



Japan Bioanalysis Forum and Worldwide Trends in Regulated Bioanalysis

バイオアナリシスフォーラム (JBF) の 取組みと世界的な動きについて

Keiko Nakai
Mitsubishi Chemical Medience Corporation

三菱化学メディエンス株式会社
中井 恵子

Contents

- Introduction
 - Medicinal Product Development and Bioanalysis
- Bioanalytical Method Validation (BMV)
- BMV Guidance/Guidelines
- Global Bioanalysis Consortium and Japan Bioanalysis Forum (GBC and JBF)

Contents

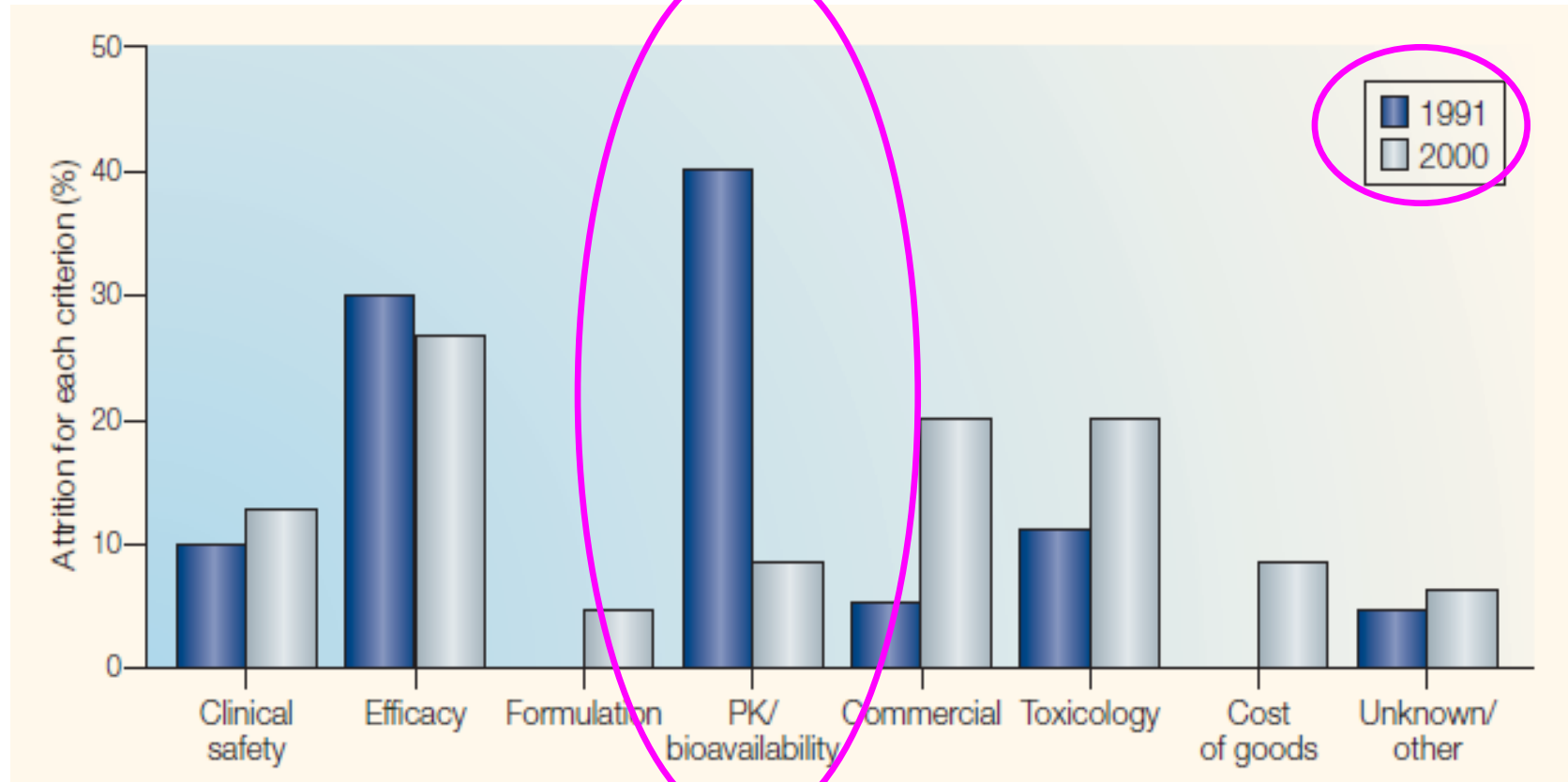
- Introduction
 - Medicinal Product Development and Bioanalysis
- Bioanalytical Method Validation (BMV)
- BMV Guidance/Guidelines
- Global Bioanalysis Consortium and Japan Bioanalysis Forum (GBC and JBF)

Introduction

Medicinal Product Development and Bioanalysis

- Pharmacokinetics and toxicokinetics are important for the medicinal product development.
- The results of pharmacokinetic and toxicokinetic studies are provided the reason for efficacy and safety of drugs.
- Bioanalysis is conducted at every stage of development for pharmacokinetics and toxicokinetics.

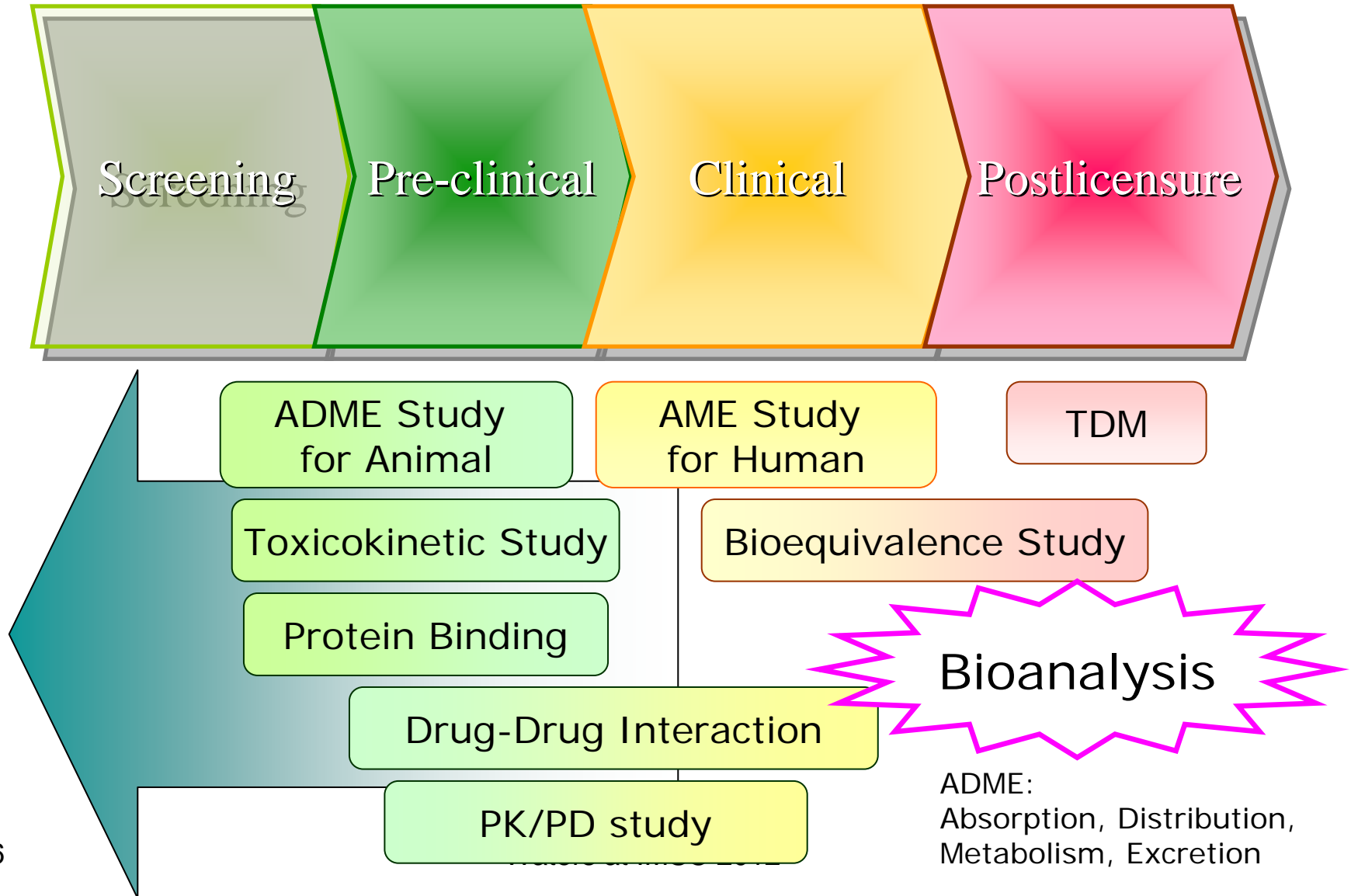
Reasons for Attrition



Ismail Kala, et. Al, Nature Reviews, Volume 3, August 2004

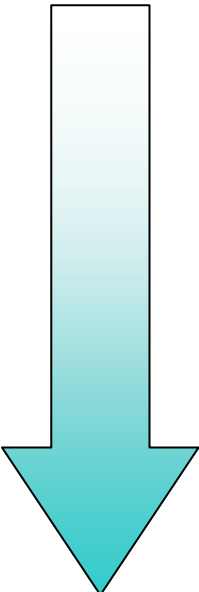
Waters at IMSC 2012

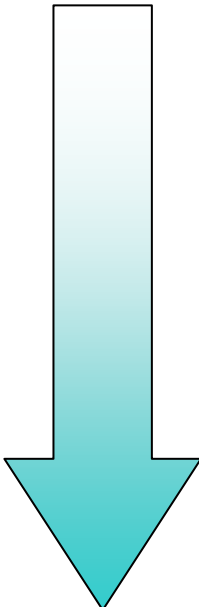
Development Stage



Concentration and Instrument on Bioanalysis (Chemical Assay)

- Lower limit level
- Instrument

- 
- $\mu\text{g/mL}$
 - ng/mL
 - Sub ng/mL
 - pg/mL
 - Sub pg/mL

- 
- GC
 - HPLC
 - GC-MS
 - LC-MS/MS
 - UPLC-MS/MS

Bioanalytical Method Validation

Contents

- Introduction
 - Medicinal Product Development and Bioanalysis
- Bioanalytical Method Validation (BMV)
- BMV Guidance/Guidelines
- Global Bioanalysis Consortium and Japan Bioanalysis Forum (GBC and JBF)



Bioanalytical Method Validation

- Measurement of drug concentrations in biological matrices is an important aspect of medicinal product development.
- It is paramount that the applied bioanalytical methods used are well characterized, fully validated and documented to a satisfactory standard in order to yield reliable results.

BMV Parameters

- Selectivity
- Limit of Quantification
- Calibration Curve
- Accuracy and Precision
(Within-run and Between-run)
- Matrix Effect
- Recovery
- Carry Over
- Dilution Integrity

BMV Parameters (Stability)

- Stability of the Analyte in the Matrix
 - Freeze and Thaw Stability
 - Short-Term Stability
 - Long-Term Stability
 - Post-preparative Stability
- Stability of the Stock Solution and Working Solutions of Analyte and Internal Standard

Incurred Sample Reanalysis (ISR)

Contents

- Introduction
 - Medicinal Product Development and Bioanalysis
- Bioanalytical Method Validation (BMV)
- **BMV Guidance/Guidelines**
- Global Bioanalysis Consortium and Japan Bioanalysis Forum (GBC and JBF)

Publication for BMV (-2011)

Date	Document	Organization
1992	Shah VP, et al., "Analytical Methods Validation: Bioavailability, Bioequivalence and Pharmacokinetic studies" Pharm Res. 1992; 9: 588-592	AAPS / FDA
2001	Guidance for Industry: Bioanalytical Method Validation	FDA
2007	Workshop/Conference Report – Quantitative Bioanalytical Methods Validation and Implementation: Best Practices for Chromatographic and Ligand Binding Assays (White Paper)	AAPS / FDA
2011	Guideline on bioanalytical method validation	EMA

BMV Guidance/Guideline

<EU-EMA> July 2011

<Canada-TPD> 2012

<China-SFDA> 2015 ?
(2010 Pharmacopoeia)

<US-FDA> May 2001
Guidance for Industry
Bioanalytical Method Validation

<Japan-MHLW>
2012-2013

2012 ?

<Brazil-ANVISA>
2012

Contents

- Introduction
 - Medicinal Product Development and Bioanalysis
- Bioanalytical Method Validation (BMV)
- BMV Guidance/Guidelines
- Global Bioanalysis Consortium and Japan Bioanalysis Forum (GBC and JBF)

Global Bioanalysis Consortium



- Late of 2010, Building the Global Bioanalysis Consortium – Working towards a functional globally acceptable and harmonized guideline on bioanalytical method validation (PSWC 2010/AAPS Annual meeting, EBF 3rd Open Symposium)
- 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.
- However, Japan did not have a forum dedicated to 'regulated' bioanalysis. Often Japanese BA scientists said "We would like to have one".

Japan Bioanalysis Forum (JBF) - Establishment -



- Jan 2011
 - GBC activity was introduced in a BA workshop in China.
- Feb 2011
 - A candidate for the SC of GBC was proposed by the attendees at the workshop and was welcomed.
- 30 Mar 2011
 - A kick-off meeting of JBF was held by foundation members.
- June 2011
 - The charter for JBF was issued by them.
- 10 Aug 2011
 - Formal establishment of JBF was announced in the 1st JBF symposium.

Japan Bioanalysis Forum (JBF) - Foundation Members-



Representative	Tatsuo Kurokawa (Prof., Keio Univ.)	
Academia	Jun Haginaka (Prof., Mukogawa Women's Univ.) Tsutomu Masujima (Prof., Hiroshima Univ.)	
Regulatory body	Noriko Katori (National Institute of Health Sciences)	
Pharmaceutical	Akira Nakayama (Ajinomoto Pharmaceuticals Co., Ltd.) Fumihiko Jinno (Takeda Pharmaceutical Company Ltd.) Hidehisa Tachiki (Towa Pharmaceutical Co., Ltd.) Hisanori Hara (Novartis Pharma AG, Switzerland) Kenji Yahata (Sanofi-Aventis) Masanari Mabuchi (Mitsubishi Tanabe Pharma Co.)	Nobuhiro Kobayashi (Daiichi Sankyo Co., Ltd.) Takahiko Osumi (Otsuka Pharmaceutical Co., Ltd.) Takahiro Kondo (Takeda Pharmaceutical Company Ltd.) Takehisa Matsumaru (Nippon Boehringer Ingelheim Co., Ltd) Tomoki Yoneyama (Takeda Pharmaceutical Company Ltd.) Yoshiaki Ohtsu (Astellas Pharma Inc.)
CRO	Masahiro Taniguchi (SCAS-BTT Bioanalysis CO., Ltd.)	Noriko Inoue (JCL Bioassay Co., Ltd.)

Japan Bioanalysis Forum (JBF)

- Scope and Mission -



- Scope
 - Small molecule bioanalysis
 - Large molecule bioanalysis
 - (Possibly biomarker measurement)
- Mission
 - To be a partner representing Japanese bioanalytical community for global harmonization
 - To facilitate to provide Japanese opinions to global harmonization in regulated bioanalysis
 - Helping setting in Japan BMV by providing scientific rationale and consensus amongst based on extensive discussions in Japanese bioanalysis

Japan Bioanalysis Forum (JBF)

- Committees -



- F&A committee
- Financial auditors committee
- Website administration committee
- Membership committee
- Event execution committee
- Public relations committee
- International affairs committee
- EBF window persons
- Documentation committee

Japan Bioanalysis Forum (JBF)

- Task Forces -



- Membership System startup
- GBC HT Support
- Small Molecule BA Method Guideline
- Large Molecule BA Method Guideline*

* To be established



Japan Bioanalysis Forum (JBF) - Steering Committee-



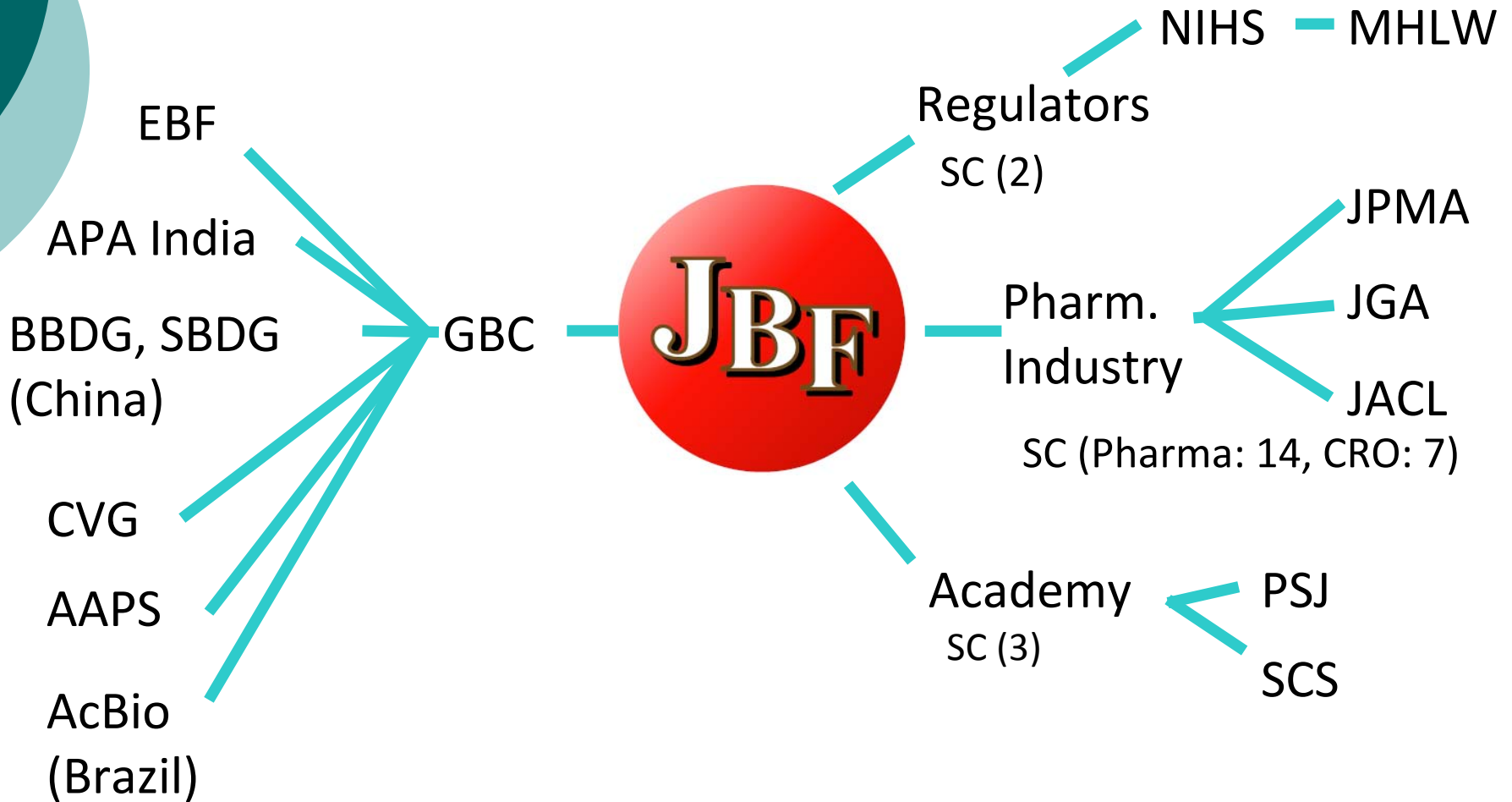
Representative	Tatsuo Kurokawa (Prof., Keio Univ.) (-June 2012) Haruhiro Okuda (National Institute of Health Sciences) (June 2012-)
Deputy Representatives	Noriko Katori (National Institute of Health Sciences) Masanari Mabuchi (Mitsubishi Tanabe Pharma Co.) Yoshiaki Ohtsu (Astellas Pharma Inc.)
GBC-SC	Tatsuo Kurokawa (Prof., Keio Univ.) (-September 2011) Shinobu Kudoh (Shimadzu Techno-Research, Inc.) (July 2011-)
Advisors	Jun Haginaka (Prof., Mukogawa Women's Univ.) Tsutomu Masujima (Prof., Hiroshima Univ.)

Japan Bioanalysis Forum (JBF) - Steering Committee (continued) -



Akira Nakayama (Ajinomoto Pharmaceuticals Co., Ltd.)	Mami Imazato (Novartis Pharma K.K.)
Harue Igarashi (GlaxoSmithKline K.K.)	Nobuhiro Kobayashi (Daiichi Sankyo Co., Ltd.)
Hidehisa Tachiki (Towa Pharmaceutical Co., Ltd.)	Noriko Inoue (JCL Bioassay Co., Ltd.)
Hisanori Hara (Novartis Pharma AG, Switzerland)	Takahiko Osumi (Otsuka Pharmaceutical Co., Ltd.)
Katsuhiko Yamamoto (Kyowa Hakko Kirin Co., Ltd.)	Takahiro Nakamura (Shin Nippon Biomedical Laboratories, Ltd.)
Kazuhiro Miya (Chugai Pharmaceutical Co., Ltd.)	Takehisa Matsumaru (Nippon Boehringer Ingelheim Co., Ltd.)
Kazutaka Togashi (Sumika Chemical Analysis Service, Ltd.)	Yoji Kuze (Takeda Pharmaceutical Company Ltd.)
Keiko Nakai (Mitsubishi Chemical Medience Ltd.)	Yoshitaka Taniguchi (Toray Research Center, Inc.)
Kenji Yahata (Sanofi-Aventis)	Yoshiyuki Minamide (Shimadzu Techno-Research, Inc.)

Relationships with Other Groups



Japan Bioanalysis Forum (JBF) - Symposiums -



- **1st:** 10 Aug 2011 in Tokyo, Japan
Attendees: 200
- **2nd:** 8 Mar 2012 in Tokyo, Japan
Attendees: 200
Guest: 2 speakers of GBC SC (EBF)
- **3rd:** 8 Aug 2012 in Tokyo, Japan
Jointly host: the 25th Symposium on
Biomedical–Analytical Sciences (BMAS 2012)
Attendees: 400
Guest: 3 speakers of GBC SC (CVG, EBF, S/BBDG)

Japan Bioanalysis Forum (JBF) - Symposiums -



Japan Bioanalysis Forum (JBF)

- GBC HT Members -



Harmonization team	Member
A1 scope & regulations	Tomoko Arakawa (Pfizer Japan Inc)
A2 tiered approach	Tomoki Yoneyama (Takeda Pharmaceutical Company Ltd.)
A3 method transfer	Masanari Mabuchi (Mitsubishi Tanabe Pharma Co.)
A4 reference std, reagents	Takahiko Osumi (Otsuka Pharmaceutical Co., Ltd.)
A5 sample management	Harue Igarashi (GlaxoSmithKline K.K.)
A6 stability	Yoshiaki Ohtsu (Astellas Pharma Inc.)
A7 repeat analysis & ISR	Masahiro Taniguchi (SCAS-BTT Bioanalysis CO., Ltd.)
A8 documentation	Hisanori Hara (Novartis Pharma AG, Switzerland)
A9 analytical inst. qualification	Hidehisa Tachiki (Towa Pharmaceutical Co., Ltd.) Makoto Niwa* (Nippon Kayaku Co., Ltd.)
A10 new frontiers	Keiko Nakai (Mitsubishi Chemical Medience Ltd.) Kohei Nozawa* (new member)

*: Additional member

Japan Bioanalysis Forum (JBF) - GBC HT Members (continued) -



Harmonization team	Member
A11 biomarkers	Yuichi Yamamoto (Pfizer Japan Inc) Yoji Kuze* (Takeda Pharmaceutical Company Ltd.)
S1 specific run acceptance	Noriko Inoue (JCL Bioassay Co., Ltd.)
S2 assay operations	Kazutaka Togashi (Sumika Chemical Analysis Service, Ltd.)
S3 chrom run quality	Junji Komaba (Ono Pharmaceutical Co., Ltd.)
L1 specific run acceptance	Katsuhiko Yamamoto (Kyowa Hakko Kirin Co., Ltd.)
L2 assay operation	Yoshiyuki Minamide (Shimadzu Techno-Research, Inc.)
L3 assay formats	Yoshitaka Taniguchi (Toray Research Center, Inc.)
L4 reagents, stab tiered	Mami Imazato (Novartis Pharma K.K.)
L5 automation	Takahiro Nakamura (Shin Nippon Biomedical Laboratories, Ltd.)
L6 immunogenicity (PK)	Kazuhiko Sonehara (Sumika Chemical Analysis Service, Ltd.)

*: Additional member

Japan Bioanalysis Forum (JBF)

- Recent Activity -



- Japanese BMV Guideline
 - Small Molecules: Ongoing
 - Large Molecules: In preparation
- HT Member/Supporters Community
 - Supporters: 45 persons (since Jan 2012)
Discussion is open, extensive and fruitful.
- Website (<http://bioanalysisforum.jp/en>)
 - Japanese: since Jan 2012
 - English: since July 2012
- Publication
- Global Vision
- JBF Membership*

Acknowledgements

- Waters Corporation
- Japan Bioanalysis Forum
- Global Bioanalysis Consortium
- Mitsubishi Chemical Medience Corporation



Thank you for your attention !

ご静聴ありがとうございました.