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Journal of Pharmaceutical and Biomedical Analysis 40 (2006) 1
JOURNAL OF PHARMACEUTICAL AND BIOMEDICAL ANALYSIS
www.elsevier.com/locate/jpba

Editorial

Spiking in analytical method development and validation A guide for authors

In the development and validation of new methods analytical scientists in both the pharmaceutical and biomedical fields rely extensively on the use of spiked samples. However, it is clear that spiked samples are not always adequate substitutes for demonstrating the utility of a method compared to the analysis of real samples. As a result there have been requests from both referees and authors for clear guidance on the extent to which spiked samples can be used for demonstrating the validity of new analytical methods. The Editors of the *Journal of Pharmaceutical and Biomedical Analysis* have therefore produced these guidelines on the subject to assist authors in the preparation of manuscripts for submission to the journal.

It is widely accepted that method development for the analysis of drugs in formulated products or of drugs and metabolites in biological fluids such as plasma initially relies on the use of spiked samples. However, it is the opinion of the Editors that, in general, a method cannot be considered properly validated until it has been applied to the analysis of real samples. Studies with real samples are the only way of demonstrating that the method works in practice, is specific, has sufficient sensitivity to define e.g. the concentration of the drug in a formulation, the pharmacokinetics of the analyte, or for therapeutic drug monitoring, etc. Also, only the application of method shows that it has the required dynamic range to cover the concentrations encountered in real samples.

In practice methods development covers a number of different cases, including e.g., a new method for a novel drug, a new method for an existing drug, and the demonstration of a new analytical principal, using a particular drug as an example of proof of principal, rather than a proposal for a new method for that particular analyte.

The opinion of the Editors is that, in the case of a new drug where little is known, then the method cannot be considered to be validated if it is only based on spiked samples and such methods *must* demonstrate an appropriate application.

Where what is proposed is a new method for a marketed drug the Editors would expect to see a justification for why the method is needed if there are already pre-existing published methods with adequate analytical properties. Such new methods must represent an advance on existing practice and the Editors would also expect to see an example of a real application, preferably with a cross validation to one of the existing methods, proving the superiority of the new approach. Lack of provision of an application would require justification on either ethical or scientific grounds. In bioanalysis a sufficient ethical reason would perhaps be a degree of toxicity that precluded administration to man whilst a scientific reason would include the knowledge that the method covered the required ranges and that the analyte was not subject to potential interferences from metabolites, etc. Proof of specificity is especially important for "non-selective" methods (e.g. UV, electrochemical, rapid chromatography, etc.).

The Editors hope that the above explanation of editorial policy will be of assistance to authors and referees alike, and lead to a continued improvement in the quality of submissions to the journal.

0731-7085/$ – see front matter © 2005 Published by Elsevier B.V.
doi:10.1016/S0731-7085(05)00788-0