# JBF Annual Report FY2014

(From 1st April 2014 to 31st March 2015)

## 1. Overview

It has been passed three years and a half since the establishment of Japan Bioanalysis Forum (JBF).

We aim to facilitate a discussion on regulated bioanalysis in Japan, to interact with Japanese regulators in the field of bioanalysis, and to represent Japan in worldwide bioanalysis communities.

JBF acts with the Steering Committee (SC), two memberships (corporate and supporting memberships), JBF partner, Discussion Group (DG), and GBC Harmonization Teams (HT) members/supporter community about broad topics of interest in bioanalysis field. At the end of FY2014, the corporate and supporting memberships are 17 companies each.

Main JBF activities of FY2014 are as indicated below.

1. Holding of JBF symposium
2. Contribution to preparation of bioanalytical method validation (BMV) guideline for Ligand Binding Assay (LBA)
3. Participation in the government working groups for regulated bioanalysis of large molecules using MS (LM-MS) and biomarkers
4. Comparison of BMV guideline/guidance among Japanese Ministry of Health, Labour and Welfare (MHLW), EMA and FDA in terms of LBA
5. The handbook on BMV LC guideline was published.
6. Promotion of DG activity

The 6th JBF symposium was held on 25th and 26th February 2015 in Tokyo with the theme, ‘Challenge of Regulated Bioanalysis’. This symposium presented the challenges regarding biomarkers and LM-MS, as well as the current circumstances for regulated bioanalysis by inviting speakers from Japan, US, EU and Asia-pacific, because biomarker measurement and LC-MS analysis of large molecule have had increasing importance in pharmaceutical development, although they are not included in the existing bioanalytical method validation guidelines in Japan. JBF DGs also presented their outcomes and openly discussed these with the attendees over 200 dedicated individuals from industry, regulatory agencies and academia. The symposium successfully reinforced the idea that fit-for-purpose approaches are necessary, and that science should drive any judgments and actions throughout drug development.

## 2. Organization and members of steering committee

The SC consists of the committee members, GBC SC members and the TF members.

The number of the SC members for FY 2014 is 26; 14 from pharmaceuticals, 7 from CROs, 3 from academia and 2 from regulatory agency.

The committees, task forces and SC members are listed below.

<Committees>

| | |
|---|---|
| F&A | Event execution |
| Financial auditors | Public relations |
| Website administration | International affairs |
| Membership | EBF window persons |
| Documentation | CBF window persons |
| Discussion group (DG) promotion | |

<Task forces>

| | |
|---|---|
| GBC HT support | Ligand binding assay BMV guideline |
| Large molecule MS guideline (LM-MS) | Small molecule BMV guideline handbook |
| Biomarker (Aug. 2014-) | |

<Steering Committee Members>

| | |
|---|---|
| Representative | Haruhiro Okuda (National Institute of Health Sciences) |
| Advisors | Jun Haginaka (Prof., Mukogawa Women's Univ.)<br>Tsutomu Masujima (Prof., Hiroshima Univ.)<br>Tatsuo Kurokawa (Prof., Keio Univ.) |
| GBC SC | Shinobu Kudoh (Shimadzu Techno Research, Inc.) |
| Deputy Representative | Noriko Katori (National Institute of Health Sciences),<br>Masanari Mabuchi (Mitsubishi Tanabe Pharma Co.),<br>Yoshiaki Ohtsu (Astellas Pharma Inc.) |

| Name | Affiliation |
|---|---|
| Harue Igarashi | GlaxoSmithKline K. K. |
| Hisanori Hara | Novartis Pharma AG, Switzerland |
| Motoki Onishi | Towa Pharmaceutical Co., Ltd. |
| Jun Hosogi | Kyowa Hakko Kirin Co., Ltd. |
| Kazuhiro Miya | Chugai Pharmaceutical Co., Ltd. |
| Kazutaka Togashi | Sumika Chemical Analysis Service, Ltd. (-Feb. 2015) |
| Takeru Yamaguchi | Sumika Chemical Analysis Service, Ltd. (Feb. 2015-) |
| Keiko Nakai | LSI Medience Co. |
| Kenji Yahata | Sanofi K.K. |
| Masaaki Kakehi | Takeda Pharmaceutical Company Ltd. |
| Noriko Inoue | JCL Bioassay Co., Ltd. |
| Yoko Urasaki | Daiichi Sankyo Co., Ltd. (-Feb. 2015) |
| Makoto Takahashi | Daiichi Sankyo Co., Ltd. (Feb. 2015-) |
| Takahiko Osumi | Otsuka Pharmaceutical Co., Ltd. (-Feb. 2015) |
| Takehisa Matsumaru | Otsuka Pharmaceutical Co., Ltd. (Feb. 2015-) |

| Name | Affiliation |
|---|---|
| Takahiro Nakamura | Shin Nippon Biomedical Laboratories, Ltd. |
| Yoshihisa Sano | Eisai Co., Ltd./Sunplanet Co., Ltd. |
| Yoshitaka Taniguchi | Toray Research Center, Inc. (-Feb. 2015) |
| Kazuhiro Takegami | Toray Research Center, Inc. (Feb. 2015-) |
| Yoshiyuki Minamide | Shimadzu Techno-Research, Inc. |
| Kazuhiko Sasaki | Taisho Pharmaceutical Co., Ltd. |
| Akemi Nagao | Japan Tobacco Inc. (May 2014-) |

## 3. Activities of steering committee

JBF SC Meetings were held monthly (3rd Apr, 8th May, 5th Jun, 3rd Jul, 20th Aug, 11th Sep, 2nd Oct, 6th Nov and 11th Dec in 2014, and 14th Jan, 5th Feb, 19th Mar [ad hoc meeting] in 2015). The minutes were finalized and distributed to the SC members.

- The operational document for SC members was updated.
- JBF annual report FY2013 in English was released.
- The handbook on BMV LC guideline was published.
- Comparison table of BMV guideline/guidance among MHLW, EMA and FDA in terms of LBA was generated.
- JBF cooperated with the BMV study group granted by MHLW with regard to preparation of BMV guidelines and other documents for large molecule analysis based on LC-MS and for biomarker measurements.
- Micro-sampling was adopted as Q&A of ICH-S3A on November 2014. JBF has participated in the implementation working group of the ICH to develop a S3A Q&A document.

In addition to the activities above, the outcome of SC activities is described in Sections 4 to 9.

## 4. New organization and activity of JBF

The BMV study group granted by MHLW has been collaborated with JBF in order to provide documents to ensure the reliability of large molecule analysis based on LC-MS and of biomarker measurements, which are not covered with the existing guidelines. LM-MS TF was formed in FY2013, and then Biomarker TF was newly formed on August 2014.

The LM-MS TF prepared the Q&A document for BMV LC guideline regarding some considerations or recommendations specific to the bioanalysis of large molecule pharmaceuticals by using LC-MS, and submitted it to the BMV study group. The consensus of the regulatory aspects to this document is not yet available because the analytical techniques are developing in this area and experiences are insufficient both within industry and amongst regulators. Further discussion with the related organizations would be needed to finalize the work product.

The biomarker TF generated the draft concept paper on quantitative analysis of human-endogenous substances as biomarkers in pharmaceutical development, and discussed the draft concept paper with Biomarker working group. The paper was submitted to the BMV study group. The TF and PMDA discussed to reach the consensus on the draft concept paper at the meeting of the BMV study group

granted by MHLW, but it has not been achieved yet, and further discussion is needed.

## 5. Symposium

### 5.1. The 6th JBF Symposium

We held the 6th symposium on 25th and 26th February 2015 in Tokyo. The theme was 'Challenge of Regulated Bioanalysis', chaired by Harue Igarashi (GlaxoSmithKline K. K.).

At this symposium, LM-MS and biomarkers were taken up as hot topics, besides implementation of the MHLW BMV guidelines and global harmonization. In addition, the outcomes of DG, in which daily bioanalytical issues/interests were scientifically discussed, presented eight topics (Seven DGs formed in 2014 and one DG formed in 2013) and more than 200 dedicated attendees from industry, agency and academia openly exchanged their views on a wide range of bioanalytical issues with DG members. Topics of these were 'The study of failure in analytical studies', 'Development of analytical method', 'Quantitative analysis of endogenous substance', 'Tiered approach for metabolite quantification', 'Partial validation (3)', 'Anti-Drug Antibody (ADA) assay', 'Quantitative analysis by LBA (PK/Biomarker)' and 'Recommendation to prepare calibration standards and QC samples'.

The conference report of the symposium was prepared by Igarashi and accepted by a journal '*Bioanalysis*'.

### 5.2. The 7th JBF Symposium

We have decided to hold the 7th JBF symposium on 9th and 10th March 2016 in Tokyo. Takahiro Nakamura (Shin Nippon Biomedical Laboratories, Ltd.) would organize the symposium.

## 6. BMV Guideline in Japan

BMV guideline for LBA and the Q&A were issued in April 2014 and those in English in May 2014.

## 7. GBC related

Outcomes of 20 GBC HTs have been published in the *AAPS Journal* to describe their best practice and/or recommendations based on their scientific discussion in each HT.

In the future, the GBC activities can be transferred to an ICH-type discussion for which GBC may play a role in bringing scientist together.

At the 6th JBF symposium, Shinobu Kudoh presented a status update on GBC and the future perspectives of GBC.

## 8. Publication and presentation

### 8.1. Publication

Akira Nakayama: *Bioanalysis*, Vol. 6, No. 7, 915-917, 2014 (in English)
Nobuhiro Kobayashi: *Bioanalysis*, Vol. 6 No. 19, 2587-2591, 2014 (in English)
Yoshiaki Otsu: *Bunseki*, 478, 591-592, 2014 (in Japanese)
Akiko Ishii: In the 4th chapter of the book 'Bioanalytical methods on drug development' (in Japanese)
Kazuaki Sakai et al: *Bunseki*, 2015(3), 98-105 (in Japanese)

**8.2. Presentation**

Noriko Katori: 41st Annual Meeting of the Japanese Society of Toxicology in July 2014 (Kobe, Japan)
Takahiro Nakamura (JBF session organizer): BMAS 2014 in August 2014 (Tokyo, Japan)
Noriko Katori: JBF session of BMAS 2014 in August 2014 (Tokyo, Japan)
Noritaka Hashii: JBF session of BMAS 2014 in August 2014 (Tokyo, Japan)
Ryuji Goda: JBF session of BMAS 2014 in August 2014 (Tokyo, Japan)
Shinobu Kudo: JBF session of BMAS 2014 in August 2014 (Tokyo, Japan)
Takahiro Nakamura: 18th Japanese Drug Metabolism Discussion Group Seminar in August 2014 (Tokyo, Japan)
Akiko Ishii: 7th EBF Open Symposium in November 2014 (Barcelona, Spain)

## 9. Other activities

The JBF session was held as a part of the BMAS 2014, and the theme of the session was 'Regulated bioanalysis for large molecules'. The organizer of the session was Takahiro Nakamura. The chairs of the session were Masanari Mabuchi and Jun Hosogi. Several members of JBF were invited there as key speakers.

The 7th EBF Open Symposium was held on November 2014. JBF received the invitation from EBF, so Akiko Ishii attended the symposium and spoke about the BMV guideline for LBA.

## 10. External Circumstances

- The Japanese guideline, "Drug Interactions Guidelines for Drug Development and Appropriate Information Provision" for public comments was issued by MHLW on July 2014.
- EMA BMV guideline was revised on September 2014.
- The white paper on Crystal City V was published by *AAPS Journal* on March 2015.

| JBF activities in 2014 (April 2014 to March 2015) | | |
|---|---|---|
| | Symposium/ Social meeting/ Guideline/ Publication | JBF Steering committee meeting/ JBF Organization |
| **April 2014** | ➢ Notification by MHLW:<br>BMV guideline for LBA and the Q&A (1st April)<br>Effective date: 1st April, 2015<br>The answers for public comments of BMV guideline for LBA (23rd April)<br>➢ The organizer and the outline of the 6th JBF symposium decided<br>➢ TC with EBF (European Bioanalysis Forum) and International affairs committee<br>➢ The program of JBF session of BMAS 2014 prepared by Program review committee for BMAS 2014 | ➢ Steering committee (SC) meeting (3rd April)<br>➢ Seven new topics and the leaders of FY2014 DGs decided<br>➢ Recruiting DG members started<br>➢ The membership regulations of JBF released<br>➢ The operational document for SC members released |
| **May** | ➢ Notification by MHLW:<br>BMV guideline for LBA and the Q&A in English (30th May)<br>➢ Publication:<br>Akira Nakayama: *Bioanalysis*, Vol. 6, No. 7, 915-917, 2014<br>➢ The invitation to speak about BMV guideline for LBA at the 7th EBF Open Symposium from EBF accepted | ➢ SC meeting (8th May)<br>➢ Contact person of BMV study group granted by MHLW decided |
| **June** | ➢ Sharing information with Bioanalysis Study Group (the academic society)<br>➢ Large molecule MS guideline TF submitted the report on the discussion about bioanalysis for large molecule MS to the large molecular LC-MS Working group.<br>➢ Preparation of Comparison table of BMV guideline/ | ➢ SC meeting (5th June)<br>➢ The first draft of the handbook on MHLW LC guideline finished by the small molecule BMV guideline handbook TF |

| JBF activities in 2014 (April 2014 to March 2015) | | |
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| | guidance for LBA among MHLW, EMA and FDA decided | |
| **July** | ➢ Presentation:<br>Noriko Katori: the 41st Annual Meeting of the Japanese Society of Toxicology (2nd July, Kobe, Japan)<br>➢ The meeting of the BMV study group granted by MHLW participated (31st July, Tokyo, Japan). The BMV study group requested JBF to prepare the draft concept paper for bioanalysis of biomarkers. Regarding bioanalysis of the large molecule MS, preparation of Q&A decided. | ➢ SC meeting (3rd July)<br>➢ The JBF scope of bioanalysis of large molecules decided<br>➢ The first draft of the handbook on MHLW LC guideline reviewed |
| **August** | ➢ Presentation:<br>Takahiro Nakamura (JBF session organizer): BMAS 2014 (20th August, Tokyo, Japan)<br>➢ Presentation:<br>Takahiro Nakamura: The 18th Japanese Drug Metabolism Discussion Group Seminar (22nd August, Tokyo, Japan)<br>➢ Conference report of the 5th JBF symposium accepted by *Bioanalysis* | ➢ SC meeting (20th August)<br>➢ JBF Biomarker TF formed<br>➢ JBF Biomarker TF members recruited and decided<br>➢ Kick off meeting of the DGs |
| **September** | ➢ Notification by EMA:<br>Minor revision of BMV guideline (16th September)<br>➢ Request for cooperation on imaging MS from JPMA accommodated<br>➢ Upload to JBF website:<br>Presentation slide on the JBF session of BMAS 2014 | ➢ SC meeting (11th September)<br>➢ Comparison table on LBA of BMV guideline/guidance among MHLW, EMA and FDA prepared by LBA Guideline TF and International Affairs Committee<br>➢ Draft Q&A of bioanalysis of the large molecule MS prepared by Large molecule MS guideline TF<br>➢ Kick off meeting of the JBF Biomarker TF |

| JBF activities in 2014 (April 2014 to March 2015) | | |
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| **October** | ➢ Publication:<br>Nobuhiro Kobayashi: *Bioanalysis*, Vol. 6 (19), 2587-2591, 2014<br>➢ Publication:<br>Yoshiaki Otsu: *Bunseki*, 478, 591-592, 2014<br>➢ Draft concept paper submitted to the BMV study group granted by MHLW by JBF biomarker TF<br>➢ Draft Q&A submitted to the BMV study group granted by MHLW by Large molecule MS guideline TF<br>➢ The meeting of the BMV study group granted by MHLW participated (30th October, Tokyo, Japan)<br>➢ The paper on preparation of standard solution (the topic of DG2013-02) to *Bunseki* submitted | ➢ SC meeting (2nd October)<br>➢ The division of roles between the Deputy Representative altered<br>➢ The draft submitted to the publish company by Small molecule BMV guideline handbook TF |
| **November** | ➢ Presentation:<br>Akiko Ishii: the 7th EBF Open Symposium (Barcelona, Spain)<br>➢ Revised draft concept paper prepared by JBF biomarker TF reviewed by PMDA<br>➢ Micro-sampling as Q&A of ICH-S3A adopted<br>➢ The paper on tiered approach (the topic of DG2013-03) to *Bioanalysis* submitted | ➢ SC meeting (6th November) |
| **December** | ➢ Publication:<br>'Bioanalytical methods on drug development'<br>In the 4th chapter of the book, the explanation of BMV guideline for LBA contained | ➢ SC meeting (11th December)<br>➢ Draft comparison table of LBA with chromatographic assays submitted by International affairs committee |

| JBF activities in 2014 (April 2014 to March 2015) | | |
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| **January 2015** | ➢ Working group for micro-sampling, Q&A of ICH S3A, formed<br>➢ Request for cooperation on imaging MS from JPMA accommodated<br>➢ Kick off meeting with JPMA for imaging MS (22nd Jan) | ➢ SC meeting（14th January）<br>➢ The JBF scope of bioanalysis of biomarkers decided |
| **February** | ➢ The 6th JBF symposium（25th and 26th February, Tokyo, Japan）<br>➢ Closed meeting with the foreign guests on the 6th JBF symposium and International affairs committee<br>➢ The organizer and the outline of the 7th JBF symposium decided<br>➢ Closed meeting among the DG members<br>➢ The handbook on MHLW LC guideline published<br>➢ The paper on tiered approach (the topic of DG2013-03) accepted by *Bioanalysis*<br>➢ Comparison table of LBA with chromatographic assays completed by International affairs committee<br>➢ Draft of supporting data for generic drug review procedure (BMV format) based on BMV guideline submitted by Japan Generic Medicines Association (JGA) and invited public comments<br>➢ Upload to JBF website:<br>Comparison on LBA with Japanese BMV Guideline, EMA guideline and draft FDA guidance (2013)<br>➢ The paper on the characteristics of BMV guideline for LBA | ➢ SC meeting（5th February）<br>➢ Four SC members changed with new members<br>➢ JBF annual report FY2013 in English released |

| JBF activities in 2014 (April 2014 to March 2015) | | |
|---|---|---|
| | to *Bioanalysis* submitted | |
| **March** | ➢ Publication:<br>Kazuaki Sakai et al: *Bunseki*, , 2015(3), 98-105<br>➢ The paper on tiered approach to *Pharmaceutical and Medical Device Regulatory Science* accepted (DG2013-03)<br>➢ The paper on partial validation (the topic of DG-2) to *Yakugaku Zasshi* submitted<br>➢ JBF attended as the observer at the conference on imaging MS sponsored by JPMA<br>➢ Upload to JBF website:<br>Presentation slide on the 6th JBF symposium<br>➢ International affairs committee translated the answers from MHLW to EBF comments on BMV guideline for chromatographic assays in English, and submitted to EBF. | ➢ Ad hoc SC meeting（19th March） |