VALIDATION OF MULTI-PARAMETER METHODS – REVISITING AN EU-COORDINATED IN-HOUSE VALIDATION STUDY FOR NSAID COMPOUNDS IN BOVINE MILK

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In the framework of monitoring residues in food of animal origin, EU laboratories face the challenge of validating analytical methods for numerous (sometimes several hundred) analytes and matrices. It is thus highly desirable to propose an approach, which will reduce the associated workload while maintaining the required level of reliability. One such approach consists in identifying relationships between the different analytes in order to constitute groups within which the method can be expected to exhibit uniform validation characteristics. This poster examines one possible approach consisting in selecting a subgroup of analytes for the validation. This approach is tested on the basis of a "coordinated" in-house validation study for a multi-parameter LC-MSMS method for NSAID compound residues in bovine milk.

This validation study involving 14 EU laboratories was conducted in 2011. Each laboratory was asked to perform an in-house validation for a multi-parameter LC-MSMS method for 16 NSAID compounds in both lyophilised and fresh bovine milk. The main advantage of this confirmatory method is the simultaneous determination of different groups of NSAID compounds. Within each laboratory, measurements were conducted according to a factorial design (with factors such as operator, sample storage and SPE lot) in accordance with the CD 657-2002 alternative approach as extended by QuoData and implemented in the software package InterVAL PLUS. The results for all 14 laboratories then formed the basis for a combined validation across laboratories, i.e. in-house validation parameters such as the in-house repeatability, intermediate and reproducibility standard deviations and the critical concentration CC_α were determined on the basis of the results of all 14 laboratories. Similarly, the contributions to uncertainty corresponding to the different factors (including matrix) were quantified on the basis of the results of all 14 laboratories. Finally – and this is the decisive aspect here – it was possible to compare the laboratory-specific CC_α values. The following result was observed: on the one hand, for many laboratories, the method yielded satisfactory performance characteristics (e.g. CC_α values lying below the maximal admissible value according to CD 657-2002) *for all compounds,* while, for the remaining laboratories, the performance characteristics were unsatisfactory *for several compounds.*

These results suggest the following approach: First, identify all analytes which have caused difficulties in the past or which are known as "critical" for example in terms of concentration level or correct identification. Then select randomly at least 6 of the remaining analytes. A complete in-house validation is then conducted on the basis of this selection. For the other analytes, an individual "ad-hoc" validation could also be performed. This approach works very well with the available data set of the NSAID compounds in bovine milk. Further studies are required to investigate whether it is also successful for other compounds and matrices.