



## Tutorial

## Tutorial review on validation of liquid chromatography–mass spectrometry methods: Part II



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## HIGHLIGHTS

- The status of validation of LC–MS methods is comprehensively reviewed.
- Clarity is brought into validation-related terminology.
- Recommendations on difficult validation-related issues in LC–MS are given.

## GRAPHICAL ABSTRACT



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## ABSTRACT

This is the part II of a tutorial review intending to give an overview of the state of the art of method validation in liquid chromatography mass spectrometry (LC–MS) and discuss specific issues that arise with MS (and MS–MS) detection in LC (as opposed to the “conventional” detectors). The Part II starts with briefly introducing the main quantitation methods and then addresses the performance related to quantification: linearity of signal, sensitivity, precision, trueness, accuracy, stability and measurement uncertainty. The last section is devoted to practical considerations in validation. With every performance characteristic its essence and terminology are addressed, the current status of treating it is reviewed and recommendations are given, how to handle it, specifically in the case of LC–MS methods.

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**Abbreviations:** CRM, certified reference material; CV, coefficient of variation; EMA/EMEA, European Medicines Agency; ESI, electrospray ionization; FDA, United States Food and Drug Administration; ICH, International Conference on Harmonization; ILC, interlaboratory comparison; ILIS, isotopically labeled internal standard; IS, internal standard; IUPAC, International Union of Pure and Applied Chemistry; LC–MS, liquid chromatography–mass spectrometry; LLoQ, lower limit of quantitation; LoD, limit of detection; LoF, lack-of-fit; LoQ, limit of quantitation; ME, ionization suppression/enhancement (matrix effect); MU, measurement uncertainty; PE, process efficiency;  $r$ , correlation coefficient;  $R$ , recovery;  $r^2$ , coefficient of determination; RSD, relative standard deviation;  $s$ , standard deviation; SLV, single lab validation; ST%, stability; ULoQ, upper limit of quantitation; VIM, International Vocabulary of Metrology.

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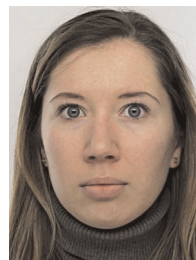
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