

# Standardization of the measurements of creatinine and new markers of renal insufficiency: an update

F. Ceriotti

*Diagnostica e Ricerca San Raffaele, IRCCS H.S. Raffaele, Milano, Italia*

The publication, in 2003, of the National Kidney Foundation Practice Guidelines for Chronic Kidney Disease, recommending the use of the MDRD formula to estimate GFR put an enormous relevance on the need for standardization of serum creatinine measurement. In fact the eGFR is highly dependent on the accuracy of the creatinine method in use. Relevant progresses occurred in the last years and a reference measurement system for creatinine was clearly defined by the Joint Committee on Traceability in Laboratory Medicine (JCTLM). Nonetheless the work published by Delanghe in 2008 (but performed in autumn 2005) to compare the performances of several analytical systems throughout Europe, demonstrated a high dispersion of the results. The problems were of two types: incorrect calibration, not traceable to the IDMS reference measurement procedure and non specificity of the alkaline picrate based methods. Correct calibration is an important issue: still in 2007 only 22% of the laboratories in USA were using IDMS traceable calibrated systems. To allow traceable calibration for Jaffe methods the positive interference due to proteins was corrected by some manufacturers introducing a "compensation" factor. It is now clear from recent publications (Panteghini, Cobbaert, Schwartz) that this correction is able to improve the average performance, but cannot work on specific patients and, especially with children, can introduce an overcorrec-

tion. Only the enzymatic methods, being more precise and specific, allow really to obtain results traceable to the IDMS based primary reference measurement procedure. An IFCC Working Group on the standardization of GFR assessment is performing a study on the specificity of creatinine assays that will provide soon useful information on this matter. The availability of a frozen certified reference material from NIST (SRM 967), that proved to be commutable with a large number of field methods, gives to the manufacturers a substantial help to guarantee traceability. Moreover EQA providers are launching programs using materials with values assigned by the reference method, giving to the clinical laboratories a real accuracy reference.

Several authors are proposing cystatin C as an alternative to creatinine in formulae to estimate GFR. The main problem of this measurement is lack of a reference measurement system that makes difficult a wide application. The IFCC working group on cystatin C standardization has produced a candidate primary recombinant reference material. The pure cystatin C has been used to prepare a secondary reference preparation spiking with the primary preparation a stabilized serum matrix. The work is in progress, stability, value assignment and commutability trials are ongoing. The availability of such a preparation will provide a sound basis for standardization and will probably allow the use of cystatin C on a worldwide scale.