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

Towards harmonized regulations for bioanalysis: moving forward!

“Looking at the current initiatives, the bioanalytical community is motivated to make 2010 the year in which we set the stage for a global bioanalytical guideline.”

It is a little over 1 year since the European Medicines Agency (EMA) committee for medicinal products for human use (CHMP) efficacy working party (EWP) released a concept paper on the need for a guideline on bioanalytical method validation (BMV) [101]. Until then, the US FDA guidance on bioanalytical method validation [102] was the only regulatory document fully dedicated to bioanalysis that existed. Although this FDA guideline has been recognized by the bioanalytical community as the standard, in essence it was based on the technology and thinking of the 1990s and left the bioanalytical scientist with a lot of questions and uncertainties. A necessary revisit of the guidance took place at the Crystal City III workshop in May 2006 and the outcome of the discussions was published in 2007 [1]. The conference report did provide a number of clarifications and, although the topic of incurred sample reproducibility caused more than a few lively debates [2–5], the bioanalytical community was happy to adopt the new standards and returned to ‘business as usual.’

“The atmosphere in the auditorium can perhaps be best described by ‘we all want it. Now why don’t we make it happen?’”

This peace only lasted until January 2009 when the concept paper by the EMA was released [101]. The European Bioanalysis Forum (EBF) and other organisations, as well as a number of pharmaceutical companies, presented comments to the EMA. The EBF’s comments followed one leading thought: “There should not be an important guideline that, even if only in some parts, contradicts any other leading guideline also dealing with the topic.” The EBF described their processes and thinking and

expressed their strong desire for a globally harmonized guideline, not only in their comments but, additionally, in an editorial in *Bioanalysis* last year [6].

As a stimulant towards this global harmonization, the EBF decided to dedicate the first day of its second open symposium [7] to this draft guideline and invited speakers representing the broader bioanalytical community, including Dr J Welink (Dutch Medicines Evaluation Board [MEB] for EMA), Dr O Le Blaye (AFSSAPS) and Dr CT Viswanathan (FDA/Center for Drug Evaluation and Research [CDER]) as representatives from the health authorities, Dr S Lowes (Advion for AAPS) and Dr B Lausecker (F Hoffmann-La Roche for EBF) as industry speakers. During this session there was a strong plea from industry to the EMA not to deviate too much from the current FDA guideline and subsequent White Papers. Dr Welink explained that the EMA guideline will largely be in alignment with the aforementioned documents, but will also be somewhat different on certain aspects. Dr Viswanathan pointed out that with more and more laboratories from more and more countries entering the field of regulated bioanalysis, the need for international standardization is becoming apparent.

During the forum discussion, most of the general questions and comments from the audience subscribed to the wish to come to one global bioanalytical guideline. The atmosphere in the auditorium can perhaps be best described by: “we all want it. Now why don’t we make it happen?”

Harmonization processes can be lengthy and cumbersome, so the sooner the start and the higher the motivation of interested parties, the bigger the chance of success will be. We must use and maintain the momentum we have now.

Peter van Amsterdam
Author for correspondence
Abbott Healthcare
Products B.V.
E-mail: peter.vanamsterdam@abbott.com

Berthold Lausecker
F Hoffmann-La Roche
E-mail: berthold.lausecker@roche.com

Authors continued overleaf...

All authors are members of the EBF Steering Committee

**FUTURE
SCIENCE**

part of
fsg

Silke Luedtke
Boehringer-Ingelheim
E-mail: silke.luedtke@boehringer-ingenheim.com

Philip Timmerman
Johnson & Johnson
E-mail: ptimmerm@its.jnj.com

Margarete Brudny-Kloeppel
Bayer Schering Pharma AG
E-mail: margarete.brudny-kloeppel@bayerhealthcare.com

So what happened after that memorable day in December 2009? First, and most importantly, the EMA draft guideline, which was announced to be made available to the public in December by Dr Welink at the EBF open meeting, was published on the EMA website on 8 December 2009 [103]. Following the EBF conference, Dr Viswanathan repeated his desire to come to international harmonization in bioanalysis as well as in GLP at the Société Française d'Assurance de Qualité (SoFAQ) meeting in Paris.

“...to help facilitate reaching for alignment in the conduct of regulated bioanalysis, a number of meetings have been set up.”

The industry understood the message. The EBF, AAPS, BSAT/APA and Calibration and Validation Group (CVG)/Canadian LC-MS Group intensified contacts to discuss and present the first steps in inviting and supporting authorities to work on a global bioanalytical guideline. A first action point they identified was to write an open letter from these organisations to the attention of the regulatory authorities, which is published in this issue of *Bioanalysis* [8].

Next, to establish platforms for discussion to help facilitate reaching for alignment in the conduct of regulated bioanalysis, a number of meetings have been set up. In Europe, EBF and The European Federation for Pharmaceutical Sciences (EUFPS) will jointly run a meeting to discuss the draft guideline. This meeting will take place in Brussels from 15–16 April 2010. In North America, the 4th Workshop on Regulated Bioanalysis (in Montreal, Canada from 22–23 April 2010), has as a key topic “Global Harmonization of Bioanalytical Method Validation Guidelines (BMV) and Sample Analysis.” Furthermore,

EBF-IGM (Interest Group Macromolecules of the European Bioanalysis Forum) and the AAPS Ligand Binding Assays Bioanalytical Focus Group will jointly run a symposium on “Update on EMA and FDA Bioanalytical Method Validation Guidelines” at the AAPS National Biotechnology Conference in San Francisco. Later in 2010, meetings run by both the AAPS-FIP (New Orleans, 14–18 November 2010) and the EBF (Barcelona, Spain, 1–3 December 2010) will touch on global harmonization of bioanalytical guidelines. All these efforts have one combined goal: to come to a better understanding of the BMV guidelines and increase the awareness and possibilities within bioanalytical laboratories to come to a more harmonized form of implementation of the guideline(s).

What is now known as Crystal City I was a landmark bioanalysis workshop held in 1990 [9]. The next major international bioanalysis meeting was Crystal City II in 2000 [10], and recommendations from the workshop found their way into the FDA BMV guideline. Looking at the current initiatives, the bioanalytical community is motivated to make 2010 the year in which we set the stage for a global bioanalytical guideline.

Disclaimer

The views expressed in this article are those of the EBF and do not necessarily reflect the respective company's position on the subject.

Financial & competing interests disclosure

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

No writing assistance was utilized in the production of this manuscript.

Bibliography

- Viswanathan CT, Bansal S, Booth B *et al.* Bioanalytical method validation and implementation: best practices for chromatographic and ligand binding assays. *AAPS J.* 9(1), E30–E38 (2007).
- Fast D, Kelley M, Viswanathan C *et al.* Workshop report and follow-up-AAPS workshop on current topics in GLP bioanalysis: assay reproducibility for incurred samples – implications of crystal city recommendations. *AAPS J.* 11(2), 238–241 (2009).
- Savoie N, Booth BP, Garofolo F *et al.* The 2nd Calibration and Validation Group Workshop on recent issues in good laboratory practice bioanalysis. *Bioanalysis* 1(1), 19–30 (2009).
- Timmerman P, Luedtke S, van Amsterdam P, Brudny-Kloeppel M, Lausecker B. Incurred sample reproducibility: views and recommendations by the European Bioanalysis Forum. *Bioanalysis* 1(6), 1049–1056 (2009).
- Savoie N, Garofolo F, van Amsterdam P *et al.* White Paper on recent issues in regulated bioanalysis from the 3rd calibration and validation group workshop. *Bioanalysis* 2(1), 53–68 (2010).
- Lausecker B, van Amsterdam P, Brudny-Kloeppel M, Luedtke S, Timmerman P. European Bioanalysis Forum and the

- way forward towards harmonized regulations. *Bioanalysis* 1(5), 873–875 (2009).
- 7 Abbott R. The broadening scope of validation: towards best practices in the world of bioanalysis. *Bioanalysis* 2(4), 703–708 (2010).
 - 8 Timmerman P, Lowes S, Fast DM, Garofolo F. Request for global harmonization of the guidance for bioanalytical method validation and sample analysis. *Bioanalysis* 2(4), 683 (2010).
 - 9 Shah VP, Midha KK, Dighe S, McGilveray IJ, Skelly JP. Analytical methods validation: bioavailability, bioequivalence and pharmacokinetic studies. *Pharm. Res.* 9, 588–592 (1992).
 - 10 Shah VP, Midha KK, Findlay JWA *et al.* Bioanalytical method validation – a revisit with a decade of progress. *Pharm. Res.* 17, 1551–1557 (2000).
- Websites
- 101 European Medicines Agency concept paper/ recommendations on the need for a (CHMP) guideline on the validation of bioanalytical methods. EMA/CHMP/EWP/531305/2008 www.ema.europa.eu/pdfs/human/ewp/53130508en.pdf
 - 102 US FDA. Guidance for Industry: Bioanalytical Method Validation. Rockville, MD, USA: US Department of Health and Human Services, FDA, Center for Drug Evaluation and Research, 2001 www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM070107.pdf
 - 103 European Medicines Agency draft guideline on validation of bioanalytical methods. EMA/CHMP/EWP/192217/2009 www.ema.europa.eu/pdfs/human/ewp/19221709en.pdf