

Editorial

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Lessons from controversy: biomarkers evaluation

The discovery and development of biomarkers presents exceptional challenges; despite the contribution of numerous authors who have described valuable guidelines and roadmaps designed to improve the different steps in the development pipeline, the biomarker saga is still riddled with failures [1].

This issue of *Clinical Chemistry and Laboratory Medicine (CCLM)* contains an editorial by Rifai and colleagues [2] that was recently published in *Clinical Chemistry* dealing with the current predicaments and providing the guidelines for the evaluation of commercial research immunoassay kits; the decision to republish it in *CCLM* was made for several reasons. First, mounting evidence underlines the need to establish and implement sound criteria for the evaluation and validation of commercially available assays, particularly because the great promises of some biomarkers in predicting the risk, yielding a prognosis, and facilitating the management of lethal diseases have not been realized [3]. Second, some countries are now using the revised frameworks for the regulation of in vitro diagnostic devices, including diagnostic kits and reagents [4], sometimes without the active involvement of laboratory professionals and thus with the likelihood of negative outcomes. Third, the *Journal* intends to maintain its promise to update and promote a debate among laboratory medicine professionals to honor the agreement made with the International Federation of Clinical Chemistry and Laboratory Medicine and, above all, the European Federation of Clinical Chemistry and Laboratory Medicine, presided over by a coauthor of the highlighted editorial. The evaluation of laboratory diagnostic tests has been stimulated by recent technological developments, namely, the so-called “omics” and the advent of new-generation laboratory tests expected to help in risk assessment, diagnosis, and prognosis of disease, as well as to guide in patient treatment [5]. Of course, a gold standard for comparing the performance of different laboratory tests is not always available, and clinical-laboratory interactions are expected to change thanks to the introduction of this new generation of diagnostics [6]. In their seminal article, Price and Christenson [7] underlined the current limitations and the lack of requirements in the process

used for evaluating and adopting new assays. These limitations are now expected to become even more apparent in the light of the growing demand for relevant outcomes when evaluating new medical technologies, including laboratory diagnostics [8].

The editorial by Rifai et al. stresses the need for manufacturers of “for Research Use Only” reagent kits to provide more details in the descriptions of the assays they produce, together with the definitions of their performance characteristics, and to specify the source of the calibration materials. However, the most important take-home message is that the “users (laboratorians) must validate the analytical performance of the assay they intend to use, and confirm the manufacturer’s claims before they use it ...”. In other words, the evaluation and validation of commercially available kits is still the duty and responsibility of laboratory professionals and cannot be ignored and also includes assays sold as “for Research Use Only”. Although the analytical evaluation of an assay is reasonably straightforward and based on valuable guidelines, more emphasis should be placed on the evaluation of its clinical validity and utility, a crucial step before moving the candidate biomarker closer to the patient [8]. This validation, in turn, calls for closer cooperation between laboratory professionals, clinical researchers, and clinicians as well as the design of appropriate clinical studies and trials, according to the hierarchical levels suggested in the ACCE framework [9]. Up to now, the process of evaluating the diagnostic tests differs substantially from that of studying pharmaceutical products that are based on randomized and double-blind trials before the commercialization of new drugs. The clinical relevance of the new generation of laboratory testing and its value in patient care has long been neglected, but the changing face of laboratory tests has finally sparked a debate conducive to developing a better framework for evaluating and regulating all laboratory testings [10]. It is time to close the gap between “what we know and what we practice” also in laboratory testing, and the editorial by Rifai et al. represents an important step forward in recognizing the urgent need to improve the evaluation and validation of novel biomarkers.

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