

# Harmonizing best practices in bioanalytical methods

**Abbreviations:** BMV, bioanalytical method validation; NDA, new drug applications; ANDA, abbreviated new drug applications; AAPS, american association of pharmaceutical scientists; GCC, global cro consortium

## Editorial

Currently, the US pharmaceutical industry is outsourcing more bioanalytical work and more studies are submitted to multiple regulatory agencies all over the world. Thus, harmonization of the current EMA and US FDA guidance documents on bioanalytical method validation (BMV) is becoming an important issue in order to overcome difficulties in complying with many different regulatory guidelines. Presently, BMV guidance from the EMA and US FDA are the most recognized document throughout the bioanalytical industry and regulatory bodies. Although this guidance was first issued in 2001, the constant updates reflect the evolution of the field through the years. The guidance is believed to have brought some uniformity to the bioanalytical community. Recognizing that, in July 2011 EMA issued its own BMV guidelines. Interaction between the FDA and EMA will be very crucial to align the two respective guidelines in an attempt to globalize guidance's.<sup>1</sup>

The EMA guideline on BMV was issued, to regulate bioanalytical work submitted to European agencies. If facilitated harmonization within Europe. The EMA guideline on BMV was also intended to be part of global harmonization as it took into account the US FDA bioanalytical method validation guidance for industry (2001), different published papers such as the AAPS/FDA Crystal City III White Paper, and the AAPS workshop on incurred sample reproducibility, as well as EMA experience based on issues seen during review of dossiers and inspections.<sup>1</sup>

In light of the necessity to comply with international standards in the highly regulated environment of drug development and submission of New Drug Applications (NDA) or Abbreviated New Drug Applications (ANDA), bioanalysis remains the primary source for quantitative measurements of active drug ingredients and their respective metabolites in biological matrices. Assays must therefore be suitable for the purpose of their respective applications. Among others, these applications include: BA/BE studies as well as pharmacokinetic and pharmacodynamic studies, toxicokinetics and ADME studies. The quality of bioanalytical data is directly related to design, conduct, and analysis of the bioanalytical process. Consequently, a holistic approach which ensures good bioanalytical practice must be well defined and implemented.

The majority of bioanalysts around the world have become familiar with the regulatory requirements and guidance documents provided by the US FDA and EMA. These guidelines, in many instances may confuse bioanalysts, due to the following reasons:

- (1) Misinterpretation of guidance's is common among non-research based bioanalytical laboratories, and regulators in different parts of the world.
- (2) Analytical procedures used for investigating key validation parameters vary among different bioanalytical laboratories, depending on the analysts understanding of the "fitness for

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purpose", and the methodology employed for "quantifying uncertainty" in analytical measurements.

- (3) Application of statistical methods to validation data has been relegated to a subordinate role in bioanalytical methods validation literature. Consequently, acceptance criteria were almost generalize.
- (4) Analysts understanding of validation parameters is inhibited by the fact that many of the technical terms used for evaluating methods vary in different sectors of analytical measurement; both in terms of their meaning and in the way they are determined.
- (5) The problem-solving role of chemical analysis is not emphasized as a process, or a chain of operations. As a consequence, in some labs bioanalysts are consigned to pigeonholes, where they function as sample drop-off points, rather than as active participants in solving an analytical problem.
- (6) Both the analytical and pharmaceutical sciences are dynamic disciplines in which today's regulations may not fit tomorrow's problems. An essential element of the analytical requirement is that it should fit the purpose for bioequivalence decision-making while giving a realistic estimate of uncertainty.

Scientific meetings are still being held between the American Association of Pharmaceutical Scientists (AAPS) and the US FDA to allow the scientific and regulatory communities to come together to discuss best practices within the regulated bioanalysis. The goals and objectives of such meetings are to align science- based perspective with new proposals in the draft BMV guidance, to increase understanding and evolution of revisions and present new aspects in the draft US FDA bioanalytical method validation guidance.<sup>2</sup>

In 2010, the global CRO consortium (GCC) was created as a globally independent consortium to bring many senior level CRO representatives to openly discuss and share opinions on scientific and regulatory issues related to bioanalysis. Several white papers were published by the GCC. The eighth GCC closed forum for bioanalysis, held in Baltimore, USA, was specifically dedicated to perform an in-depth review of the draft revised FDA guidance on BMV, issued in September 2013.<sup>3</sup>

Globalization of US FDA guidance is different from its harmonization. Globalization will require acceptance from everybody to form unified single bioanalytical guidance. This may render the process of harmonization more complex.<sup>1</sup>

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## Conflict of interest

The author declares no conflict of interest.

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