



## Letter to the editor

## Why harmonization is essential to realize the manifesto for the future of laboratory medicine



Dear editor

A manifesto for the future of laboratory medicine was recently published by Plebani et al. [1,2]. The manifesto describes 10 points that focus the role of clinical laboratory professionals to provide effective collaboration with physicians to achieve optimal value in healthcare. A central theme of the manifesto is cooperation and optimization of the path of workflow to implement the brain to brain loop between clinical care providers and laboratory medicine experts first described by Lundberg in 1981 [3].

Harmonization and standardization of the laboratory testing process are essential to achieving high quality laboratory service [4]. Harmonization of the pre-examination components such as patient preparation, test ordering and sample procurement as well as the post-examination components such as reporting units, reference intervals and interpretive information is critical to avoid misunderstanding and misinterpretation of test results. Harmonization of the laboratory test results themselves is critically important to realizing several points in the manifesto.

The manifesto point 3 to develop laboratory medicine stewardship emphasizes that false positive or false negative test results be avoided. Since a positive or negative interpretation involves a decision value, there will always be some misclassification due to uncertainty in measured values. Reducing the measurement uncertainty to an acceptable level is thus required. However, harmonization of results among measurement procedures from different manufacturers used in different laboratories must be achieved to minimize the occurrence of false positive or false negative interpretations based on decision values for medical actions.

The manifesto point 5 recommends improving the quality and reliability of reference intervals and decision limits for use in clinical decisions. In principle, reference intervals are intended to provide suitable interpretive information for use with a particular measurement procedure in a particular population. As such, again in principle, reference intervals could compensate for differences in calibration among different measurement procedures for the same laboratory test. In practice, different measurement procedures sometimes use the same or very similar reference intervals even when those measurement procedures are not harmonized to give the same result values.

Frequently, fixed decision values derived from clinical trials or clinical practice recommendations are used to apply clinical actions based on laboratory test results. When decision values are applied to results from different measurement procedures that do not give harmonized results, serious errors in medical decisions and patient treatment or non-treatment can occur. Realizing the manifesto point 5 requires increased focus and resources be applied to achieving

harmonized or standardized results among different measurement procedures for the same laboratory test.

The manifesto point 6 emphasizes the importance of the laboratory professional getting out of the laboratory silo and becoming part of the interdisciplinary diagnostic team. In this context, a laboratory test result is assessed for its impact on patient management. As stated in the preceding point, when laboratory test results are different from different measurement procedures, errors in medical actions will occur especially when test results are interpreted using fixed decision values, but also when inappropriate reference intervals are used. One goal of manifesto point 6 is the laboratory professional can bring knowledge of non-harmonized test results to the diagnostic team. However, the laboratory professional may not be aware of all non-harmonized test results. Consequently, the laboratory profession needs to better educate laboratory medicine specialists as well as clinical practitioners on such testing limitations. A better solution is to achieve harmonized results for all laboratory tests.

The manifesto conclusion proposes the concept of “diagnostic calibration” which has been defined as the relationship between diagnostic accuracy and physician confidence in that accuracy [1]. Diagnostic calibration requires diagnostic accuracy that in turn requires harmonized or standardized results from different measurement procedures for the same laboratory test. The insidious influence of non-harmonized laboratory test results on medical errors is underappreciated by clinical care physicians and also by laboratory medicine professionals. It is essential that laboratory medicine embrace the importance of harmonized test results and increase the resources to achieve harmonized results among all measurement procedures for the same laboratory test.

## References

- [1] M. Plebani, M. Laposata, G. Lippi, A manifesto for the future of laboratory medicine professionals, *Clin. Chim. Acta* 489 (2019) 49–52.
- [2] M. Plebani, M. Laposata, G. Lippi, Driving the route of laboratory medicine: a manifesto for the future, *Intern. Emerg. Med.* (2019), <https://doi.org/10.1007/s11739-019-02053-z> (accessed 28 February 2019).
- [3] G.D. Lundberg, Acting on significant laboratory results [editorial], *JAMA* 245 (1981) 1762–1763.
- [4] G.L. Myers, W.G. Miller, The roadmap for harmonization: status of the International Consortium for Harmonization of Clinical Laboratory Results, *Clin. Chem. Lab. Med.* 56 (2018) 1667–1672.

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