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JOURNAL OF CHROMATOGRAPHY B: BIOMEDICAL APPLICATIONS

Editorial

Validated assays in the Journal of Chromatography B: an initial editorial position

In the coming year, the Editors of the Journal of Chromatography B will be examining the scope and policies of this publication. One of the key issues is the definition of a validated assay. This is a central question since this journal is often the vehicle for the initial publication of bioanalytical assays. These methods are then used in metabolic, pharmacokinetic and clinical studies which are reported in pharmacological journals with reference to the analytical methods. Thus, we must assure our colleagues reviewing the pharmacological data that the analytical method works and that they can trust the data, in other words, that it is a valid method.

There are many definitions of a validated assay. An extensive definition of method validation has been previously published by Shah et al. [1] and is generally accepted as the validation criteria for regulatory agencies. However, the Journal of Chromatography B is not a regulatory journal; it is a scientific publication designed to disseminate reports of the development and application of a wide range of bioanalytical methods.

The challenge facing the journal is to develop a set of criteria to define a validated assay in the context of a broad scientific journal. An analytical method which satisfies these criteria will have the phrase "a validated assay" added to the title of the article; the sentence "This method has been validated according to the criteria established by the Journal of Chromatography B" added to the abstract; the keywords "validated assay" added to the keyword indices.

The draft validation criteria are:

1. Linearity of calibration: The concentration versus detector response curves (calibration curves) must be linear over the concentration range chosen for the study and inter-day reproducibility of the calibration curves should be presented. The studies must be performed in the same biological matrix (or matrices) as the final study.

2. Repeatability: The method must be able to reliably measure high and low calibrators (relative to the range of the standard curve) multiple times within a single day and during the course of several consecutive days. Repeatability infers that the assay was performed by one person using the same equipment. If possible, reproducibility data should be presented, in which the method has been reproduced by another person.

3. Accuracy: The method must be able to accurately determine the concentration of high and low calibrators and/or blinded unknowns within a single day and during the course of several consecutive days.

4. Limits: The lower limits of quantitation and detection (LOQ, LOD) must be reported. Chromatograms from the assay of blank matrices should be included for the establishment of the "background noise" in the assay.

5. Recoveries: Where applicable, average recoveries (with standard deviations) must be reported for high and low concentrations within the concentration range of the study. Recoveries should be calculated from the results of the full analytical method.

6. Proof of applicability: The results from the application of the method to samples from the actual study in which it was utilized must be included. For example, if an assay has been developed for a pharmacokinetic study, then the authors must demonstrate that the method can indeed be used to

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analyze the range of samples obtained during the study. In addition, if known metabolites or interfering concomitant drugs are present, then the authors must verify that these compounds do not interfere with an assay.

As stated above, this is a draft document. Copies have been sent to the Editorial Board of this journal as well as to some of the referees who regularly review articles submitted as "validated assays". We urge you, our readers and contributors, to join in this process also and we look forward to your suggestions and contributions. We hope to publish a final set of guidelines before the end of 1996.

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References

[1] V.P. Shah et al., Analytical methods validation: Bioavailability, bioequivalence and pharmacokinetic studies, J. Pharm. Sci., 81 (1992) 309–312.