

Letter to the Editor

## Commutability of the ERM-DA470k Reference Material for two assays measuring serum albumin using immunochemical principles

Ilenia Infusino<sup>1,2,\*</sup>, Federica Braga<sup>1,2</sup>,  
Cristina Valente<sup>2</sup> and Mauro Panteghini<sup>1,2</sup>

<sup>1</sup> Centro Interdipartimentale per la Riferibilità Metrologica in Medicina di Laboratorio (CIRME), Università degli Studi, Milan, Italy

<sup>2</sup> Laboratorio Analisi Chimico-Cliniche, Azienda Ospedaliera 'Luigi Sacco', Milan, Italy

The standardization of measurements is a high-priority in Laboratory Medicine; its purpose being to achieve closer comparability of results for the same analyte obtained using different commercial systems (1). The promotion of result traceability to available higher-order reference measurement procedures and reference materials is the recommended approach (2). A major prerequisite for guaranteeing comparability of results among different methods is the availability of suitable reference materials, appropriately and thoroughly defined by a set of characteristics (3, 4). Reference materials can be used for calibration of routine methods. However, when reference materials are intended for direct value assignment to manufacturer's calibrators, they should be extensively investigated for commutability (5).

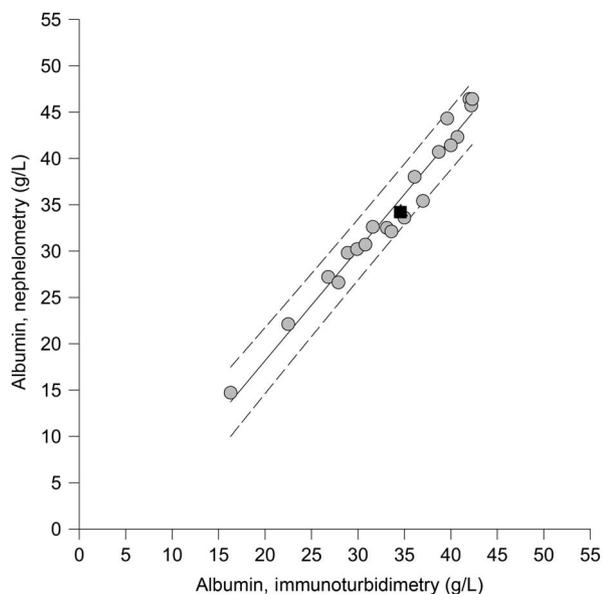
The main serum proteins are among the best standardized analytes in clinical laboratories. In 1993, the Bureau Communautaire de Reference of European Commission released the certified reference material (CRM) 470 (later renamed to ERM-DA470), developed in collaboration with the IFCC, resulting in a highly significant reduction of the among-laboratory variance for most proteins (6, 7). The ERM-DA470k/IFCC is a new serum protein reference material prepared to replace ERM-DA470, and to ensure continuity of the standardization of serum protein measurements (8, 9). With regard to serum albumin, the availability of these serum protein reference materials, both including albumin in the list of certified proteins, together with immunochemical methods based on turbidimetry-nephelometry principles, recognized as reference measurement procedures by the Joint Committee on Traceability in Laboratory Medicine (JCTLM),

provides the basis for maintaining assay traceability to the US National Reference Preparation no. 12-0575C, representing the highest level of the albumin traceability chain (10). However, we recently showed that some problems with accuracy of albumin measurements still persist, even if highly specific immunochemical methods are used (11).

To exclude that the lack of standardization of serum albumin measurements was, at least in part, due to some matrix effects of the new ERM-DA470k/IFCC employed in the accuracy studies, we tested its commutability using two immunochemical assays based on turbidimetric (Tina-quant Albumin Gen. 2, Roche Diagnostics, Basel, Switzerland) and nephelometric (A/S Albumin, Radim Diagnostics, Pomezia, Italy) approaches performed using the Cobas c501 platform (Roche Diagnostics) and on the Delta analyzer (Radim Diagnostics). A total of 20 leftover human serum samples (albumin concentrations, 16.3 g/L–42.3 g/L, Cobas c501 values) were collected, aliquoted, and stored at +4°C for  $\leq 24$  h before analyses. We measured albumin concentrations with the two systems in each biological sample and in the ERM-DA470k/IFCC [Institute for Reference Material and Measurements (IRMM), Geel, Belgium] in duplicate in two different runs on the same day. The reference material was reconstituted according to the procedure recommended by the IRMM, and the analyzers were handled according to the manufacturer's instructions. The recommended manufacturer's control materials were used to validate the analytical runs. The commutability of the reference material was estimated from Deming regression analysis of the measured results in native samples using the 95% prediction interval (95PI) and multiples of the standard error of regression ( $S_{y-x}$ ), in accordance with the CLSI C53-A standard (12).

The regression equation was as follows: nephelometry = 1.16 [95% confidence interval (CI): 1.06–1.26] turbidimetry – 4.6 g/L [95% CI: –7.7 g/L to –1.5 g/L], with  $r=0.984$ . As shown in Figure 1, the albumin results for reference material fall inside the 95PI based on the results for the native clinical samples. In addition, using an acceptance criterion for commutability of  $\pm 2$  times the experimental  $S_{y-x}$  ( $\pm 3.135$ ), the relative residual for the reference material (–2.107) was within the acceptable range. Both results confirmed the good commutability of the ERM-DA470k/IFCC between the two methods we evaluated. In agreement with our previous results (11), there was, however, an important bias in mean albumin concentrations for reference material obtained with both analytical systems (34.6 g/L for turbidimetry).

\*Corresponding author: Ilenia Infusino, Laboratorio Analisi Chimico-Cliniche, Ospedale Luigi Sacco, Via GB Grassi 74, 20157 Milan, Italy  
Phone: +39 02 3904 2290, Fax: +39 02 503 19835,  
E-mail: infusino.ilenia@hsacco.it  
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**Figure 1** Regression analysis (regression line – continuous and 95% prediction interval – dashed lines) to evaluate commutability of ERM-DA470k/IFCC (black square) between turbidimetry and nephelometry assays for serum albumin. Gray circles identify native serum samples.

etry and 34.2 g/L for nephelometry) when compared with the certified value ( $\pm$  uncertainty) ( $37.2 \text{ g/L} \pm 1.2 \text{ g/L}$ ).

In conclusion, our results demonstrate that the relationship between native clinical samples and the ERM-DA470k/IFCC is the same within stated statistical limits, showing that the newly available reference material for serum albumin is commutable between the evaluated immunochemical assays and can be used as a basis to maintain their traceability to higher-order references. However, some inconsistency in the assignment of values to the working calibrators of commercial assays used in this study is likely and should be verified by manufacturers.

### Conflict of interest statement

**Authors' conflict of interest disclosure:** The authors stated that there are no conflicts of interest regarding the publication of this article.

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