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Editorial

Requirements for Initial Assay Validation and Publication in J. Chromatography B

In the 683/2 issue of this journal, we published a draft editorial position regarding assay validation for manuscripts submitted to the Journal of Chromatography B. 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 that the methods published in the Journal of Chromatography B work and that the data can be trusted. In other words that it is a valid method.

We received a large number of responses to the draft guidelines. All of the responses were positive and most contained suggestions for the improvement of the document. We have modified the guidelines according to the recommendations from our Editorial Board and general readership and the resulting document is presented below. An analytical method which satisfies these criteria will have the phrase ''This method has been validated according to the criteria established by the Journal of Chromatography B'' added to the abstract and the keywords ''Validated assay'' added to the key word indices.

The validation criteria are:

1. Peak purity and selectivity: the authors must demonstrate that there are no peaks in the chromatogram which interfere with the analytes and internal standard. This should be demonstrated for all biological matrices investigated and with all sample preparation procedures. The authors must also demonstrate that there are no interferences with metabolites and coadministered drugs.

2. Linearity of calibration: the concentration versus detector response curves (calibration curves where $n=5$) must correlate over the concentration range chosen for the study and interday reproducibility of the calibration curves should be presented. Linear correlations are preferable, but non-linear curve fitting is acceptable. The studies must be performed in the same biological matrices from the same species as the final study.

3. Repeatability: the method must be able to reliably measure high and low calibrators, relative to the range of the standard curve, multiple times (preferably $n\geq5$) within a single sequence and during the course of several consecutive sequences. Where applicable, the repeatability of quality control (QC) samples should be reported where the minimum acceptance criteria for relative standard deviations (RSDs) are 10% for the high QC sample and 20% for the low QC sample. 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 in the same or different laboratory.

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

5. Analyte stability: the authors must indicate the stability of the analyte throughout the total bioanalytical method, including storage conditions.

6. Limits: the lower limits of quantitation and detection (LOQ, LOD) along with statistical bases for these limits must be reported and must be within

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the calibration range. Data from the assay of blank matrices should be included for the establishment of the ''background noise'' in the assay.

7. Absolute recoveries: where applicable, average absolute recoveries (with standard deviations) for analytes and internal standard must be reported for high and low concentrations within the concentration range of the study. Recoveries should be calculated using the full bioanalytical method. Absolute recovery is defined as the yield obtained in comparison to the theoretical maximum defined by complete transfer of a compound from the natural matrix into the solution studied by the quantitating instrumentation.

8. Proof of applicability: the manuscript must include results from the application of the method to authentic samples from the actual study it will be utilized in. 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 analyze the range of samples obtained during the study.

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