Feed back from SC

3 December 2010

Margarete Brudny-Klöppel (Bayer Schering Pharma AG)
on behalf of EBF SC

EBF

EBF vwz

- Start: 14 April 2010
- Belgium non-profit organization
- Name: European Bioanalysis Forum vwz (EBFvwz)

- Charter was signed by 5 founders
  - Pharma only association

Closed Meetings I

- January (EBF), June (EBF and IGM), December (IGM)
  - January - Main Topics (EBF):
    - Feed back SC and EBF Future
    - Final discussion on MIST paper
    - Discussion of surveys
    - DBS
  - June - Main Topics (EBF):
    - Feed back SC and EBF Future
    - Agenda of Open Meeting
    - Final Preparation of DBS Meeting
    - EMA BMV guideline and feed back from Brussels WS
    - GBC
    - Discussion of surveys

Closed Meetings II

- January (EBF), June (EBF and IGM), December (IGM)
  - June - Main Topics (IGM):
    - Feed back SC and EBF Future
    - EMA BMV guideline and feed back from Brussels WS and NBC
    - Sample condition and whole blood stability
    - Drug Tolerance and Assay Dissociation
    - Integrated PK/PD analysis
    - Acceptance criteria for validation
    - Anomalous results

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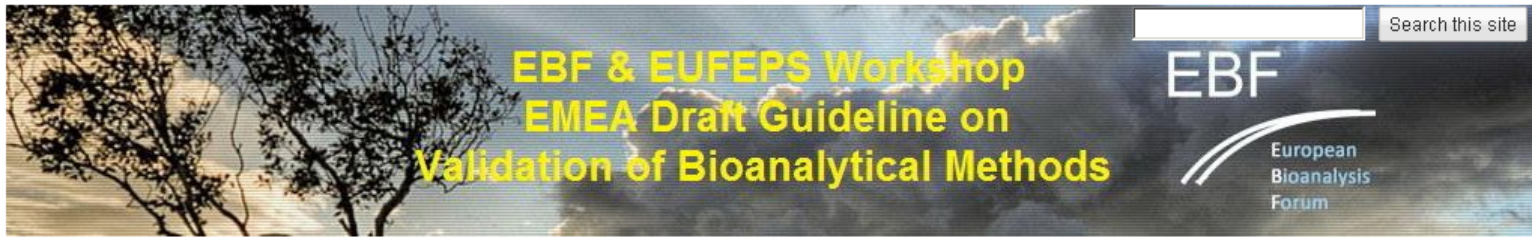
Closed Meetings II

- January (EBF), June (EBF and IGM), December (IGM)
  - December - Main Topics (IGM):
    - Stability of assay reagents
    - Activity assays
    - Follow up on discussion on dilution QCs versus assay acceptance QCs
    - Outsourcing
    - Comments on new guidelines

EBF - EUFEPS - EMA Workshop



Home
Announcements
Contact
Organisation
Program
Publications
Registration
Speakers
Venue
Directions
Maps
Sitemap

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Home

EBF & EUFEPS Workshop

EMEA Draft Guideline on Validation of Bioanalytical Methods

April 15-16 ▪ 2010 ▪ Sheraton Hotel Brussels
Brussels ▪ Belgium

The Workshop will open on Thursday, April 15, 2010, at 09:00 and it closes on Friday, April 16, 2010, at 14:30.

The European Medicines Agency (EMEA) Committee for Human Medical Products (CHMP) released a concept paper on the "Need of a Guideline for the Validation of Bioanalytical Methods" in December 2008. All interested parties were invited to provide input by the end of March 2009. Having collected and collated all input, the CHMP subcommittee released a Draft Guideline in December 2009 on their website, which is now in the cycle of consultation, until the end of May 2010, i.e. for final comments.

The aim of this Workshop is to discuss the current scientific knowledge in the area of bioanalysis, the regulatory requirements and their subsequent translation into the work in the bioanalytical laboratory. Examples of topics to be discussed include the GLP-status of the process of method validation; acceptance criteria of methods to be used in the area of chromatography and ligand-binding based assays; incurred sample reproducibility (ISR), study sample reanalysis for PK purposes and re-integration (to list only a few).

The intention of this Workshop is to give scientists from industry and academia, managers and representatives of company regulatory functions the opportunity to discuss the new regulation with representative from regulatory authorities in Europe. Input for the Workshop Programme includes comments submitted to the organisers in the run-up phase to the event. All participants are invited to present their views and suggestions, based on own experience, during the discussion, and to support these proposals by experimental data.

EBF

EBF - EUFEPS - EMA Workshop

- Meeting in Brussels: 15. – 16. April
  - Organized by EBF (Berthold, Michaela, Margarete), EUFEBS (Gabriele Rohde, Erich Brendel, Hans Linden and CROs (Christoph Siethoff)
    - Each sessions has a presentation and podium discussion part
    - Session key topics and discussion points were identified survey
    - Presentation of consolidated discussion points by OC
  - Moderated discussions
    - Howard Hill and Kamal K. Mitha
  - Representatives from EMA on podium
    - Rapporteur: Jan Welink
    - Co-rapporteur: Jerome Barré
    - Inspector: Olivier Le Blaye
  - 140 Participants from Pharma, CROs, Academia and HA

EBF - EUFEPS - EMA Workshop

- 14 Sessions according to key topics
  - **(1) Legal Basis**
  - **(2) Method Validation**
  - **(3) Accuracy**
  - **(4) Calibration Curve and Anchor Points**
  - **(5) Selectivity**
  - **(6) Specificity**
  - **(7) Matrix Effect**
  - **(8) Dilution Integrity**
  - **(9) Heterogeneity**
  - **(10)Stability**
  - **(11)General Comment**
  - **(12)Incurred Sample Reanalysis**
  - **(13)Size of a Run**
  - **(14)Study report**
- Conference report in preparation

EBF
European Bioanalysis Forum

WELCOME

EBF Workshop

Connecting Strategies on Dried Blood Spots

June 17-18, 2010 • Sheraton Hotel Brussels, Belgium

EBF

EBF Focus Meeting - DBS

- Evaluation of Survey 1 (Response rate: 23/28)
  - Questions relate to:
    - Are we already using DBS, and if so in which development phase
    - Did we develop DBS internal or external
    - Since when do we use DBS?
    - Why did we start using DBS (or want to start using it)?
    - Number of compounds/methods?
    - Did we already submit DBS analyzed studies to authorities?
- Evaluation of Survey 2 (Response rate: 23/28)
  - Do DBS methods require special validation criteria
  - Do studies analyzed with validated DBS methods need special acceptance criteria?

EBF Focus Meeting - DBS

Program highlights

- 5 plenary session – first 3 with panel discussions
  - DBS in non regulated environment
  - DBS in Toxicology (combined with Reg/QA session)
  - DBS in clinical
  - DBS and bioanalysis – tools
  - DBS and bioanalysis – applications
- Combined Tutorial/poster sessions
- Breakout and final panel discussion

EBF Participation in International Conferences I

- Bioanalysis in Clinical Research, London, UK
  - Presenter: Philip
  - Topic: Towards European Pharma Companies best practice on Metabolite Quantification
  - Presenter: Berthold
  - Topic: EBF and EMEA concept paper on Bioanalysis and EMEA draft Guideline on Bioanalytical Method Validation: EBF's recommendations towards harmonization
- WS on Recent Issues in Regulated Bioanalysis CVG Meeting, Montreal, Canada
  - Presenter: Peter
  - Topic: EBF Perspective on the New EMA Guidelines on Bioanalytical Method Validation (BMV) and input on global BMV harmonization

EBF Participation in International Conferences II

- National Biotechnology Conference (NBC) in San Francisco
  - Symposium on EMA Draft BMV Guideline
    - Organized by EBF-IGM SC (Michaela, Peter, Margarete) and AAPS LBABFG (Maria Kelley)
    - Invited Speaker: Jan Welink
    - Best populated session at NBC
      - Presentation of EMA and Guideline (Jan Welink)
      - EBF perspective (Margarete)
      - LBABFG perspective (Marian)
      - Comparison of EMA and FDA guideline (Michaela)
  - Symposium on Anomalous Results
    - Organized by CVG (Fabio Garofolo)
      - EBF-IGM perspective on procedures how to handle anomalous results (Margarete)
      - Biotherapeutics Case Studies from the North American Pharmaceutical Companies (Joe Marini)

EBF Participation in International Conferences III

- APA-BSAT Meeting, Baltimore (MD), USA
  - Presenter: Philip
  - Topic: ICH M3 and metabolite quantification: Views and Recommendations of EBF
- AAPS Meeting, New Orleans, 16 Nov 2010
  - Presenter: Philip
  - Topic: Towards an EBF Recommendation on Validation of Dried Blood Spots Assays

EBF Response to Draft Guidelines I

- FDA Guideline on Assay Development for Immunogenicity Testing of Therapeutic Proteins
  - Announced: 04 Dec 09
  - Very short response time (31 Jan 10)

Jan	Who	Action
8	SC*	Feedback form to all IGM members
19	All	Response back to *IGM SC
20 - 22	SC	3 TC to consolidate response
22	SC	Draft out for review to IGM members
25	All	Response back to SC
27	SC	Final draft out for review to IGM members
28	All	Response back to SC
30	SC	Final update
		Consolidated final response to FDA and all IGM members

EBF-IGM member companies providing comments (70%):

Bayer Schering Pharma AG, Boehringer-Ingelheim, Crucell, Ferring, Johnson & Johnson, H. Lundbeck A/S, Merck Serono, Micromet, Hoffmann-La Roche, Sanofi-Aventis, Merck Sharpe and Dohme, Solvay Pharmaceuticals, UCB

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EBF Response to Draft Guidelines II

- EMA Guideline on Bioanalytical Method Validation
  - Announced: 08 Dec 09
  - Response time (31 May 10)
  - Preparation via Feed back form and EBF-EUFEPs-EMA WS
  - Consolidation of responses from 23 member companies
  - Timely submission to EMA

<u>EBF and EBF-IGM member companies providing comments (80%)</u>:

Actelion Ltd, Active Biotech, Almirall, Bayer Schering Pharma AG, Boehringer-Ingelheim, Crucell, Ferring Pharmaceuticals A/S, Grünenthal GmbH, GlaxoSmithKline, F. Hoffmann-La Roche, Johnson & Johnson, H. Lundbeck A/S, Merck Serono, Novartis Pharma AG, Novo Nordisk, Nycomed, Orion Corp. Orion Pharma, Sanofi-Aventis, Schering-Plough/MDS, Servier, Shire Pharmaceuticals, Solvay Pharmaceuticals/Abbott, UCB Pharma

EBF Publications

WHITE PAPER

For reprint orders, please contact reprints@future-science.com

Best practices in a tiered approach to metabolite quantification: views and recommendations of the European Bioanalysis Forum

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The relationship between the exposure to drug metabolites and overall drug safety has become an integral part of the drug-development process. In-depth discussions in the scientific community, as well as recent guidelines on Drug Safety Testing of Metabolites from the US FDA (often referred to as the MIST guidance and ICH M3(R2) from the International Conference on Harmonization (ICH), has brought clarity to the regulatory requirements of the sponsor company in providing documentation on circulating levels of qualifying metabolites. However, less attention has been given to the challenges now faced by the bioanalytical community in supporting these new guidance policies. In this paper, the European Bioanalysis Forum (EBF) is providing a recommendation on which quality standards to apply when assessing the (relative) abundance or absolute concentrations of metabolites. This paper is the result of both an intensive consultation within the EBF (through internal surveys amongst EBF member companies and discussions) and consultation of the broader bioanalytical community (through discussions at international conferences). These recommendations will provide an increased understanding of how to apply a tiered approach to metabolite quantification as part of the bioanalytical strategy. As such, it aims to provide support to the bioanalytical community on the appropriate level of validation required at each stage of the drug-development process.

Bioanalysis (2010) 2(7), 1185–1194

EBF

EBF Surveys and Mini-surveys via Mail

- WBS
- Choice of anticoagulant and Comparison of counter ions
- Stability of Reagents
- Dilution Integrity
- Non-clinical Dose Formulation - Method Validation / Sample Analysis
- Regulatory Status of lab performing Met ID in human ADME trials

EBF - GBC Interaction

EBF – CRO Interaction

Workshop in Brussels: 12 Oct 2010

EBF SC representatives: **Philip / Margarete**	**Peter /**
CRO representative: **representative per CRO**	**1**
Number of CROs participating:	**27**

1. GBC involvement:

- CRO involvement as part of harmonization teams
  - Level of partnership: member of EBF-external contact group

2. EBF involvement:

- Additional involvement will be developed as appropriate:
  - CRO invited to join Topic Teams as they emerge during 2010/2011.
  - Level of partnership: scientific partners (as per charter) and co-authorship in publications/recommendations

EBF-CRO-Coalition Group's Contribution

EBF Perspective:

- Participation in surveys, e.g.:
  - WBS
  - DBS
  - Anomalous Results
  - Quality
- Comments to draft Guidelines
  - BMV
  - Immunogenicity
- Contribution to technology evaluation
  - LIMS Systems
  - Assay platforms
  - New Mass Spectrometrer technology
- Sharing experience from RA inspections

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EBF-CRO-Coalition Group's Contribution:

CRO Perspective:

Evaluation of Survey

- 27 participants (all meeting participants)
- 9 questions
- Two sections
  - GBC interaction
  - EBF - CRO interaction
- Results
  - GBC
    - Participate in Harmonization Teams is appreciated
  - EBF - CRO interaction
    - Further discussions in strategic team
      - CROs: Maria, Tim, Christoph
      - EBF: Philip, Peter, Margarete

EBF

EBF activities in 2011

- GBC International Conference in February
- Strategic Meeting in March
- EBF 2nd Focus Meeting in June
- EBF 4th Conference in November, 14 -16
- Participation in international conferences
  - NBC
  - BSAT
  - AAPS