

Editorial

Mario Plebani*, Philippe Gillery, Ronda F. Greaves, Karl J. Lackner, Giuseppe Lippi, Bohuslav Melichar, Deborah A. Payne and Peter Schlattmann

Rethinking internal quality control: the time is now

<https://doi.org/10.1515/cclm-2022-0587>

In this issue of the *Journal*, two papers deal with a fundamental issue in the practice of clinical laboratories, leading us to rethink the management of internal quality control (IQC) in the traceability era. As we really believe that these articles reflect “two schools of thought”, their publication should provide further information and a valuable source of knowledge for laboratory professionals, which may translate into a better operational approach to assure the quality and reliability of laboratory results. From one side, the father of statistical quality control (SQC) Dr James Westgard, and colleagues, highlight the principles of the “risk-based statistical quality control” that comprise six steps: 1) define the quality specifications for the test; 2) select appropriate control materials and levels; 3) determine the stable (in control) performance of the measurement procedure; 4) identify candidate quality control strategies; 5) specify desirable goals for the QC performance characteristics; and 6) select a quality control strategy (control rules, number of control measurements),

whose predicted performance meets or exceeds the quality control performance goals [1]. Quality specifications and stable imprecision are used to calculate a Sigma-metric and candidate QC procedures are indeed identified using a Sigma-Metric Run Size Nomogram which, in turn, permits the risk-based SQC strategy. The SQC strategy, as emphasized by Westgard and colleagues, is based on the traditional Total Error (TE) framework.

In their work, Westgard and colleagues reiterate criticisms of the articulated proposal to rethink IQC in the traceability era by Mauro Panteghini and colleagues [2, 3]. The *Journal* has previously published the articles of Panteghini et al., as well as many other articles which are strictly related to the First Strategic Conference organized in Milan in 2014 by the European Federation of Clinical Chemistry Laboratory Medicine (EFLM). The conference was entitled “Defining analytical performance goals 15 years after the Stockholm conference”, as it was considered timely to address the topic of performance specifications both because it was a long time since it was previously addressed, because performance specifications are central for the clinical application of test measurements and are also of “vital importance for quality control measures that should be taken in the laboratories” [4]. As emphasized in the final part of the cited sentence above, therefore, properly derived analytical performance specifications (APS) play a central role not only in setting operational goals and defining the uncertainty of laboratory measurements, but provide a more objective tool for establishing IQC in the traceability era. As emphasized by Panteghini commenting on the Westgard article, the question is not to “reiterate the debate between the Total Error (TE) advocated and those conversely supporting the importance of measurement uncertainty (MU)” but some points should be better highlighted [5]:

First, the proposal by Panteghini et al. to rethink IQC cannot be considered a step back to the “fixed clinical limits” to be used as an “acceptability range on a control chart”. The interpretation of the so-called component I of

***Corresponding author: Mario Plebani**, CCLM Editor-in-Chief, Honorary Professor, Medical School, University of Padova-Italy, Padova, Italy, E-mail: mario.plebani@unipd.it. <https://orcid.org/0000-0002-0270-1711>

Philippe Gillery, Laboratory of Biochemistry-Pharmacology-Toxicology, University Hospital of Reims, Reims, France

Ronda F. Greaves, Biochemical Genetics, Victorian Clinical Genetics Services Ltd, Parkville, VIC, Australia

Karl J. Lackner, Medical Center of the Johannes Gutenberg-University, Institute of Clinical Chemistry and Laboratory Medicine, Mainz, Germany

Giuseppe Lippi, Section of Clinical Biochemistry, University Hospital of Verona, Verona, Italy. <https://orcid.org/0000-0001-9523-9054>

Bohuslav Melichar, Oncology, Palacky University Medical School, Olomouc, Czech

Deborah A. Payne, CPDP Consulting, LLC, Denver, CO, USA

Peter Schlattmann, Computer and Data Sciences, University Hospital Jena, Institute of Medical Statistics, Jena, Germany

the new model of IQC seems to be reductive, as Panteghini et al. highlighted the need to take into consideration not only a single checked value but also “temporal trends” [3].

Second, the proposal to rethink IQC is addressing a fundamental shift to allow clinical laboratories to check the system alignment to higher-order references, which should be granted by manufacturers, thus providing evidence of surveillance of IVD metrological traceability and stimulating IVD manufacturers to provide control materials as a qualified part of the measuring system, as recommended in the new EU IVD regulations [6, 7]. Laboratory professionals need to adopt valuable systems to verify in real-time the traceability of their clinical results.

Third, the proposal by Panteghini et al. stresses the need to take into higher consideration not only imprecision but also the trueness (bias) of laboratory results, and this is a major concept to be emphasized in the traceability era.

However, we would add some additional considerations.

First, the *Journal* has already regularly considered and would like to continue with this tradition, the topics related to analytical quality as fundamental requirements for the daily practice of clinical laboratories, thus encouraging laboratory professionals to submit other manuscripts dealing with this topic.

Second, while rethinking IQC in the traceability era is now mandatory, we still need new and better proposals to revise the traditional approach to IQC for the measurands (about 300 and more) for which no reference measurement procedures (RMP), nor reference materials (RM) are available, but are of pivotal significance and value in clinical practice. Is the traditional statistical quality control the unique practice to be used? Is the real-time quality control (RTQC) and its eventual integration with SQC a better strategy? In addition, other promising proposals, such as the use of machine learning in IQC are receiving increasing interest [8].

Third, the special issue of the *Journal* dedicated to biological variation and the updated information on this essential topic [9], should be a further stimulus to upgrade our knowledge and practices on analytical quality, including IQC.

Finally, we believe that the analytical quality of laboratory results, and particularly the improvement due to better efforts to comply with APS and to adopt better IQC

and external quality assessment/proficiency testing systems, should be notified in some universally agreed means to clinicians, to allow better and more evidence-based interpretation and utilization of laboratory information. This, in turn, should ultimately assure a better quality of care and enhanced patient safety.

We strongly believe that these topics still require further contributions and debate, and the *Journal* will offer a valuable platform to continue the discussion.

Research funding: None declared.

Author contributions: All authors have accepted responsibility for the entire content of this manuscript and approved its submission.

Competing interests: Authors state no conflict of interest.

References

1. Westgard JO, Bayat H, Westgard SA. How to evaluate fixed clinical QC limits vs. risk-based SQC strategies. *Clin Chem Lab Med* 2022;60: e199–201.
2. Panteghini M. Application of traceability concepts to analytical quality control may reconcile total error with uncertainty of measurement. *Clin Chem Lab Med* 2010;48:7–10.
3. Braga F, Pasqualetti S, Aloisio E, Panteghini M. The internal quality control in the traceability era. *Clin Chem Lab Med* 2020;59:291–300.
4. Panteghini M, Sandberg S. Defining analytical performance specifications 15 years after the Stockholm conference. *Clin Chem Lab Med* 2015;53:829–32.
5. Panteghini M. Reply to Westgard et al: keep your eyes wide ... as the present now will later be the past. *Clin Chem Lab Med* 2022; 60:e202–3.
6. Cobbaert C, Smit N, Gillery P. Metrological traceability and harmonization of medical tests: a quantum leap forward is needed to keep pace with globalization and stringent IVD-regulations in the 21st century. *Clin Chem Lab Med* 2018;56: 1598–602.
7. Cobbaert C, Capoluongo ED, Vanstapel FJLA, Bossuyt PMM, Bhattoa HP, Nissen PH, et al. Implementation of the new EU IVD regulation – urgent initiatives are needed to avert impending crisis. *Clin Chem Lab Med* 2022;60:33–43.
8. Zhou R, Wang W, Padoan A, Wan Z, Feng X, Han Z, et al. Traceable machine learning real-time quality control based on patient data. *Clin Chem Lab Med* 2022. July 2022. <https://doi.org/10.1515/cclm-2022-0548>. [Epub ahead of print].
9. Sandberg S, Carobene A, Aarsand AK. Biological variation – eight years after the 1st strategic conference of EFLM. *Clin Chem Lab Med* 2022;60:465–8.