Editorial

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Progress towards standardization: an IFCC Scientific Division Perspective

The aim of the Scientific Division (SD) of the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) is to advance the science of Laboratory Medicine [1]. In this regard, IFCC-SD identifies research areas of relevance in Laboratory Medicine and related scientific and technological problems, and provides solutions and guidelines on how to resolve them. Especially, SD focuses on standardization issues in order to facilitate the development and implementation of new methods and their optimal use in clinical practice.

To facilitate its work, IFCC-SD has established over time a number of committees (Cs) and working groups (WGs) devoted to various areas of Laboratory Medicine. In most cases, the outcome has been the description of reference measurement procedures (RMPs) and the validation of certified and commutable reference materials [1]. The list of active Cs and WGs in 2012 is shown in Table 1.

Standardization of methods is a complex process which requires the development of a full reference measurement system and a traceability chain. For some measurands, the path from description of a RMP to implementation of standardized tests in clinical laboratories is a long and complex one. In this special issue, several Cs or WGs provide state-of-the-art reviews or experimental data illustrating the different steps of the standardization process and the potential difficulties encountered.

Metrological traceability is a major concept in SD’s strategy for standardization, which aims at obtaining equivalent measurement results regardless of the assay. This implies traceability to RMPs through an unbroken chain of steps, each contributing to the measurement uncertainty [2]. In addition, since the use of an agreed terminology is needed to ensure the correct reporting of results generated by specialists in Laboratory Medicine to clinicians, definition and update of metrological terms and units are major roles of the Joint Committee for Nomenclature, Properties and Units of the IFCC and The International Union of Pure and Applied Chemistry (IUPAC) (C-NPU) [3].

Many efforts of SD WGs are devoted to the establishment of RMPs and of convenient commutable reference materials. In this issue, the example of the development and the validation of a candidate LC-MS/MS RMP for urinary albumin is described by the Working Group on Standardization of Albumin Assays in Urine (WG-SAU), together with the validation of candidate reference materials for urinary albumin and creatinine [4]. As highlighted in this paper, the availability of such procedures and materials will enable standardization of this important marker of kidney damage and risk factor for progression of renal and cardiovascular diseases. Another example is given with carbohydrate-deficient transferrin (CDT), a clinically relevant biomarker of alcohol abuse, by the WG-CDT. While an HPLC candidate reference method has already been proposed, the availability of convenient secondary reference materials is now necessary for harmonizing CDT measurements by different methods before achieving their full standardization against the RMP [5].

However, achieving full standardization is challenging and various pitfalls may occur along the path from RMP to routine practice. A major practical difficulty, the sourcing of relevant clinical samples for establishing metrological traceability, is discussed in this issue [6]. The experience of the Working Group on Standardization of Thyroid Function Tests (WG-STFT, since transformed into a Committee) in obtaining relevant panels from normal and non-euthyroid patients illustrates the difficulty of collecting sufficient numbers of samples from patients covering the whole range of clinical interest while adhering to approved ethical and regulated procedures. This experience demonstrates that those leading similar projects should collaborate with both manufacturers and clinicians to allow the constitution of sample panels which could support the efforts of method standardization.

Another challenge is related to the transfer of new methods from basic research laboratories to clinical laboratories. This is especially the case for quantitative mass spectrometry, which is entering the field of Laboratory Medicine after having been a major tool of structural investigation in basic research, especially
regarding peptides and proteins. The use of such methods in routine laboratories requires standardized procedures for sample pre-treatment, analysis, data processing and quality assurance, as reviewed by the Working Group on Clinical Quantitative Mass Spectrometry Proteomics (WG-cMSP) [7].

When a range of methods are available, the question of equivalence of results becomes crucial for many measurands. In this regard, the implementation of assays giving metrological traceability of results is necessary, and acceptable limits for errors in the traceability chain have to be defined. The Working Group on Allowable Error for Traceable Results (WG-AETR) has proposed guidelines to evaluate acceptable limits and dependent on clinical requirements when establishing new assay methods [8].

The maintenance of traceability in Laboratory Medicine must be ensured by appropriate external quality assessment schemes and establishment of adequate networks. The 10-years’ experience of the IFCC External Quality Assessment Scheme for Reference Laboratories in Laboratory Medicine (RELA) clearly shows the positive impact of such schemes on the performance of participating laboratories and the coherence of reference laboratory networks, as reported by the Committee for Traceability in Laboratory Medicine (C-TLM) [9].

The optimal clinical use of laboratory test results necessitates the establishment of reference intervals adapted to age, sex and ethnicity, or decision limits defined according to clinical need and utility. Achievement of these goals requires the design of wide-scale studies performed in large and well-characterized populations, using well-controlled assay methods that provide results traceable to a reference measurement system. The statistical approaches used to define reference ranges and decision thresholds are of paramount importance and their scientific validity has to be clearly demonstrated. In this issue, two papers prepared by the Committee on Reference Intervals and Decision Limits (C-RIDL) propose: 1) a statistical methodology to allow transferability of reference intervals for different measurands from different countries using linear regression analysis [10]; 2) a protocol and standard operation procedures for conducting a multicenter study on reference values in several countries [11]. The merit of these two papers is to propose original approaches to solve the difficult problem of determining reference values for disparate populations. This task has not yet been completed, and the validation of the hypotheses raised is part of the C-RIDL current terms of reference. The publication of these manuscripts creates an opportunity for members of the international scientific community to discuss and refine the methodological approaches and concepts proposed. The wish of IFCC-SD is to enrich debate in this area and to promote the emergence of validated strategies in this important field.

When methods are eventually used in patients, the definition of analytical goals for the determination of a given measurand is a key step in the interpretation of results at the clinical level. Taking the example of HbA2, increased in patients with β-thalassemia, the Working Group on Standardization of HbA2 (WG-HbA2) has demonstrated that limits derived from a statistical approach
and from the opinion of clinical experts were significantly different [12]. This clearly showed that communication between specialists in Laboratory Medicine and clinicians is an essential step in the correct use of biological test results.

The use of biological diagnosis outside laboratories through point-of-care testing (POCT) is another challenging matter that has been addressed by the working group on glucose POCT (WG-GPOCT). The widespread use of glucose meters in various clinical settings other than critical care units generates difficulties related to the possible unsuitable use of the devices by health professionals. In this regard, quality specifications for glucose meters must be clearly defined and adapted to the clinical use in order to provide reliable results, traceable to the reference system. WG-GPOCT has especially focused on the characteristics of the performances and the limitations of glucose meters [13]. A special emphasis has been given to professionals’ education and to collaboration with manufacturers in order to improve performance and standardization of glucose strips. The broadened field of action of the WG has led the IFCC Executive Board to decide to close the WG and to create a new Task Force for POCT, with a larger range of activities, including education and communication.

To conclude, the experiences or opinions reported in this special issue illustrate the significant progress towards standardization of laboratory tests that has characterized IFCC-SD actions for many years. The clinical challenge is of such importance that the efforts made by the numerous professionals involved in these actions must be continued and encouraged. This remains one of SD’s major goals.

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References


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