2nd JBF Symposium

- International Harmonization of Bioanalysis Regulation &
Current Situation of a New Bioanalysis Guideline in Japan-

8 March 2012, 10:00-17:10

Venue: Tower Hall Funabori (Tokyo, Japan)

Opening remarks	**10:00-10:10**
Tatsuo Kurokawa, Ph.D. (JBF Representative: Professor, Keio University)	
1. Bioanalytical Method Validation in Japan and activities of the Japan Bioanalysis Forum	**10:10-10:30**
Noriko Katori, Ph.D. (National Institute of Health Sciences)	
2. Outline of Global Bioanalysis Consortium	**10:30-10:45**
Shinobu Kudoh (Shimadzu Techno-Research, Inc.)	
3. Towards Global Harmonization of Bioanalysis Guidelines: The Global Bioanalysis Consortium (GBC)	**10:45-11:30**
Philip Timmerman (Drug Safety Sciences, Janssen Research and Development for EBF/GBC)	
Lunch break	**11:30-12:50**
4. The EMA Bioanalytical Method Validation Guideline: process, history, discussions and evaluation of its content	**12:50-13:35**
Peter van Amsterdam (Global Bioanalytics, Abbott Healthcare Products BV for EBF/GBC)	
5. Overview of GBC discussion	**13:35-15:15**
Takehisa Matsumaru, Ph.D. (Nippon Boehringer Ingelheim Co., Ltd.) Tomoko Arakawa (Pfizer Japan Inc.) Yoshiaki Ohtsu (Astellas Pharma Inc.) Masanari Mabuchi (Mitsubishi Tanabe Pharma Corporation) Yoshiyuki Minamide, Ph.D. (Shimadzu Techno-Research, Inc.)	
Coffee break	**15:15-15:45**
6. Preparation of Guideline for Bioanalytical Method Validation in Japan	**15:45-16:15**
Tomoki Yoneyama (Takeda Pharmaceutical Company Limited)	
7. General discussion	**16:15-17:00**
Closing remarks	**17:00-17:10**
Yasuo Ohno, Ph.D. (Director General, National Institute of Health Sciences)	
Exhibition and gathering (at Event Hall)	**17:30-19:30**

Chair: Yoshitaka Taniguchi (Toray Research Center, Inc.)

This document is a translation of the official handout for the 2nd JBF Symposium.

Dear Sirs/Madams,

It is our greatest pleasure to welcome you to the 2nd Japan Bioanalysis Forum (JBF) Symposium.

Since the 1st Symposium in August 2011, the JBF has worked devotedly to establish its scope, framework and organization, with a great help from experts and stakeholders. Today the JBF is holding the 2nd Symposium, having a firm organizational structure, owing to your kind and continuous support so far.

Recently we have seen a significant progress in discussions on Bioanalytical Method Validation (BMV) in the Global Bioanalysis Consortium (GBC). In addition, establishment of the BMV Guideline in Japan is currently in progress, which is the topic of interest. We believe that it is high time for this country to solidify the scope and framework of regulated bioanalysis, from a perspective of pharmaceutical R&D, quality assurance (QA) and quality control (QC).

It has been a long time since pharmaceuticals became a topic of international harmonization and global competition, and there has been a great movement in this regard especially in Asia. Considering these situations, we invite oversea guest speakers to see global trends and to clarify the overall picture and future steps in regulated bioanalysis.

In addition, thanks to supporting companies, exhibition booths are set up during this Symposium, where latest technological information is available.

As discussion about regulated bioanalysis is rapidly growing, communication in this field should be open, mutual and constructive from the early stage. We would highly appreciate your contribution and participation in this Symposium and future bioanalysis in Japan.

Sincerely yours,

Tatsuo Kurokawa, Ph.D.
Professor, Keio University
On behalf of the Japan Bioanalysis Forum

1. Bioanalytical Method Validation in Japan and activities of the Japan Bioanalysis Forum

Since the Japan Bioanalysis Forum (JBF) was established in March 2011, there have been active discussions on the regulated bioanalysis in Japan. We the JBF held the 1st Symposium in Tokyo on 10 August, followed by a Workshop on bioanalysis by BMAS 2011 (The BioMedical Analytical Chemistry Symposium) in the end of August. The BMAS 2011 raised awareness of the importance of Bioanalytical Method Validation (BMV) among academic field representatives. The 3rd JBF Symposium will be held in collaboration with the BMAS 2012.

In addition to these local activities, the JBF is acting globally: after its establishment was officially announced in the 5th WRIB in Montreal (April 2011), we confirmed in the 4th EBF Open Symposium in Barcelona (November 2011) that the EBF and JBF will be a partner in BMV harmonization. From now on, the JBF seeks possibility of collaboration with Asia-Pacific nations, e.g., Korea and China, with regard to BMV.

Meanwhile, some Task Forces are working within the JBF: The most active one is the HT Task Force, which has been supporting Japanese members in Global Bioanalysis Consortium Harmonization Teams (GBC-HT) from the very early stage. In addition, we have established the Guideline Task Force upon request by the BMV Study Group in the Japanese Ministry of Health, Labour and Welfare (MHLW). The Task Force members have worked aggressively and made the first draft of the Japanese BMV Guideline (small molecule area) in 3 months. They are expected to work for drafting the FAQ section and large molecule area Guideline as well.

We have to admit that Japan fell behind Europe and the US in the BMV Guideline; however, BMV in advanced areas such as biomarkers and micro-dosing is still under discussion, and the JBF is expected to be a tractive power in these novel technologies.

Noriko Katori, Ph.D.
Chief of Third Section, Division of Drugs, National Institute of Health Sciences

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2. Outline of Global Bioanalysis Consortium

The Global Bioanalysis Consortium (GBC) works in collaboration with about 150 bioanalytical experts from four global regions: EU/Middle East/Africa, Asia-Pacific, Latin America and North America. The GBC consists of: All molecules (A) group for discussion on both chromatographic (CA) and ligand binding assay (LBA); Large molecules (L) group dedicated to LBA-specific topics; and Small molecules (S) group dedicated to CA-specific topics. The GBC has 20 Harmonization Teams (HTs), each of which has a specific theme. The JBF has successfully sent Japanese members to all of the 20 HTs, and they aggressively participate in the team discussion through regular teleconferences.

The mission of the GBC is to* "create an all inclusive Global Bioanalysis Consortium (GBC) consisting of represented scientific associations with world wide influence to merge existing or emerging bioanalytical guidance to create one, unified consensus document that can be presented to the regulatory bodies/health authorities in various countries". It will enable us to: create quality bioanalysis data around the globe; facilitate the regulatory review process; eliminate useless work and retests; and deliver quality drugs to patients and the medical front more quickly.

The goals and objectives of the GBC are*:

- To bring together stakeholders from the pharmaceutical industry, contract research organizations and academia to share current understanding of bioanalysis guidelines, identify differences in these guidelines or differences in the interpretation or application thereof to routine regulated bioanalysis.
- To come forward with recommendations to Health Authorities and regulatory bodies worldwide on globally agreed best practices for Bioanalytical Method Validation (BMV) and application of such methods/technologies to the analysis of drugs of all molecular sizes in support of clinical and nonclinical studies.
- To invite relevant stakeholders, from industry, academia, Health Authorities and regulatory bodies, to jointly discuss the GBC recommendations at a global conference(s) in order to achieve globally agreed guidelines on bioanalysis.
- Going forward, to serve as a pivot point on the continued harmonized interpretation and/or updates of globally agreed guidelines

The GBC will hold a Global Conference this September and is preparing for disclosure of a unified draft bioanalysis guideline. After some revision and fortification by discussions in this Conference, the Consortium plans to contribute the draft guideline to a journal.

The unified guideline will be established based on scientific findings and discussions by experts from all around the globe; therefore it will help bioanalysts create quality data and the regulatory authorities provide scientific and consistent review.

* Quoted from the GBC website.

Shinobu Kudoh
Shimadzu Techno-Research, Inc.

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3. Towards Global Harmonization of Bioanalysis Guidelines: The Global Bioanalysis Consortium (GBC)

Throughout the eighties and nineties, Regulated bioanalysis has been influenced by different evolutions in the pharmaceutical industry, science, evolution in technology or economic factors, resulting in the 2001 FDA Guidance on Bioanalytical Method Validation (BMV). Certainly the last 10 years, the increased globalization and rapid progress in technology has created an additional complexing factor in allowing the industry to come to a common view on the application of these established Guidelines. In addition, new Guidelines are emerging in addition to the FDA Guidance. In 2010, following up on the Open Letter to the authorities (Bioanalysis, April 2010), AAPS-APA-CVG and EBF joined hands and founded the Global Bioanalysis Consortium (GBC). Endorsed, supported and even stimulated by health authorities, the GBC has create an all inclusive Global Consortium consisting of represented scientific associations with worldwide influence, to merge existing or emerging bioanalytical Guidances to create a industry consensus that can be discussed with the regulatory bodies/health authorities globally.

Throughout 2011 and 2012, GBC brought together stakeholders from the pharmaceutical industry, contract research organizations and academia to share current understanding of bioanalysis Guidelines, identify differences in these Guidelines or differences in the interpretation or application thereof to routine Bioanalysis.

Currently within GBC, 20 teams are discussing all aspects of regulated bioanalysis.

Under the umbrella of GBC, they intend to come forward with recommendations to Health Authorities and regulatory bodies worldwide on globally agreed best practices for BMV and application of such methods/technologies to the analysis of drugs of all molecular sizes in support of clinical and nonclinical studies.

The recommendations will be discussed and shared at a global conference to be held in The Netherlands in September 2012

In this presentation, an overview will be presented of the history of Regulated bioanalysis and the activities of the GBC.

Philip Timmerman
Drug Safety Sciences, Janssen Research and Development for EBF/GBC

Session Chair: Shinobu Kudoh (Shimadzu Techno-Research, Inc.)

4. The EMA Bioanalytical Method Validation Guideline: process, history, discussions and evaluation of its content

The Crystal City conference reports and the FDA bioanalytical method validation guidance (May 2001) have long been recognized as the standard documents for regulated bioanalysis, also in Europe.

At the End 2008 the European Medicines Agency (EMA), formerly known as European Agency for the Evaluation of Medicinal Products (EMEA), issued their "Concept paper/recommendations on the need for a (CHMP) guideline on the validation of bioanalytical methods" in which the agency presented their intention to issue a guideline on bioanalytical method validation and short description of the intended contents. The EBF collected comments from its members on this concept paper and presented them in a consolidated format to the EMA in March 2009. Further the EBF included a session in their December 2009 Open Symposium with presentations by the EBF, AAPS and EMA representatives to discuss the concept guideline with the bioanalytical community.

End 2009 the draft bioanalytical method validation guideline was issued by the EMA and subsequently the EBF started the process to collect comments from its members. Further the EBF organised a workshop in collaboration with the EUFEPS to discuss the draft guideline in great depth with the regulators and the bioanalytical community in April 2010. In parallel a symposium dedicated to large molecules/ligand binding analysis was organised by the IGM group of EBF, held at the May 2010 National Biotech Conference in San Francisco. Comments from the EBF were submitted to the EMA per end May 2010.

August 2011 EMA released their final guideline, which has become effective per February 2012. EBF provided the opportunity for discussion on the interpretation of the final document during their 2011 Open Symposium and has organized a workshop for March 2012 with their members focusing on the implementation within the bioanalytical laboratories.

In this presentation, an overview will be presented of the processes and history of the EMA bioanalytical method validation guideline and the activities of EBF and the interactions EBF had with the authors of the guideline.

Peter van Amsterdam
Global Bioanalytics, Abbott Healthcare Products BV for EBF/GBC

Session Chair: Nobuhiro Kobayashi, Ph.D. (Daiichi Sankyo Co., Ltd.)

5. Overview of GBC discussion

The GBC has 20 Harmonization Teams (HTs) and Japanese members take part in all of them. To help the Japanese GBC-HT participants, the JBF has set up a HT-supporter community, which is currently having active discussion. The current status on GBC-HT activities and Japanese HT members is presented, followed by presentation of four topics of interest.

Takehisa Matsumaru, Ph.D.
Nippon Boehringer Ingelheim Co., Ltd.
JBF HT Task Force

Session Chair: Kazutaka Togashi (Sumika Chemical Analysis Service, Ltd.)

A1: Scope and regulations

The HT-A1 is discussing the regulation on bioanalytical method validation and sample analysis, and the Scope and Glossary of the harmonized document. What we have discussed so far and the current Scope draft will be presented.

Tomoko Arakawa
Pfizer Japan Inc.

A3: Method transfer, partial and cross validation

The following are the topics in HT-A3: How to define each of the Method Transfer, partial and cross validation; how to use them properly; how we think about their acceptance criteria. The interim report will be presented.

Masanari Mabuchi
Mitsubishi Tanabe Pharma Corporation

A6: Stability

The summary of HT-A6 activities, scope and team agreement will be presented. In addition, some topics will be introduced that have not been fully discussed in Japan so far (e.g., Incurred sample stability, ISS).

Yoshiaki Ohtsu
Astellas Pharma Inc.

L2: Large molecule specific assay operation

Ligand binding assays (LBAs) are widely used in bioanalysis of antibodies and proteins; however, LBAs tend to have greater variability and have unique characteristics such as the Hook Effect. The HT-L2 is discussing assay operations to properly evaluate the LBA systems, considering these characteristics. What we have discussed will be presented.

Yoshiyuki Minamide, Ph.D.
Shimadzu Techno-Research, Inc.

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6. Preparation of Guideline for Bioanalytical Method Validation in Japan

In the history of Bioanalytical Method Validation (BMV), the US Food and Drug Administration (FDA) released the Guidance for Industry in 2001, whereas no detailed guideline has been established in Japan. With the discussion on global harmonization of BMV guidelines started by the GBC in 2011, the Japan Bioanalysis Forum (JBF) was established in August 2011, involving experts from academia, government and industry. This has lead to a request from the industry for establishment of a BMV guideline in Japan.

Considering these trends, in October 2011, the Ministry of Health, Labour and Welfare (MHLW) set up a Study Group that aims at establishment of the BMV Guideline in Japan. The Study Group asked the JBF, the only entity for BMV dedicated experts in Japan, to draft the Guideline.

The JBF immediately set up a Task Force and started drafting the Guideline. The scope of the Guideline is firstly the method validation and sample analysis with chromatographic assays for small molecules. In the future the Guideline for large molecules and biomarkers will be in scope. The draft Guideline refers to the FDA Guidance and the European Medicines Agency (EMA) Guideline and is largely harmonized with them. As for the Glossary, the Japanese Pharmacopoeia, the ICH and other relating guidelines/guidance are referred to (e.g., non-clinical PK, clinical PK and BE guidelines); when a proper definition was not found in these documents, the JBF had a discussion on term definition as well. The draft Guideline provides minimal requirement and allows us to apply currently used techniques and methods; for some areas in question, supplements or FAQs may be provided as well.

In this session, the process of drafting the BMV Guideline by JBF, points of discussion, our conception and term definitions will be presented, in comparison with the existing guidelines/guidance.

We the JBF expect that the draft Guideline will bring active discussions about regulated bioanalysis and BMV in Japan.

Tomoki Yoneyama
Takeda Pharmaceutical Company Limited

Session Chair: Noriko Katori, Ph.D. (Chief of Third Section, Division of Drugs, National Institute of Health Sciences)

7. General discussion

Session Chair: Takahiko Osumi (Otsuka Pharmaceutical Co., Ltd.)

Panelists: Noriko Katori, Ph.D. (Chief of Third Section, Division of Drugs, National Institute of Health Sciences)

Shinobu Kudoh (Shimadzu Techno-Research, Inc.)

Takehisa Matsumaru, Ph.D. (Nippon Boehringer Ingelheim Co., Ltd.)

Tomoko Arakawa (Pfizer Japan Inc.)

Yoshiaki Ohtsu (Astellas Pharma Inc.)

Masanari Mabuchi (Mitsubishi Tanabe Pharma Corporation)

Yoshiyuki Minamide, Ph.D. (Shimadzu Techno-Research, Inc.)

Tomoki Yoneyama (Takeda Pharmaceutical Company Limited)

Symposium Executive Committee Members

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Tsutomu Masujima, Ph.D., Professor (Hiroshima University)

Committee chair: Kazutaka Togashi (Sumika Chemical Analysis Service, Ltd.)

Committee members: Harue Igarashi (GlaxoSmithKline K.K.)
Noriko Inoue, Ph.D. (JCL Bioassay Corporation)
Mami Imazato (Novartis Pharma K.K.)
Takahiko Osumi (Otsuka Pharmaceutical Co., Ltd.)
Yoshiaki Ohtsu (Astellas Pharma Inc.)
Noriko Katori, Ph.D. (National Institute of Health Sciences)
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Yoshitaka Taniguchi (Toray Research Center, Inc.)
Keiko Nakai (Mitsubishi Chemical Medience Corporation)
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