Fresenius Z Anal Chem (1988) 332:718–721

Fresenius Zeitschrift für Analytische Chemie

Quality assurance, interlaboratory comparisons

Meeting the need for reference measurements

P. De Bièvre[1], J. Savory[2], A. Lamberty[1], and G. Savory[2]

[1] Central Bureau for Nuclear Measurements, Commission of the European Communities – JRC, B-2440 Geel, Belgium
[2] Departments of Pathology and Biochemistry, University of Virginia Medical Center, Charlottesville, VA, USA

Wie der Notwendigkeit von Referenzmessungen entsprochen werden kann

Summary. Reference materials do fulfil a very useful function in that they provide means to check, verify and calibrate measurement procedures and instrumentation. However, the material is often "idealized" compared to "real life" samples: it is either (very) pure or does not correspond in concentration level or matrix to the "real life" case. It is shown how this situation could be remedied if "real life" samples with carefully assessed "reference values" could be made available regularly as unknowns to measurement laboratories. Comparison of the latter's measurements with the "reference values" then would provide a picture of the real performance of the particular measurement community in general and of each participating laboratory in particular. The opinion is expressed that isotope-specific methods have now matured to the stage that, if they are correctly applied under rigorous control and based on highly skilled expertise, they can provide such "reference values" against which laboratories can then evaluate their routine performance in regular Interlaboratory Measurement Evaluation Programmes (IMEPs).

1 Introduction

The role of reference materials (RMs) in measurement science is well established: RMs provide the means to check, verify and calibrate measurement procedures and instrumentation. The essence of their function is that they carry a certified value with uncertainty of a given quantity (not "amount" but "Grösse", "grootheid", "grandeur") in a given material.

The role of the RM is undisputed and, in fact, the only major problem is that there are insufficient reference materials available.

There are, however, limitations to the usefulness of RMs and they cannot help to solve all problems in measurements. In fields where regular measurements on "real life" samples are important (clinical, life-essential, toxic, quality-limiting impurities, etc.), RMs are not always successful in identifying problems for the following reasons:

a) their "best" value is known (within a given uncertainty range), so users sometimes give special care to obtain this certified value; they tend to work "towards" this value,

b) the material is often "idealized" compared to "real life" samples: it is (very) pure or does not correspond in concentration level and/or unknown element and/or matrix to the "real life" case.

This fact is illustrated by one of the Central Bureau for Nuclear Measurements' (CBNM) interlaboratory programmes to assess the true capability of the nuclear measurement community to assay uranium (see Fig. 1) [1, 2]. As can be seen, several of the laboratories experienced some difficulty with the measurement.

The question now arises how to help laboratories such as those in Fig. 1 resolve their problems. Obviously, RMs do not help as all of the laboratories in Fig. 1 had used existing (and excellent!) RMs to the best of their ability.

The help which CBNM and National Bureau of Standards (NBS) offered in a cooperative effort, is illustrated in Fig. 2: a "reference value" or "reference measurement" was provided, having been obtained using the following information:

1) using all of our present knowledge of chemistry and physics of the particular measurement process,

2) performing a complete ("orthodox") uncertainty assessment,

3) refining the measurement until its uncertainty was smaller than the interlaboratory spread expected,

4) using an isotope-specific method [isotope dilution mass spectrometry (IDMS) rather than an element-specific method (classical analytical chemistry)].

Isotope-specific methods have now matured to a stage that they can provide very good values for element amounts or concentrations because of their specificity: they use isotopes of the element under investigation and isotopes are excellent "representatives" of the elements.

The reason why IDMS has proved to be particularly interesting, is that it directly relates an unknown number N_X of atoms of one isotope in an unknown sample X to a known number N_Y of atoms of another isotope in a known sample Y (the added "spike") through a direct measurement of their ratio R_B by means of a suitable instrument (the mass spectrometer):

$$\frac{N_X}{N_Y} = R_B \,^{1}.$$

[1] The corrections for the presence of other isotopes in both X and Y are easy and do not detract from the above statement:

$$\frac{N_X}{N_Y} = \frac{R_Y - R_B}{R_B - R_X} \cdot \frac{\Sigma R_{iX}}{\Sigma R_{iY}}$$

Offprint requests to: P. De Bièvre

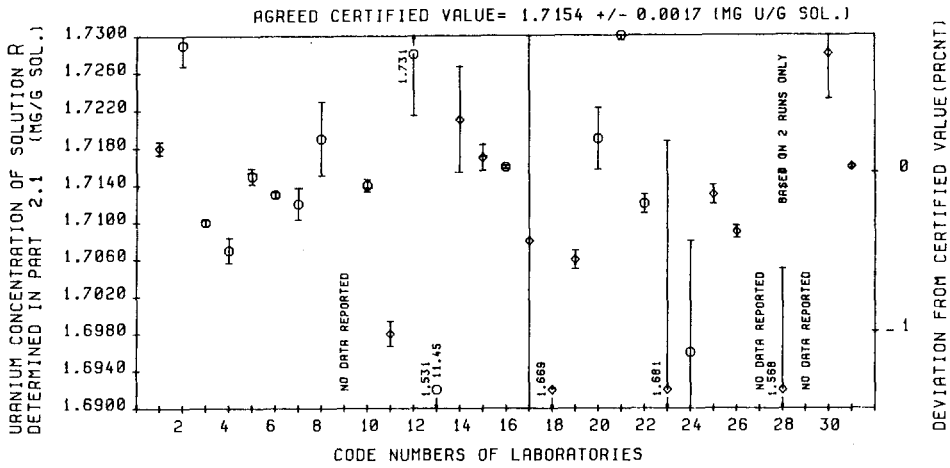

Fig. 1
Interlaboratory measurement evaluation of assay measurements of uranium concentration [1, 2]

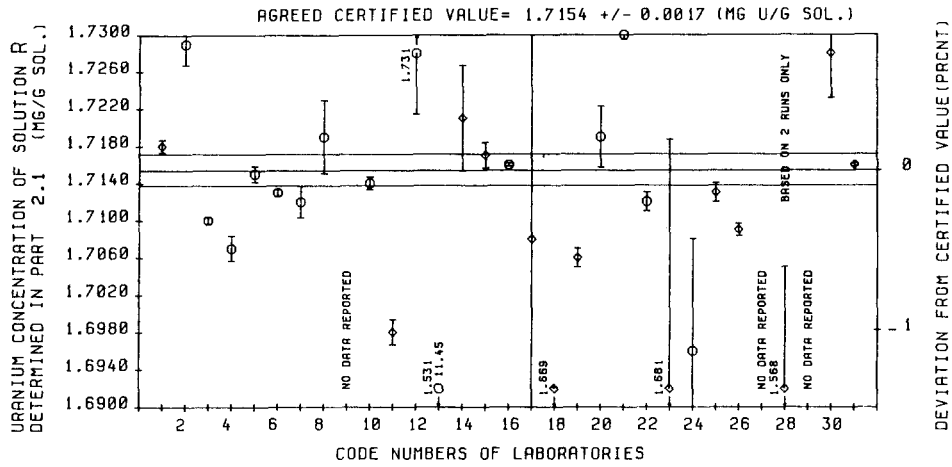

Fig. 2
Same as Fig. 1 but equipped with a "reference value" established by an isotope-specific technique (IDMS) [1, 2]

Table 1. Results of Li interlaboratory measurement evaluation (Li in mmol · l^{-1})

Lab.	Method	I	II	III	IV	Aqueous
CBNM	Isotope dilution mass spectrometry	0.0193 ± 0.0011	0.621 ± 0.017	1.205 ± 0.018	2.195 ± 0.022	1.514 ± 0.020
A	Flame photometry[a]	0.08 0.08	0.69 0.69	1.30 1.31	2.40 2.41	1.5 1.5
B	Ion selective electrode	0.10 0.08	0.62 0.62	1.21 1.22	2.17 2.17	[b]
C	Atomic absorption spectrometry	0.1 0.1	0.7 0.6	1.3 1.2	2.3 2.3	1.0 1.1
D	Atomic emission spectrometry	0.03 0.03	0.61 0.60	1.16 1.19	2.17 2.16	1.42 1.38
E	Flame photometry	0.07 0.06	0.65 0.65	1.25 1.25	2.26 2.26	1.41 1.42
F	Flame photometry[a]	0.05 0.06	0.65 0.64	1.23 1.25	2.20 2.21	1.36 1.35

[a] Same laboratory results obtained on separate days
[b] The aqueous specimen was unsuitable for use with a lithium ion-selective electrode

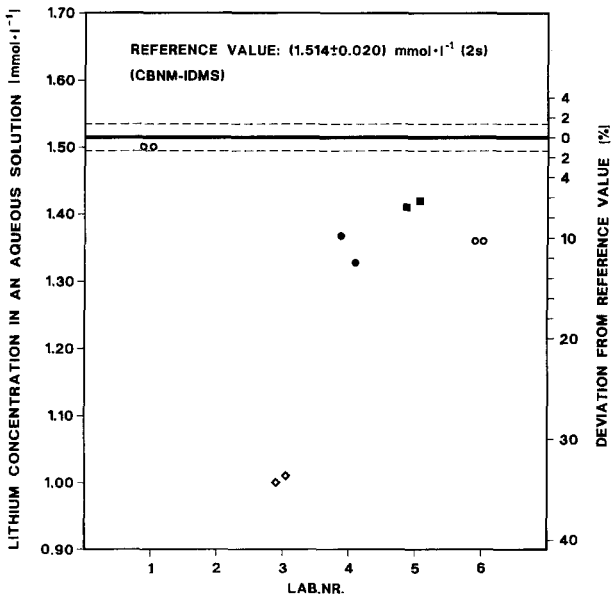

Fig. 3. Lithium concentrations in an aqueous solution

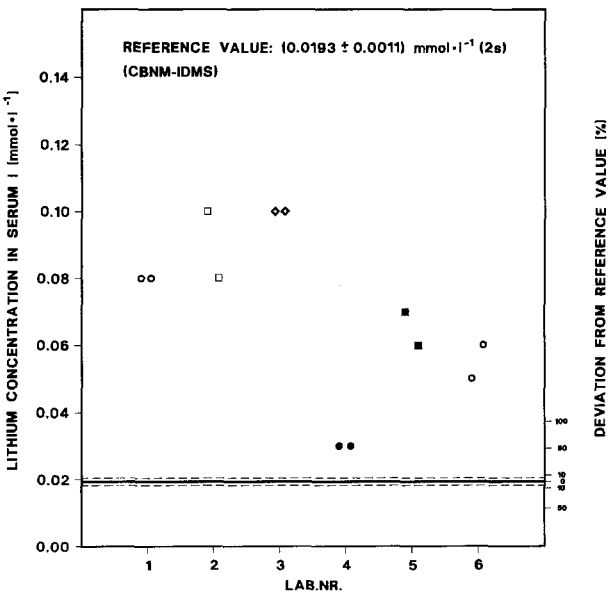

Fig. 4. Lithium concentrations in Serum I

Note that this measurement is directly performed in ratios of amounts, i.e. fractions of our basic SI unit for amount of substance: the mol (an amount of $6.023137 \cdot 10^{23}$ atoms). Thus a "Reference Value" was provided to the measurement laboratories in Fig. 2.

We recently were made aware by a request for "Reference Values" for trace elements in biological materials from the Clinical Chemistry Division to the Inorganic Chemistry Division within the International Union of Pure and Applied Chemistry (IUPAC) [3] and confirmed at the IUPAC General Assembly 1985 in Lyon. We tested the same approach and presented the results as a "feasibility experiment" to the IUPAC Inorganic and Clinical Chemistry Divisions at their General Assembly 1987 in Boston. The approach was warmly received and plans for expansion of the concept approved. A budget has been allocated for work meetings in 1988 and 1989 in order to perform similar work and prepare those results for the IUPAC 1989 General Assembly in Lund, Sweden.

2 Experimental

2.1 Preparation of four serum pools and an aqueous solution containing varying concentrations of lithium

A serum base was obtained commercially and was certified to be free of infectious agents (Pel-Freez Clinical Systems, Brown Deer, WI, USA). Four pools were prepared at the University of Virginia, Charlottesville, by spiking the serum with various amounts of lithium carbonate with approximate lithium concentrations of 0, 0.6, 1.2 and 2.2 mmol/l together with an aqueous solution of 1.5 mmol/l of lithium.

2.2 Determination of the reference values by isotope dilution mass spectrometry (IDMS)

From each of the four serum pools and from the aqueous solution, 3 different samples from 2 different tubes were each spiked with about 5 µmol ^{6}Li in the form of ^{6}Li enriched Li_2CO_3. After a $HClO_4/HNO_3$ digestion of the matrix, lithium was separated on a cation exchange column, eluted with HCl and measured on an isotope mass spectrometer. Mass spectrometric measurements were corrected for mass fractionation using Isotopic Reference Materials CBNM IRM-015 and CBNM IRM-016.

The sample preparation method was tested by assaying NBS-SRM 909.

The ^{6}Li enriched spike was characterized by reverse IDMS using NBS-SRM 924 Li_2CO_3 certified for chemical purity.

3 Distribution to laboratories

Five competent laboratories were selected and asked to perform a measurement of the Li content of the "blind" samples in duplicate. The list of methods used by the participants can be found in Table 1.

4 Results

The results of this Interlaboratory Measurement Evaluation Programme (IMEP) are shown in Table 1 and in Figs. 3 through 7.

5 Conclusions

1. The work model appears to work as in previous application fields (nuclear) and should be successful for identifying measurement problems in other fields.

2. A distinct advantage over other means of assessing accuracy was that the specimens used were "real life" samples. Besides no reconstitution was necessary, hence any dilutional errors due to reconstitution of a lyophilized material were eliminated.

3. Some methods could not distinguish between "non-toxic" and "toxic" concentration levels.

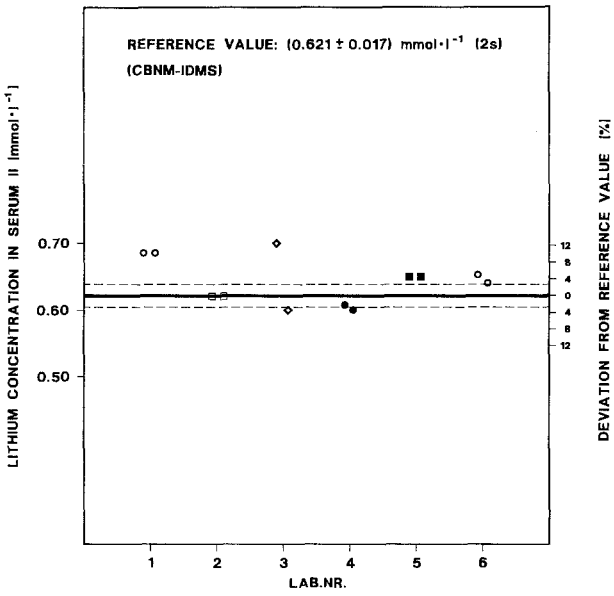

Fig. 5. Lithium concentrations in Serum II

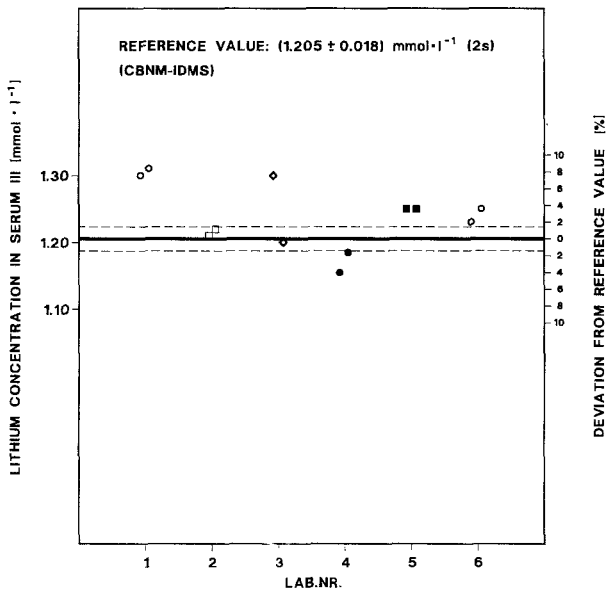

Fig. 6. Lithium concentrations in Serum III

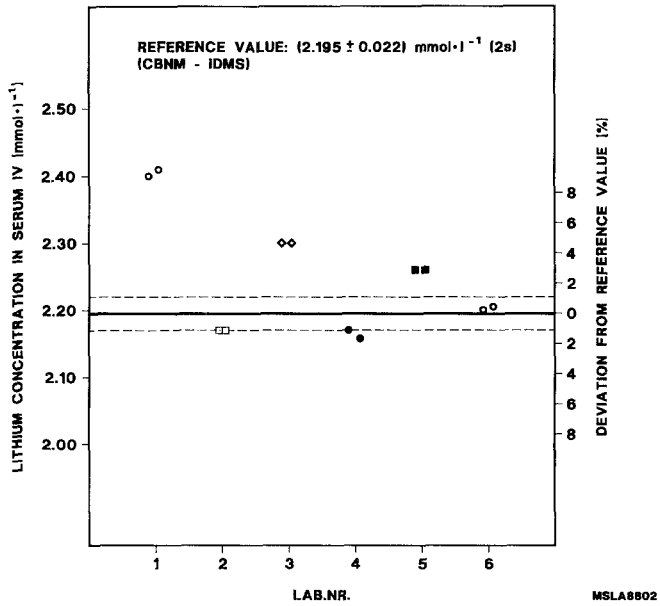

Fig. 7. Lithium concentrations in Serum IV

4. The question for a "reference" could be answered by integrating in an interlaboratory survey the use of an isotope-specific method to establish "reference" values.

5. The main result from this limited experiment is probably to create "awareness" about possible problems amongst measurement scientists. Hence the approach demonstrated could provide a tool or incentive to work on the problem situation.

6. The approach puts a severe burden on "standards laboratories" to carry out the tedious work needed to substantiate the "reference values" but this is in fact what they have been created for!

References

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Received July 1, 1988