Bundesamt für Verbraucherschutz und Lebensmittelsicherheit

Department 5
European Reference Laboratory for Residues of Pharmacologically Active Substances (EURL)

European Commission

Proficiency Tests with SI-Traceable Reference Values – Example of an Interlaboratory Comparison on Chloramphenicol in Plasma

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Introduction

Official food control laboratories in Europe have to be accredited according to ISO 17025. One of the requirements of ISO 17025 is that results should be metrologically traceable to SI (international system of units) whenever possible.

Organising interlaboratory comparisons for proficiency testing purposes is one of the key tasks of European Union and National Reference Laboratories (EURL / NRL). As discussed by de Bievre [1], PT programme organizer have, besides the often used consensus value evaluation, also the possibility to decide on a reference value evaluation, ideally based on metrological evidence originating fully from outside the PT programme.

As German NRL and designated institute (DI) for residues in food, the BVL organised an interlaboratory comparison for the official German routine laboratories for chloramphenicol (CAP) in plasma.

Statistics

The proficiency of the laboratories was evaluated by means of the classical consensus value evaluation with z_u-scores (DIN 38402-A45) using the robust mean and the robust reproducibility standard deviation (according to ISO 13528:2015, Annex C).

In addition a second evaluation based on a metrological traceable reference value was performed. This evaluation was done in the form of a "degrees of equivalence evaluation" [2] using the results of the participants and their reported uncertainties as well as the reference value and its associated uncertainty. The reference value was assigned by the NRL on the basis of its status as designated institute acquired pursuant to its proven competence in key comparisons of the CCQM at the BIPM).

The study material was tested and calibrated at the BVL. For the material a reference value and a respective measurement uncertainty was calculated.

Sample preparation and characterisation

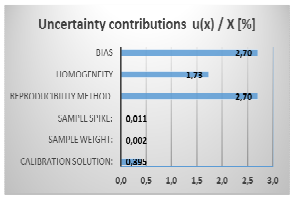
Incurred sample material derived from a pig which was medicated with chloramphenicol. Plasma was collected, pre-tested and subsequently diluted with blank plasma in order get a final CAP content of about 0.3 ng/g, followed by lyophilisation.

The homogeneity was checked according to ISO 13528. For the test material a relative between bottle standard deviation of 1.7 % was calculated, the material proved to be homogenous.

The stability of the lyophilised material was tested for duration of 5 month at temperatures of -30°C, +4°C, +25 °C and – 80°C as reference temperature. The samples proved to be stable even at + 25°C for at least five months.

Reference value and uncertainty

Assigning of the reference value was done using the isotope dilution technique by applying the method BVL/CAP_013 as listed in the calibration and measurement database ("CMC"-database) of the BIPM [3]. The reference value of the study material is traceable to a chloramphenicol standard material provided by the National Metrology Institute of Turkey (UME, TÜBITAK Ulusal Metroloji Enstitüsü).



The reference value was calculated as 0.396 +/- 0,031 ng/g (uncertainty as expanded uncertainty with k=2).

Participants and results

12 German official control laboratories and the NRL participated in the interlaboratory comparison. Each laboratory received a sample to be examined for the total chloramphenicol content. The laboratories were asked to provide additionally an uncertainty budget for their measurements.

Evaluation

A consensus value of 0.392 ng/g with a reproducibility standard deviation of 0.048 ng/g was calculated from the 13 received results.

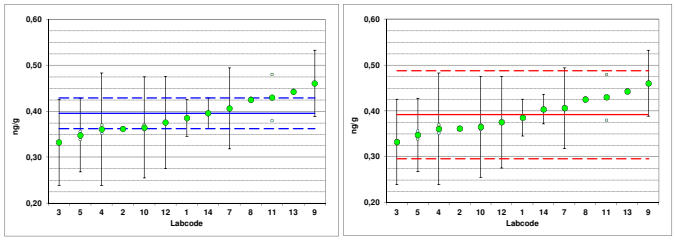


Fig. 1: Results of Interlaboratory comparison CAP in Plasma with different evaluations :
a) results with reference value (▬ traceable to SI), its expanded uncertainty (– –) and reported values (●) including reported measurement uncertainties
b) results with robust mean as target value (▬) and expanded reproducibility standard deviation (Hampel, k=2 ; – –) and reported values (●) including reported measurement uncertainties

DoE calculation

The calculation [2] of the degrees of equivalence (DoE) might be used to demonstrate the equivalence of the participant´s own measurements and the SI traceable reference value with the stated uncertainties. This calculation requires stated uncertainties from the participants, which was not always the case.

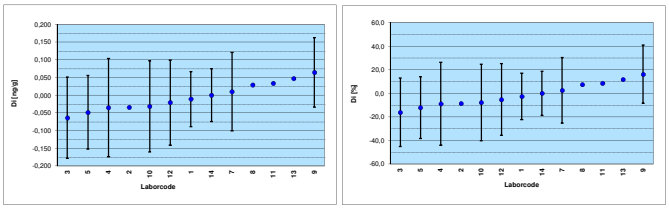


Fig. 2: Relative and absolute DoE taking into account the uncertainty of the reference value and the reported uncertainty (the equivalence of the own measurement and the SI traceable reference value is given if some overlap to the zero level is given).

Summary

- The SI traceable reference value and the calculated robust mean value in this study are in very good agreement (which might not always be the case)
- The use of a reference value in an interlaboratory comparison offers a feasible way of providing traceability to SI, a DoE calculation can be an approach to show the equivalence of results.
- Presently only few interlaboratory comparison providers in residue control in food are able to provide SI traceable reference values.

References

[1] P. de Bievre, Accred Qual Assur (2016) 21:167–169

[2] CCQM Guidance note: Estimation of a consensus KCRV and associated Degrees of Equivalence, Version 10, 2013-04-12, www.bipm.org

[3] CMC database at http://kcdb.bipm.org/appendixC/default.asp

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