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Editorial

"Harmonization of laboratory testing — A global activity"

The harmonization of laboratory testing is a high priority topic in Laboratory Medicine. It is more than harmonized terminology, units of reporting, methodology and reference intervals but, rather, covers a wide range of topics from the "pre-pre-analytical" phase ('Right test at the Right time for the Right patient') to the analytical aspects and reporting of critical results through to consumer education and the meaning of laboratory tests in lay terms ("post-post-analytical" phase). Harmonization should lead to safer and more accurate interpretation of patient results [1].

Any new concept requires innovative and practical ideas if it is to succeed. This special themed issue of 26 articles explores how we might achieve the closer comparability of processes to achieve closer comparability of laboratory outcomes globally. Experts provide reviews, commentaries and critical opinions about the benefits of harmonization and its future directions. Aarsand and Sandberg [2] suggest practical ways of achieving harmonization of laboratory testing and describe the potential barriers. They recommend close interaction with all stakeholders including the Laboratory Medicine community, diagnostic industry, clinicians, professional societies, IT providers, consumer advocate groups and the government as essential for harmonization projects to be successful and to achieve improved clinical effectiveness of critical tests and greater patient safety.

In particular, harmonization initiatives should improve procedures and processes at the laboratory-clinical interface. As Plebani and Panteghini discuss [3], it is essential to promote close relationships between laboratorians and clinicians to improve the laboratory testing process. As a practical example, Berg [4] describes the elements of a global harmonization model based on the United Kingdom harmonization initiative and the importance of marketing communications as an inclusive approach involving key pathology and clinical professional groups. Misra and Barth [5] go on to describe how when being developed guidelines on test selection require an integral interaction between clinicians and laboratory specialists, and that this should help to harmonize practice, reduce inappropriate test selection and reduce treatment variations secondary to analytical variations.

Harmonizing the pre-analytical phase requires use of standardized operating procedures for correct test selection, sample collection and handling. However, standardized protocols for patient preparation for laboratory testing are currently lacking. Simundic et al. [6] for the European Federation of Clinical Chemistry and Laboratory Medicine Working Group on the Pre-analytical Phase (EFLM WG EFLM WG-PA) discuss the need to provide a framework for the harmonization of definitions for fasting requirements for laboratory tests. In a more contentious article, Dolci and Panteghini [7] raise the possibility of harmonizing automatic hemolysis index (HI) assessment and, in particular, the need to develop a harmonized response for reporting results of unsuitable samples with significantly increased HI. Finally, in this section, Plebani [8] describes the model of Quality Indicators (QIs) developed by the International Federation of Clinical Chemistry and Laboratory Medicine WG on Laboratory Errors and Patient Safety (IFCC WG-LEPS) and the need for promoting the harmonization of available QIs in the pre-analytical phase.

Standardized test terminology and units, and traceability to international standards are required to ensure equivalency of assay measurement results. Greenberg [9] describes the importance of ensuring the equivalence of test results among different measurement procedures, different laboratories and healthcare systems, over time. He explains the critical concepts of *standardization*, *traceability* and *harmonization*. Braga and Panteghini [10] go on to critically review the status of metrological traceability of IVD assays and the importance of clinical laboratory professionals understanding how manufacturers have implemented the traceability of their calibrators and estimated the corresponding uncertainty. They stress that external quality assurance (EQA) programs must be able to evaluate the traceability of the assay calibration and of patient results as well as the equivalence of measurement results among laboratories. In this way those analytes needing improved harmonization are identified and standardization initiatives that are needed to support clinical practice guidelines are sustained.

The concept of method harmonization in Laboratory Medicine is not new as Ross et al. [11] describe in their empirical approach to harmonizing growth hormone measurements in the Netherlands several years ago. What is new is the global strategy proposed by an International Consortium for Harmonization of Clinical Laboratory Results [12] to use method harmonization as a pragmatic procedure for achieving the closer comparability of patient results, in particular, for high priority measurands where a clinical decision level is used and measurement inaccuracy can cause clinical misclassification. Wieringa et al. [13] and Sturgeon [14] in their papers emphasize the need for harmonization of growth hormone and other immunoassays where there is a common decision limit yet significant differences still exist between methods. Van Uytfanghe et al. [15] explain the practical aspects involved with the "Step-Up" design for method harmonization which comprises a sequence of method comparisons with selected sets of commutable samples and uses a statistically valid measure as the surrogate reference measurement procedure.

A key message in this issue is the need for monitoring of harmonization activities and the analytical quality of laboratory measurements through surveillance by EQA schemes. Ceriotti [16] emphasizes the role of EQA schemes in monitoring and improving the standardization process and the need to use commutable materials with target values assigned by reference methods. Examples of the success of standardization and

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harmonization through EQA schemes are described by Perich et al. and Jansen et al. [17,18].

An important key to harmonization of laboratory testing is the use of harmonized or common reference intervals (RIs) which will reduce inaccurate clinical interpretation and unnecessary additional laboratory testing due to different reference limits. The use of common RIs will benefit the task of integrating results from different laboratories into future national e-health frameworks. Koerbin et al. [19] describe an evidence-based approach for harmonizing reference intervals for traceable analytes where platforms share allowable bias requirements. To complement this approach Jones [20] describes how common RIs can be validated for use in individual laboratories by considering the appropriateness of the interval, methodological factors and population factors. At the global level the use of common RIs is more complex due to possible ethnic differences between populations. Ichihara [21] describes the statistical considerations for harmonization of global reference values, which is a part of the major multicenter study being coordinated by the IFCC Committee on Reference Intervals and Decision Limits.

Hyltoft Petersen and Klee [22] describe in their opinion paper how diagnostic decisions based on guideline-based decision limits may be fraught with inaccuracy. They explain how assay quality, as measured by analytical bias and imprecision, can profoundly impact on the number of false positive results observed when using decision limits, and that there is the need for strict bias specifications when applying these limits.

Harmonized procedures for the management of critical laboratory test results are required to improve service quality and ensure patient safety. Campbell and Horvath [23] systematically review current international critical laboratory practices and, based on literature review findings, propose a harmonized terminology and a conceptual framework for designing more evidence-based systems for the timely notification of critical laboratory results.

The current reporting practices of patient results are heterogeneous and may lead to an increased risk of interpretation errors, possibly endangering clinical safety. It is these factors that are driving the requirement for standardization of information technology structures and terminology in Laboratory Medicine. Legg [24] in his paper describes the IT standardization required to achieve interoperability for laboratory test requesting and reporting, and to preserve the shared meaning of data or information when it is electronically exchanged. Laboratory Medicine needs to better interact with IT specialists if our reporting is to be harmonized and the health informatics data are to be reliable.

Often the final 'post-post analytical phase' seems to be out of the reach of the clinical laboratory. We need to become more involved as described by Florkowski et al. [25] in their contribution, where they outline the managed process taken nationally in New Zealand by the laboratory and clinical professions to implement the HbA_{1c} IFCC unit from the laboratory to the consumer. Its successful adoption was the result of a robust consultation process and a phased introduction designed to increase familiarity and comfort with the new units. Importantly, it required a close collaboration between the diabetes clinical and laboratory communities.

Finally, Campbell et al. [26] detail the work of Lab Tests Online and the important contribution it is making to consumer understanding of laboratory testing. With the advent of the Personalized Health Record and consumers becoming increasingly involved in the management of their own healthcare, the Lab Tests Online global websites are an important educational tool.

It has become apparent that harmonization of laboratory testing globally is a significant project and requires input from a range of national and international stakeholders to gain momentum and uptake. This will require a planned communication and marketing strategy in order to roll out the relevant changes, educate clinicians, and gain acceptance of these processes by all stakeholders. In so doing it raises the profile of Laboratory Medicine and our input into decision-making and education.

The idea behind this themed issue has been to highlight the importance of harmonization of laboratory testing and provide impetus for the profession to progress harmonization activities globally. The editors and authors of the issue invite the clinical laboratory community to participate in the many varied quality activities that contribute to the process of harmonization. No matter what discipline of Laboratory Medicine you may work in, the same principles of harmonization apply. As consumers of laboratory testing ourselves, we above all have the expectation of receiving the 'Right test at the Right time for the Right patient' and the 'same results and interpretation for a sample irrespective of the laboratory that produced the result'. It is only by having a harmonized approach to laboratory testing that we can hope to achieve these goals.

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