Report: International Symposium on Bioequivalence Testing – 2012

An **International Symposium on Bioequivalence Testing** was held on August 21. and 22 in Bangkok Thailand, under the sponsorship of the International Pharmaceutical Federation (FIP), the American Association of Pharmaceutical Scientists (AAPS), The Pharmaceutical Association of Thailand under Royal Patronage (PAT), Thai Industrial Pharmacist Association (TIPA), Regulatory Affairs Pharmaceutical Association (Thailand), Thai Food and Drug Administration and Burapha University, Thailand.

Almost 200 delegates, mostly from the Thai industry and regulatory authority but with some representation from other Asian countries e.g. Indonesia, attended the Symposium, which was organized by Prof. Sompol Prakongpan (Burapha University, Thailand) and Prof. Jennifer Dressman (Goethe University, Germany).

The Symposium opened with a welcoming address from Prof. Sompol Prakongpan and Opening Remark from Mr. Teera Chakajnarodom, President of The Pharmaceutical Association of Thailand under Royal Patronage. The first session opened with a presentation by Jennifer Dressman on the "why and how" of bioequivalence testing, providing a framework on why and when bioequivalence must be assessed and which methods are available to do so. Anita Nair (Goethe University) and Sandra Klein (University of Greifswald) followed with detailed descriptions of pharmacokinetic assessment of bioequivalence, for both standard situations and special cases such as drugs with narrow therapeutic index, those that are to be administered with food, those with long half-lives in plasma etc. Vinod Shah (FIP) rounded out the morning session by detailing the dissolution studies required to support pharmacokinetic assessment of bioequivalence.

The afternoon session focused on the BCS based biowaiver as an alternative to pharmacokinetic assessment of bioequivalence. Vinod Shah opened the session with a description of the BCS and how drugs can be classified according to this system, also mentioning the ramifications of BCS category for the application of the biowaiver. Jennifer Dressman then gave an overview of which drug/product combinations are eligible and how to determine whether a particular drug/product can be approved by this procedure. Having identified which drug products might be eligible for the biowaiver, Sandra Klein then discussed in detail which dissolution tests are needed for the biowaiver based approval and how the results need to be evaluated. Anita Nair then illustrated how to assess whether the BCS biowaiver is applicable for an individual drug product using case examples of Biowaiver Monographs.

Wednesday morning kicked off with a session devoted to further alternatives to pharmacokinetic BE testing. Vinod Shah outlined requirements for obtaining a biowaiver for lower dosage strengths, emphasizing the requirement for proportional composition of the drug product at the lower dosage strength and explaining how proportional composition is defined. Sandra Klein and Jennifer Dressman focused on setting up in vitro-in vivo correlations as another way of obtaining a waiver of pharmacokinetic assessment of bioequivalence. While Sandra Klein discussed the classical approaches using deconvolution techniques which are the focus of current guidances, Jennifer Dressman presented what the future could look like, employing

physiologically based pharmacokinetic models to convolute biorelevant dissolution data into simulated plasma profiles.

In the last session, on Wednesday afternoon, the specifics of bioequivalence testing in Thailand were the focus of discussion. Two presentations were given, one presented by Tharnkamol Chanprapaph (Thai FDA) and the other by Ariya Khunvichai (Medica Innova, Thailand). Thereafter followed a long and lively –almost two hours - Question and Answer session with the full panel of speakers, moderated by Sompol Prakongpan. Although Thailand, as part of the ASEAN alliance, basically follows the EMA rules for bioequivalence, it was clear that differences among the guidances of the US FDA, WHO and EMA create confusion on the part of sponsors and also create headaches for the local regulatory authorities. It was also clear that there is a need to better address requirements for fixed dose combinations, which are important in this region, and to clarify rules for approval of lower dose strengths based on proportionality of the formulation composition.

Feedback from the Symposium was extremely positive and it is to be hoped that further such Symposia can be organized in other non-ICH countries so that scientists in these regions can have an opportunity to discuss the various bioequivalence guidances directly with seasoned experts in the field.

Submitted by Jennifer Dressman and Sompol Prakongpan