biowaiver procedures for drug product approvals in Ukraine. Several real cases were described, and the structure of the biowaiver dossier was provided. Then there were three short communications. The first, given by **I. G. Smekhova**, Asst. Prof., **SPCPA**, Saint Petersburg, Russia, was “Application of Biowaiver Procedure to Russian Generic Drug Products.” She said that to prevent the manufacture of pharmaceutically nonequivalent drugs and to improve the quality of solid oral dosage forms, the use of the dissolution test is necessary for medicines with the same active ingredient. She shared experiences of the application of the dissolution test and biowaiver procedure to the evaluation of generic drugs marketed in Russia and

provided the results of work in this field carried out in Saint Petersburg State Chemical Pharmaceutical Academy (SPSCPA) in the Department of the Technology of Medicinal Forms. The second short talk was given by **M. A. Gushina** of **Hanson Research**; she presented an overview of Hanson Dissolution equipment. The last short communication was given by **R. I. Moustafine**, Prof., **KazSMU**, Kazan, Russia, who spoke on drug release from the polymeric complex Eudragit. The combination of chemically complementary grades of Eudragit copolymers in oral, modified-release matrix and reservoir types of solid dosage forms (tablets, microspheres, micropellets) and technological methods of their preparation, including film coatings were explained. Interactions between reactive groups of copolymer pairs, which control the drug release process inside matrices and within multilayer or combined coatings, were discussed. He stated that analysis of these processes has a key significance for representing poly(meth)acrylate complexes as a new class of drug carriers in constructing modern oral drug delivery systems.

Evangelos Kotzagiorgis from the **EMA** discussed the European Regulatory Perspective on Dissolution Testing. The last speaker was **Galina Ramenskaya** (Prof., head of chair of pharmaceutical and toxicological chemistry in **First MSMU**; Director of Institute of Pharmacy, Russia), who discussed "Russian Regulatory Perspective on Dissolution, BE and Biowaivers." Prof. Ramenskaya

provided information about current laws, guidelines, and other regulations for bioequivalence studies in Russia and a draft of biowaiver and dissolution kinetics guidances. Vivian Gray closed the workshop with remarks of thanks to the organizers and speakers and appreciation for the fine hospitality shown to the Focus Group speakers.

There were about 450 attendees from six countries: Russia, Ukraine, Belarus, Armenia, Hungary, and Kazakhstan



From left to right: Johannes Krämer, Igor Shonin, Prof. Ramenskaya, Evangelos Kotzagiorgis, Nikoletta Fotaki, Vivian Gray, and Terry Way.