Data Supplement:

to

COMPARISON OF PROCEDURES USED TO EVALUATE LABORATORY PERFORMANCE IN EXTERNAL QUALITY ASSESSMENT SCHEMES FOR LEAD IN BLOOD AND ALUMINUM IN SERUM DEMONSTRATES THE NEED FOR COMMON QUALITY SPECIFICATIONS

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Results

Aluminum in serum and plasma

The performance limits used by European EQASs for monitoring measurement of aluminum in serum at 100 and 200 µg/L are as follows: 16.5 and 34.0 µg/L (Belgium, France and United Kingdom), 23.4 and 41.4 µg/L (Germany), 10.4 and 18.5 µg/L (Italy). Aluminum is not included in the schemes from Denmark, or Spain and performance targets are not set by the organisers of the Dutch scheme. As with blood lead the variation among accepted performance levels is more than one hundred percent.

Typical between-laboratory SDs associated with these concentrations of aluminum are given in Table 5. The concentration ranges monitored by the Belgian scheme did

not include samples at 200 µg/L. Again, as with blood lead there are large variations in performance evident among the schemes. Consequently, the sensitivity for detection of poor performance will be similarly varied.

Table 6 shows the serum aluminum results obtained in different exercises carried out in the Italian and UK schemes and used for the comparison of scoring systems. The differences between the distribution of values observed in the Italian and UK schemes is likely to be a consequence of the greater number of specialised laboratories that participate in the UK Scheme (8). The table also shows the number of results that were outside the limits agreed at the Second Network Meeting (Rome, November 2000) as being indicative of minimum acceptable analytical performance *i.e*: 80 - 120 at 100 µg/L, 160 – 240 at 200 µg/L.

The data sets were examined as for the blood lead results to determine how many results would be reported as unacceptable according to the scheme criteria above. The number and percentage of unacceptable results is shown in Table 6.

Figure 3 shows, as for blood lead, the individual results provided by participants in the Italian scheme for sample C compared to the superimposed acceptance limits used in the Italian and other European EQA s. It can be observed that the judgement of individual result in different EQASs varies even more than for blood lead results.

Figure 4 shows the z-scores based on the between-laboratories SDs given in Table 5, determined for the results observed for sample C. The number and percentage of results scoring >3 are given in Table 7.

Goals based on current state of the art

a. As demonstrated by data from EQASs. The data in Table 5 are very variable (4.3-20.0% at 100 μg/L) among different schemes implying that there is no specific state of the art.

b. Other data. Coefficients of variation associated with the UK and German reference laboratories are around 9.0% and 7.8% at 40 and 100 μg/L, respectively.

Performance goals set by

a. Regulatory bodies

There are no legal requirements relating to the measurement of aluminum in serum.

b. Organisers of EQASs

Goals set by the organisers of the European schemes are indicated in Table 5. As previously noted, some are based only on analytical grounds while others attempt to account also for the clinical usefulness of the test (13, 14). These goals correspond to CVs of 10.4% to 23.4%, at 100 μg/L.

Published professional recommendations

As for lead, to our knowledge there are no published recommendations from expert bodies, groups or individuals.

Effect of analytical performance on clinical decisions

a. Data based on biological variation. In a study where serum aluminum concentrations were measured in subjects with normal renal function at bi-weekly intervals for 30 weeks, the sample-to-sample variation was less than 5 μg/L (25).

b. Data based on clinicians' opinions. In 1997 the serum aluminum acceptance limits used for the UK EQAS were revised when it was evident that those originally set were no longer appropriate to the improved performance of the participants. A group of renal physicians were asked to comment on the new limits (given in Table 5) and they agreed that these targets matched their clinical expectations (Goldie, personal communication to AT). We are unaware of any published opinions relating to performance criteria for occupational and environmental medicine.

Effect of analytical performance on clinical outcomes in specific clinical settings

On the basis of the minimum serum aluminum concentration at which symptoms first appear, from rates of increase following exposure to the metal, and from proposals for frequency of patient monitoring Taylor et al. (13) suggested analytical methods should at least meet the following criteria: bias within 13.5 μg/L, within-laboratory between-batch CV of less than 10% at 100 μg/L and a detection limit of less than 10 μg/L. These criteria refer to patients with chronic renal failure but since then interest has spread to other situations of possible exposure with the requirement for more stringent analytical procedures at much lower concentrations.

Proposed standard of performance for the measurement of aluminum in serum

We propose that, for this assay a suitable quality specification for TEa would be ± 5 μg/L or ± 20%, whichever the greater. This is equivalent to a TEa of ±5 μg/L up to 25 μg/L and a variation of ±20% for higher concentrations.

Table 5. Typical between-laboratory SDs and CVs calculated from results reported by participants in the European EQASs for measurements of aluminum in serum. *N* = approximate number of participants

	Aluminum in serum, µg/L	
Target concentration	**100**	**200**
Country (N)	**SD (CV%)**	**SD (CV%)**
Belgium (18)	14.1 (14.1)	--
France (60)	11.9 (11.9)	26.6 (13.3)
Germany (31)	20.0 (20.0)	20.6 (10.3)
Italy (47)	19.6 (19.6)	29.8 (14.9)
The Netherlands (24)	4.3 (4.3)	14.2 (7.1)
United Kingdom (65)	4.6 (4.6)	6.7 (3.4)

Table 6 Number and percentage of results that would be viewed as consistent with poor performance according to the performance limits used by the European EQASs for aluminum in serum

Sample code	**632**	**C**
Target concentration, µg/L	**108**	**151**
N	**61**	**108**
Range of results	22-162	69-308
Country	**N (%)**	**N (%)**
Belgium, France, United Kingdom	12 (19.7)	29 (26.9)
Germany	6 (9.8)	25 (23.1)
Italy	23 (37.7)	51 (47.2)
European Network “agreed limits”	9 (14.8)	28 (25.9)

Table 7 Number and percentage of results that would have a z-score >3 if typical between laboratory SDs as observed in each scheme (Table 5) were used to determine z-scores for determinations of aluminum in serum.

Target concentration, µg/L	**108**	**151**
Country	**N (%)**	**N (%)**
Belgium	2 (3.3)	----
France	3 (4.9)	9 (8.3)
Germany	2 (3.3)	9 (8.3)
Italy	2 (3.3)	6 (5.6)
The Netherlands	14 (23.0)	29 (26.9)
United Kingdom	15 (24.6)	41 (38.0)

Figure captions (Supplement)

Fig. 3 Distribution of the laboratories results for the determination of aluminum in serum in a sample with target value of 151 µg/L plotted against the acceptance limits of each scheme for that concentration (BE: Belgium; DE: Germany; EN: European Network; FR: France; IT: Italy; UK: United Kingdom).

Fig. 4 Distributions of the z-scores, determined on the basis of the SDs observed in each scheme, associated with results of the determination of aluminum in serum in a sample with target concentration of 151 µg/L (DE: Germany; FR: France; IT: Italy; NL: The Netherlands; UK: United Kingdom).