Letter to the Editor

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# The simple reproducibility of a measurement result does not equal its overall measurement uncertainty

https://doi.org/10.1515/cclm-2022-0618
Received June 27, 2022; accepted July 1, 2022;
published online July 11, 2022

**Keywords:** measurement uncertainty; metrological traceability; internal quality control.

To the Editor,

In reading the recently published discussion paper by Coskun et al. [1], I was happy to see that many of the concepts we previously promoted for correctly estimating measurement uncertainty (MU) in medical laboratories were endorsed [2, 3]. The "top-down" approach estimating MU of laboratory results is now officially recognized by the ISO Technical Specification 20914 that provides a practical guidance to be applied in medical laboratory settings for estimating MU of values produced by procedures intended to measure biological measurands [4]. It seems, however, that Authors did not fully realize that the inspiring concept behind this approach relies on the definition of MU across the entire traceability chain, starting with the uncertainty of reference materials ($u_{ref}$), extending through the IVD manufacturers and their processes for assignment of calibrator values and uncertainty ($u_{cal}$), and ending with the random variability of measuring systems ($u_{Rw}$). Although correctly, the authors only discuss how to derive this last component of MU by using internal quality control (IQC) data, ignoring, however, that the MU estimate must include all uncertainties introduced by the selected calibration hierarchy for the measurand, beginning with the highest available reference down to the assigned value of the calibrator for the commercial IVD medical device. Although reference material providers, IVD manufacturers, and medical laboratories have different roles and independent tasks across the metrological traceability chain, their performances contribute together to the MU of patient results [5–7]. The crucial point is that the estimated MU must be always combined at each level of the employed traceability chain. Particularly, the MU at the level of clinical samples ($u_{result}$) must be the combination of all uncertainty contributions accumulated across the entire traceability chain. This refutes the common misconception, which also shine through the proposal by Coskun et al., that the simple reproducibility of a measurement result equals its overall MU. A correct estimate of MU of laboratory results is indeed not possible without $u_{cal}$, which in turn should include $u_{ref}$. In the European market, the information about $u_{cal}$ shall be provided on request to the professional end-users. Sometimes, calibrators are offered without MU, but it is up to the laboratory professionals to ask manufacturers and obtain this information for the correct estimate of $u_{result}$ [8].

The characteristics of the IQC material to be used for $u_{Rw}$ estimate have been also previously described in detail and should be carefully considered [2, 3, 5, 9]. The material should be different from that used to check the correct alignment of the measuring system, be commutable and with concentration(s) corresponding to the decision cut-point(s) employed in the medical application of the test. Therefore, suggesting that "calculating MU for normal level IQC material" is a rational compromise does not consider the third requirement. IQC materials for estimating $u_{Rw}$ should have analyte concentration levels close to clinical decision limits or, at least, to employed reference limits. This is important because, for most, if not all laboratory tests, MU varies with the analyte concentration, usually decreasing with increasing concentrations.

**Research funding:** None declared.
**Author contributions:** Single author contribution.
**Competing interests:** Author states no conflict of interest.
**Informed consent:** Not applicable.
**Ethical approval:** Not applicable.

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