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The International Measurement Evaluation Programme

IMEP-17
Trace and Minor Constituents in Human Serum
EUR 20694 EN
Report to Participants

Part 2: Methodology and quality specifications

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TABLE OF CONTENTS

1. INTRODUCTION 3

2. COMMUTABILITY OF THE TEST MATERIALS 3

2.1. DEFINITIONS 3
2.2. INVESTIGATING THE COMMUTABILITY 3
2.2.1. Indications of the commutability of the IMEP-17 materials 4

3. QUALITY SPECIFICATIONS 4

3.1. 'FITNESS-FOR-PURPOSE' 4
3.2. ANALYTICAL QUALITY SPECIFICATIONS 6
3.2.1. Quality specifications for routine clinical measurements 6
3.2.2. Quality specifications for reference measurements 7

4. PERFORMANCE EVALUATION OF MEASUREMENT PROCEDURES 8

4.1. ACCURACY (TRUENESS AND PRECISION) 8
4.2. ESTIMATES OF THE BIAS FOR PROCEDURES USED BY PARTICIPANTS IN IMEP-17 9

5. RESULTS AND DISCUSSION 9

5.1. GRAPHICAL DISPLAY OF RESULTS 9
5.1.1. Explanatory remarks 9
5.1.2. The general IMEP graph 9
5.1.3. Graphs that include analytical quality specifications 9
5.1.4. Results arranged according to method groups 10
5.1.5. Overall results for specific procedures – 'bias plots' 10
5.1.6. Youden graphs 11

6. SUPPLEMENTARY INFORMATION 12

ACKNOWLEDGEMENTS 12

ABBREVIATIONS 12

ANNEX 1 - GRAPHICAL PRESENTATION 13

ANNEX 2 - FORMS, LETTERS AND DOCUMENTS 41

ANNEX 3 - REFERENCES 43

1. Introduction

Part 1 of the 'Report to participants' [1] described the background and objectives of the interlaboratory comparison IMEP-17,* organised by the IRMM in collaboration with the C-AQ IFCC and members of EQALM. Part 1 also summarised information about the production and characterisation of the two serum materials that were used [2]. The participants' results from measurements of nineteen components in Material 1 and lithium in Material 2 were displayed.

This report (Part 2) presents the participants' results for ten components in Material 2 (modified serum). Laboratory performance is displayed with Youden graphs. Special attention is paid to the performance of individual measurement procedures for creatinine, sodium and potassium. Analytical quality specifications, i.e. performance goals for routine analytical work is discussed and compared with the results in IMEP-17. The properties of the test materials are discussed from the point of view of commutability.

The combined report (Part 1 + Part 2) is available on the Internet [3].

2. Commutability of the test materials

2.1. Definitions

The 'commutability of a material' is a key term when establishing and demonstrating metrological traceability of results. A calibrator/control material is commutable if the ratio between the results of two procedures is the same for the calibrator/control material as for routine (patient) samples [4].† The standard EN ISO 17511 [5] specifies how to assure the traceability of values assigned to calibrators and control materials intended to establish or verify trueness of measurements. The calibrators and control materials are those provided by the manufacturers as part of, or to be used together with, in vitro diagnostic medical devices [6]. EQA samples, with proven commutability, whose values have been assigned by means of internationally agreed reference measurement systems or internationally agreed conventional reference measurement systems fall within the scope of EN ISO 17511.

2.2. Investigating the commutability

To ensure the validity of a metrological traceability chain, manufacturers should investigate and describe the commutability of their materials, and limits of applicability [7].

When preparing the material, an analyte is sometimes removed or, as for the IMEP-17 Material 2, added. The effect of such modifications must be validated. Spiking can introduce a heterogeneity of the analyte in the calibrator (isoforms, derivatives) making physico-chemical description difficult, e.g. in case of enzymes, antibodies, and glycoproteins. This, in turn, can affect measurement procedures having different specificity and selectivity towards the analyte in a given calibrator.

* A list of abbreviations can be found at the end of the document.

† The term 'matrix effect' is sometimes erroneously used for the lack of commutability due to a denatured analyte or an added non-genuine component meant to simulate the analyte [See Clause 3.15 in Ref. 5].

The commutability can be checked by measuring a large number (>20) of patient samples with a routine and with a reference measurement procedure [8]. If the mathematical relationship between the results of the reference measurement procedure, *x*, and the results of the routine measurement procedure, *y*, for the human samples is not significantly different from that found for the calibrator/control material, then commutability of the latter has been demonstrated. This can be demonstrated in an *x*-*y* chart if the spread of the points, (*x*, *y*), around the regression line and/or its offset are not unacceptable. A reason for non-commutability can be a difference in analytical specificity between the two measurement procedures.

A prerequisite to this approach is that both measurement procedures actually measure the same quantity. This is expected to be the case for the majority of the procedures used by the participants in IMEP-17. Creatinine, is one exception where problems with the interpretation of results from a commutability study can arise. This is because of the various approaches to measuring and reporting results for this component [1]. Another exception concerns amylase and γ-GT where the measurands are strictly defined by the applied procedure.

2.2.1. Indications of the commutability of the IMEP-17 materials

The production of the two human sera was described in detail in Part 1 of this report [1]. No formal commutability study was conducted. There are, however, good reasons to believe that Material 1 is fully commutable with normal patient samples. This material, a pool of serum from healthy donors, was sterile-filtered, transferred to inert vials, and freshly frozen without any stabilizers added.

Material 2 was prepared in a similar way. In the spiking, 'pro analysi' chemicals and pure enzyme preparations were used to achieve higher but still clinically relevant concentrations. The added γ-GT was of non-human origin,[*] and this, or other foreign substances introduced via the spiking of γ-GT, may cause interferences in certain measuring systems. However, the selected preparation had the highest available purity and the choice was approved by the enzymologists consulted. The γ-GT method is robust and insensitive to possible differences between isoenzymes of γ-GT and in fact to very small differences between γ-GTs of different animal origin [9]. A more evident problem is the higher than normal pH of Material 2 (7,77), which has an effect of +9% on the albumin result in Vitros' measuring systems [1, 10].

A strong indication of the commutability of the materials is that results for the same measurand obtained by different routine procedures agree within the uncertainties. This is demonstrated by comparing the results for Material 1, obtained by a number of specific procedures, for Na and K (Sections 4.2 and 5.1.5).

3. Quality specifications

3.1. 'Fitness-for-purpose'

The measurement results produced by the clinical laboratory should be 'fit for their intended use'. An unnecessary high quality often leads to higher costs. On the other hand, a too low

[*] γ-GT, EC number 2.3.2.2 from bovine kidney, 500 U (25 °C), cat. No., G4756 (grade 2 purity; 26 U/mg) from Sigma-Aldrich.

quality may lead to repeated analyses, an increased risk for wrong diagnoses and/or unnecessary treatments.

Most EQA schemes and other interlaboratory comparisons assess only part of the work carried out by the laboratory for a specific application. In the case of IMEP-17, it is the 'analytical phase' (Figure 1). The general graphs presented in Annex 1 and in Part 1 of the report [1] illustrate the quality of the laboratories' instrument calibration and the performance of the instruments in routine use. The errors stemming from sampling, and from sample preparation outside the instrument, are not covered [11].* The effect of those errors can very well contribute much more to the combined ('total') uncertainty of the measurement result than errors in the analytical phase.

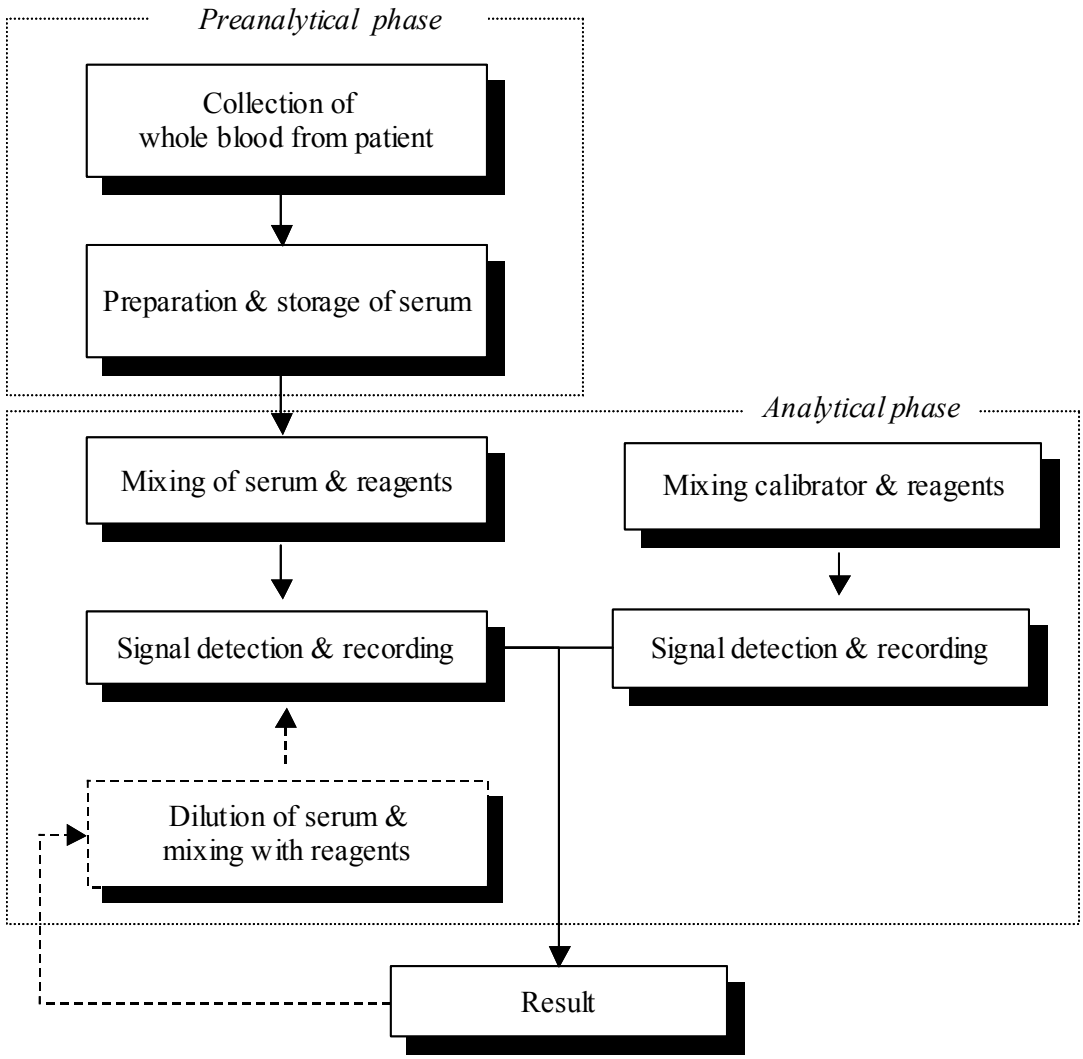


Figure 1. Overview of steps included in many general clinical chemistry measurements [12].† The technical work is often divided into a pre-analytical phase and an analytical phase. In IMEP-17, the results are used to assess the quality of the work covered by the analytical phase.

* Up to now, no quality specifications for extra-analytical steps have been set, except for results from the Q-probes and Q-tracks organized by the College of American Pathologists [11].

† All operations in Figure 1 can be summarised with the term 'measurement' since it describes work aiming at determining the value of a quantity [12].

3.2. Analytical quality specifications

3.2.1. Quality specifications for routine clinical measurements

Analytical quality specifications are set differently in different countries, which means that the goal for laboratory performance for the same component can vary. This is not satisfactory and strategies to set global quality specifications were outlined in 1999 [13]. Furthermore, the specifications are often classified as 'minimum', 'desirable'* or 'optimum' by taking into account the actual performance of methods and instruments [14].

The differences are exemplified using quality specifications for total concentration of calcium in serum from four sources (Table 1). The first specification is taken from Ricós et al. [15] and amounts to ±2,4%. It is expressed by the 'desirable total error' (TE) based on data for biological variation and performance goals for precision (I) and bias (B). It is calculated as

$$TE = 1{,}65 \cdot I + B \text{ where } I < 0{,}5 \cdot CV_W \text{ and } B < 0{,}25\sqrt{CV_W{}^2 + CV_b{}^2},$$

and where CV_w is the intra-individual biological variation (1,9%) and CV_b is the inter-individual biological variation (2,8%).

The second specification (±3,0%), currently under revision, is that used by the Finnish EQA scheme organiser Labquality. The value dates back to 1995 where an expert group re-assessed and defined values for TE for common clinical components [16]. The principles in setting these EQA performance limits complied with current findings in biological variation, overall long-term precision of the laboratories, existing reference intervals and/or clinical needs.

The third specification is based on the CLIA criteria for 'acceptable performance' in EQA [17]. The CLIA '88 regulations are based on the test complexity or the difficulty to perform the test. The acceptable performance for total S-Ca is defined as "target value ±1 mg/dL". This corresponds to ±11% when S-Ca is equal 2,33 mmol/L, which was equal to the level of Ca in IMEP-17 Material 1. The quality goal is similar in size to the fourth specification, taken from a German guideline and described as maximum allowed deviation for a single result [18]. The criteria underlying the third and forth specification have more to do with the current state of the art rather than with 'desirable' analytical quality. This difference is important.

Yet another option would be to use a target uncertainty as a quality goal [19] expressed, e.g. as a 'maximum allowed combined standard uncertainty, u_c'.

Table 1. Analytical quality specifications (quality goals) for total S-Ca from four sources.

Source and reference	Quality specification (+%)
Ricós et al. [15]	2,4
Labquality [16]	3,0
CLIA '88 [17]	11
German Bundesärzkammer [18]	11

* In some documents, 'desirable' is replaced with 'allowable'.

Table 2. Analytical quality specifications for measurement of the components in IMEP-17. The Specifications are expressed as desirable total error (TE) in % for a confidence level of 95% (P<0,05) and based on biological variation [15]. Data for Li is from Reference 20. Also given is the range of results obtained by the majority (~95%) for single measurements on Material 1 and the relative uncertainty for the certified values for Material 1 and for Li in Material 2 [2].

Component	Quality specification for routine laboratories (±TE%)	Observed approximate range for majority of participants' results relative to the certified value (±%)	Uncertainty for certified values in IMEP-17 U_{rel}, k=2 (%)
Ca	2,4	5	0,30
Cl	1,5	5	1,1
Cu	7,7	20	0,57
Fe	30,7	-15 to +5	2,8
K	5,8	4	0,56
Li	10,1	10	0,82
Mg	4,8	10	0,69
Na	0,9	2	0,68
Se	14,5	-40 to +10	3,4
Zn	11,0	20	2,1
Glucose	7,9	10	0,75
Cholesterol	9,0	5	0,41
Creatinine	6,9	-10 to +15	0,76
Urea	15,7	10	1,0
Uric acid	11,9	3	1,8
Thyroxine (T4)	8,3	-15 to +8	1,3
Albumin	3,9	10	6,5
IgG	8,0	10	4,6
Amylase	15,7	-25 to +200	4,6
γ-GT	22,2	-30 to +10	2,7

3.2.2. Quality specifications for reference measurements

Analytical quality specifications for measurements based on reference measurement procedures are discussed in a paper by Thienpont et al. [21].

To be fit for purpose, the uncertainty of a reference measurement procedure value must be significantly smaller (preferably by a factor of 5 to 10) than the expected range of the participants' results (routine level). As can be seen from Table 2, the certified values established for IMEP-17, meet, in most cases this criterion. Albumin, Cl, Na, uric acid and IgG are, however, exceptions. This is further discussed below with the intention to illustrate the limitations with some of the values serving as reference in IMEP-17. For more information, please consult the certification report [2, 3].

The uncertainty of the certified value for albumin in CRM-470 is already relatively large (~2%) and contributes significantly to the uncertainty when this CRM is used to determine albumin in the IMEP-17 Material 1. It is the experience of the reference measurement laboratory that the combined uncertainty ranges between 2 % and 7 % depending on the albumin concentration and the formation of more or less contrasted precipitation rings for the specific material of investigation [22].

For both Na and Cl, the certified values are based on an average of results from two reference laboratories, using procedures with very different metrological properties and with uncertainties that differ by a factor of 2-3 [2]. By using the value for the procedure having higher metrological qualities (gravimetry and IDMS respectively), the situation can be improved.

The uncertainty of the certified value for amylase is only about 1/3 of the desirable total error, and for uric acid, the difference between the range of participants' results and the uncertainty of the certified value is less than a factor 2. This can possibly be explained by that there is still little experience on how to identify and control all sources of error in the reference measurement procedures for these components.

4. Performance evaluation of measurement procedures

4.1. Accuracy (trueness and precision)

To evaluate the overall performance of a specific measurement procedure, protocols in ISO 5725 can be followed [23]. This standard describes performance in terms of 'accuracy', i.e. 'trueness' and 'precision'. The trueness of a measurement procedure is of interest when it is possible to have an accepted (analytical) reference value for the quantity being measured, e.g. via suitable reference materials or reference measurement procedures.

The trueness of the measurement procedure is investigated by comparing the accepted reference value with the level of the results given by the procedure. Trueness is normally expressed in terms of 'bias', i.e. the 'systematic error'. The bias $\hat{\delta}$ is calculated as

$$\hat{\delta} = \bar{\bar{y}} - \mu$$

where $\bar{\bar{y}}$ is the grand mean of the results from p laboratories using the procedure, and μ is the accepted reference value. The mean $\bar{\bar{y}}$ is calculated according to

$$\bar{\bar{y}} = \frac{1}{p}\sum_{i=1}^{p}\bar{y}_i \, .$$

The bias of results from an individual laboratory (laboratory bias, $\hat{\Delta}$) that works according to a specific measurement procedure can be calculated from the difference between the average of the laboratory's results $\bar{y}_w$ and the accepted reference value μ according to: $\hat{\Delta} = \bar{y}_w - \mu$.

It is, however, not the intention of IMEP-17 to provide a basis for calculating individual laboratory bias although some participants have multiple results. Those interested are recommended to consult Part 4 of ISO 5725 [23] for a detailed discussion on the limitations with such calculations.

4.2. Estimates of the bias for procedures used by participants in IMEP-17

The certified values for the components in IMEP-17 [2] represent suitable references that can be used to estimate the bias of specific procedures that the participants used. In doing so, we use all the available information. The participants could perform duplicate analyses during five consecutive days, i.e. a maximum of ten results per laboratory for a given component in each material [1].

The participants measurement procedures for three components, creatinine, Na and K, have been examined in detail. Some restrictions were necessary: Only procedures applied by at least ten laboratories were selected. An additional selection criterion was that the report form did not indicate modifications to the manufacturer's procedure. Further details are given in Section 5.1.5.

5. Results and discussion

5.1. Graphical display of results

5.1.1. Explanatory remarks

The measurands, i.e. the quantities subject to measurement [24] are the total amount-of-substance concentration, mass concentration or catalytic activity concentration of the components in the respective serum material. Results are presented in the units that the Finnish EQA organisation Labquality uses in its clinical chemistry surveys [25].

5.1.2. The general IMEP graph

Figure 5 in Part 1 of the report [1] was an attempt to exemplify how results are displayed in IMEP. For each set of data, the participants' results are plotted in ascending order against the certified value. The scale of the graph, from the certified value, is chosen for convenience. No results are excluded but those that are off-scale are presented in textboxes on the graphs. Unless otherwise stated, each participant's data is the result of a single measurement. This is because the main objective of IMEP-17 is to show how results obtained under routine conditions agree on an international level. General graphs have been constructed for Cu, K, Mg, Zn, glucose, creatinine, urea, uric acid, amylase and γ-GT (Annex 1).

5.1.3. Graphs that include analytical quality specifications

Annex 1 contains graphs covering results for Ca, K, Na, glucose or cholesterol reported by two or more countries (regional display). These five graphs also include an analytical quality specification expressed as the desirable total error (data from Table 2). This is indicated by solid black lines on both sides of the certified value. Note that the lines have been positioned at a distance given by U_{rel}(%) + TE(%) from the middle of the certified value. This is done

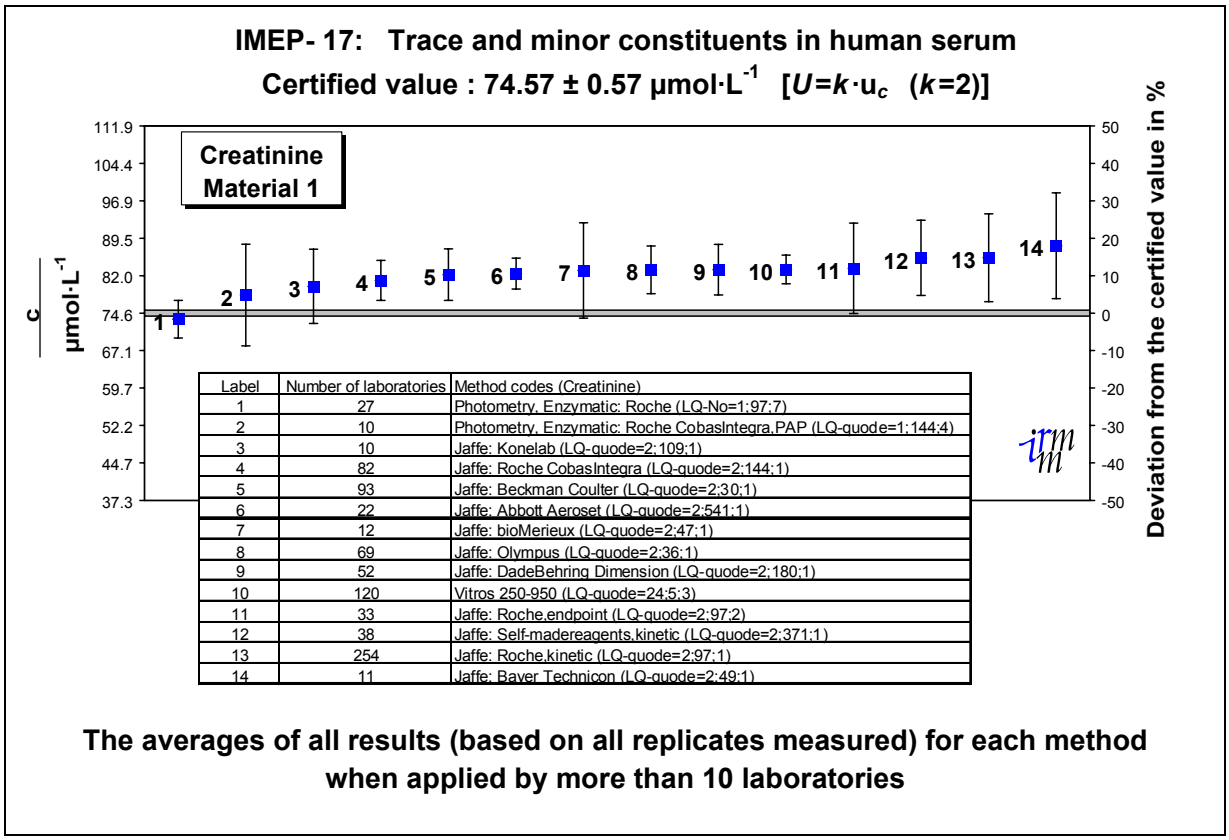
deliberately to illustrate that a value, serving as reference in a decision process, is not always perfect.

5.1.4. Results arranged according to method groups

Results obtained by procedures having similar properties are often grouped together in order for EQA scheme organisers to simplify the graphical display. The groups used in this report are taken from Reference 25. Graphs with results arranged in groups have been constructed for creatinine, uric acid and γ-GT. Results based on a single measurement and average of all replicate measurements are presented next to each other for the three components but there is little difference between the graphs (Annex 1).

5.1.5. Overall results for specific procedures – 'bias plots'

In Figure 2 estimates of the systematic error (bias) for fourteen specific creatinine procedures are displayed. The bias, calculated as the difference between the average of the participants' results (■) and the certified value, is read from the y-axis to the right in the graph. The vertical bars around the average results are simply the standard deviation (*s*) of the results for each procedure.* Similar graphs for Na and K are shown in Annex 1.



Label	Number of laboratories	Method codes (Creatinine)
1	27	Photometry, Enzymatic: Roche (LQ-No=1;97;7)
2	10	Photometry, Enzymatic: Roche CobasIntegra,PAP (LQ-quode=1;144;4)
3	10	Jaffe: Konelab (LQ-quode=2;109;1)
4	82	Jaffe: Roche CobasIntegra (LQ-quode=2;144;1)
5	93	Jaffe: Beckman Coulter (LQ-quode=2;30;1)
6	22	Jaffe: Abbott Aeroset (LQ-quode=2;541;1)
7	12	Jaffe: bioMerieux (LQ-quode=2;47;1)
8	69	Jaffe: Olympus (LQ-quode=2;36;1)
9	52	Jaffe: DadeBehring Dimension (LQ-quode=2;180;1)
10	120	Vitros 250-950 (LQ-quode=24;5;3)
11	33	Jaffe: Roche,endpoint (LQ-quode=2;97;2)
12	38	Jaffe: Self-madereagents,kinetic (LQ-quode=2;371;1)
13	254	Jaffe: Roche,kinetic (LQ-quode=2;97;1)
14	11	Jaffe: Bayer Technicon (LQ-quode=2;49;1)

Figure 2. Estimate of the bias for fourteen specific measurement procedures.

*A more detailed examination of the data is needed to calculate the so-called reproducibility standard deviation (s_R) of the respective procedure [23].

5.1.6. Youden graphs

A common approach to indicate presence of systematic errors is to use a so-called 'two-sample plot' ('X-Y chart') devised by W. J. Youden [26]. The principle involved is that each laboratory receives two similar samples and performs one determination on each. Results can be plotted, e.g. as shown in Figure 3. Each point represents a pair of results from a single laboratory. The mean of participants' results, or as done here, the certified values for each material, are indicated with a horizontal and vertical line pair. The result is a chart with four quadrants. For interpretation, see Figure 3. Annex 1 contains Youden graphs for ten components.

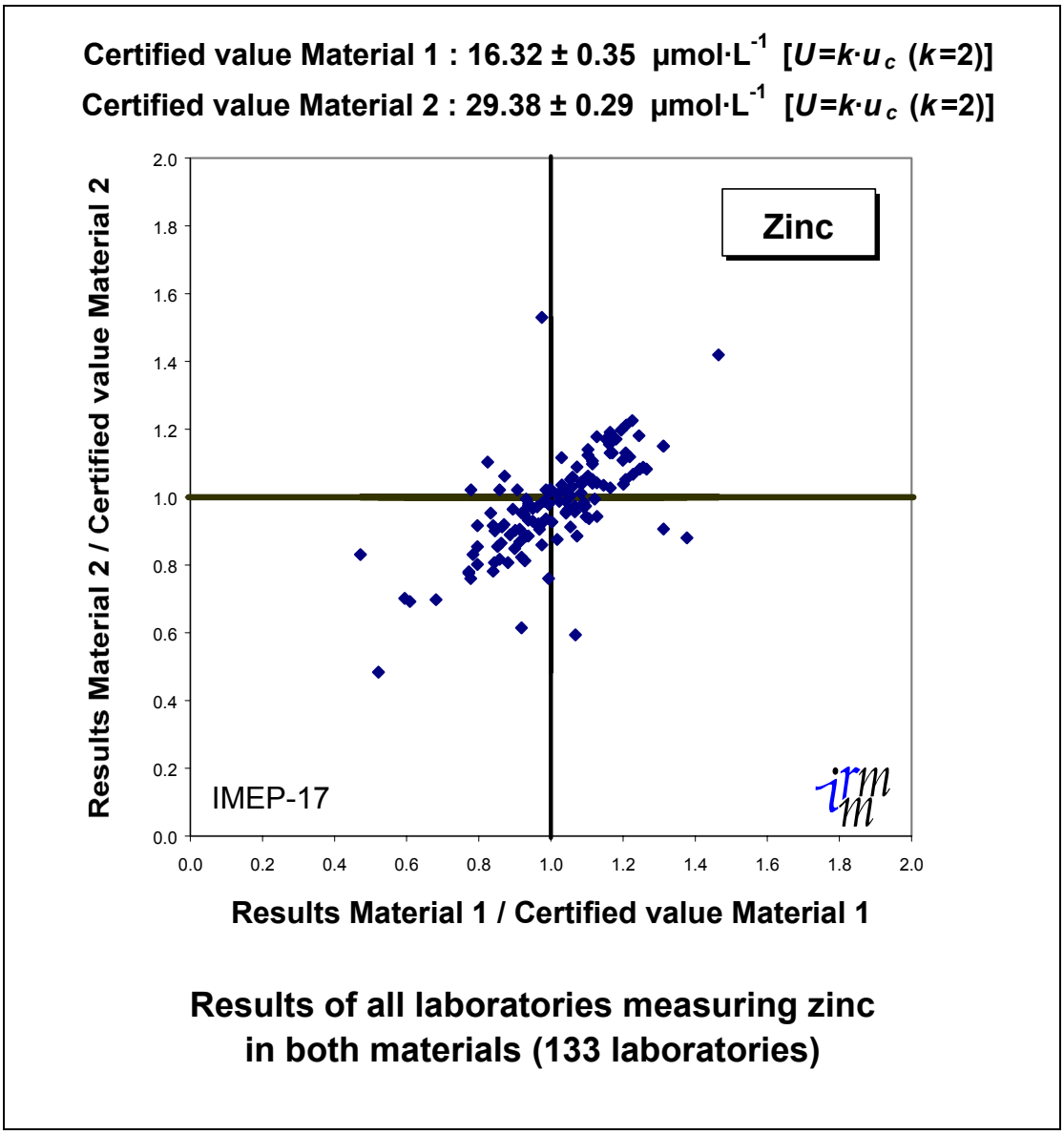


Figure 3. Example of a Youden graph for zinc. If results from different laboratories vary entirely because of random error, one would expect approximately equal number of points in each quadrant. If systematic errors were the main cause of the variation, one would expect that laboratories with a high value for Material 1, would also tend to obtain a high value for Material 2. This would lead to a predominance of points in the lower left and upper right quadrants. The graph is based on single results on the materials for each laboratory.

6. Supplementary information

The large amount of information prevents a complete graphical display to be printed here. Country-specific graphs have been prepared for all components in Material 1 and for Li in Material 2 [27]. The information is compiled in an electronic report which will be provided to regional coordinators and other interested parties via the Internet [3]. A database with all raw data (in laboratory coded form) will be made available to those interested. It will enable further analysis of the results.

Acknowledgements

The authors thank the members of the C-AQ IFCC and EQALM for their continuous support and guidance throughout the project. The work of scientists involved in the establishment of reference measurement procedure values, and the coordination of participants is gratefully acknowledged. Valuable support and advice has been received from people within the CCQM, IUPAC, Eurachem, Euromet, Eurolab and CITAC. We are indebted to Mrs M. De Smet, Dr Yetunde Aregbe, previous members of the IMEP group, and all other colleagues at IRMM who offered administrative and logistic assistance throughout this project.

Abbreviations

C-AQ IFCC	Committee for Analytical quality of the International Federation for Clinical Chemistry and Laboratory Medicine	www.ifcc.org
CCQM	Consultative Committee for Amount of Substance – Metrology in Chemistry	www.bipm.fr
CITAC	Co-operation on International Traceability in Analytical Chemistry	www.citac.cc
CV	Coefficient of variation	
EQA	External quality assessment	
EQALM	European committee for External Quality Assurance programmes in Laboratory Medicine	www.eqalm.org
Eurachem	A focus for analytical chemistry in Europe	www.eurachem.ul.pt
Eurolab	The European Federation of National Associations of Measurement, Testing and Analytical Laboratories	www.eurolab.org
Euromet	A European Collaboration in Measurement Standards	www.euromet.ch
IDMS	Isotope dilution mass spectrometry	
IMEP	International Measurement Evaluation Programme	www.imep.ws
IRMM	Institute for Reference Materials and Measurements	www.irmm.jrc.be
IUPAC	International Union of Pure and Applied Chemistry	www.iupac.org

Annex 1 - Graphical presentation

Figure nr.	Component	Material(s)	Description
General graphs			
1	Cu	2	Single results from all reporting laboratories
2	K	2	
3	Mg	2	
4	Zn	2	
5	Amylase	2	
6	Creatinine	2	
7	γ-GT	2	
8	Glucose	2	
9	Urea	2	
10	Uric acid	2	
Youden graphs			
11	Cu	1-2	Single results from all reporting laboratories
12	K	1-2	
13	Mg	1-2	
14	Amylase	1-2	
15	Creatinine	1-2	
16	γ-GT	1-2	
17	Glucose	1-2	
18	Urea	1-2	
19	Uric acid	1-2	
General method graphs			
20	Creatinine	2	Single results from all reporting laboratories arranged in method groups
21	Creatinine	2	Average of replicate results from all reporting laboratories arranged in method groups
22	Uric acid	2	Single results from all reporting laboratories arranged in method groups
23	Uric acid	2	Average of replicate results from all reporting laboratories arranged in method groups
24	γ-GT	2	Single results from all reporting laboratories arranged in method groups
25	γ-GT	2	Average of replicate results from all reporting laboratories arranged in method groups
Graphs for specific measurement procedures ('bias plots')			
26	Na	1	Average of all replicates for specific methods
27	K	1	

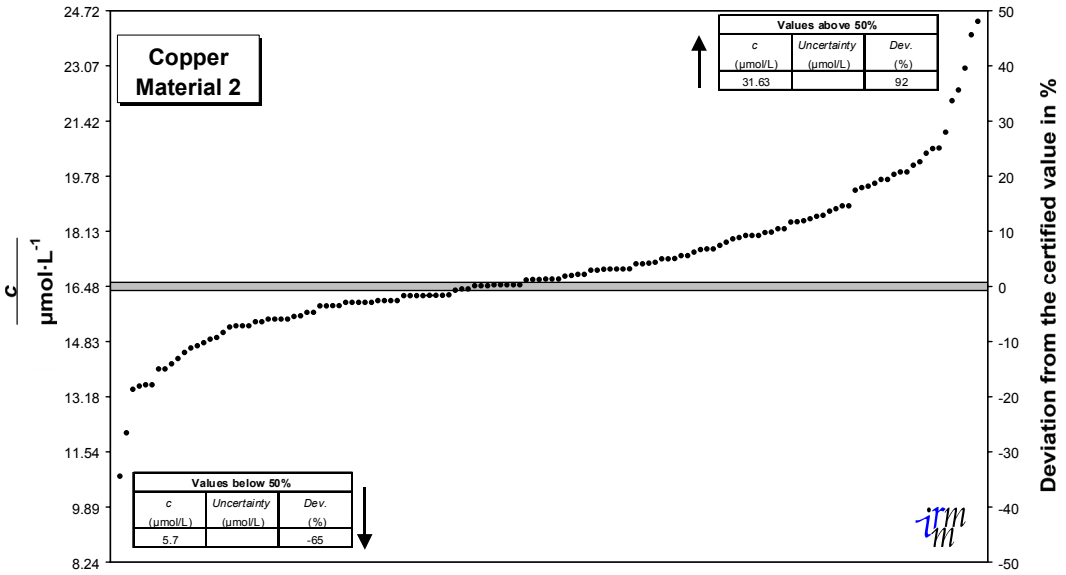
Annex 1 cont.			
National/regional graphs that include analytical quality specifications			
Figure nr.	**Component**	**Material**	**Description**
			Single results from all reporting laboratories in region:
28	Ca	1	Nordic countries
29	Glucose	1	Australia + New Zealand
30	Na	1	North America
31	K	1	EU candidate countries
32	Cholesterol	1	South America

IMEP-17
Participants' results.
General graphs by component

Fig. 1

IMEP- 17: Trace and minor constituents in human serum

Certified value : 16.48 ± 0.12 µmol·L^{-1} [$U=k\cdot u_c$ (k=2)]

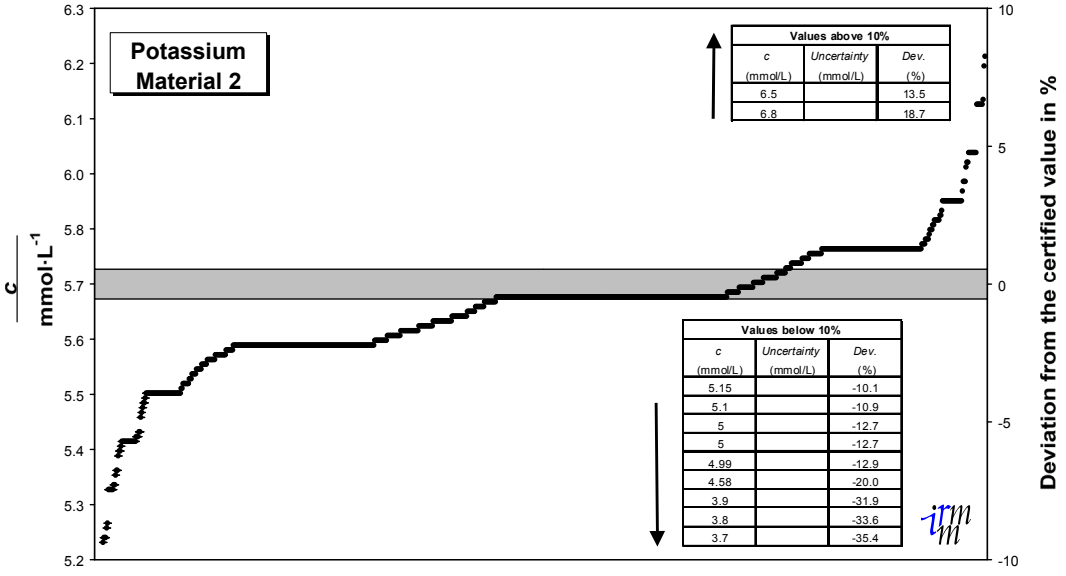


Results from all participants (136 laboratories)

Fig. 2

IMEP- 17: Trace and minor constituents in human serum

Certified value :5.727 ± 0.031 mmol·L^{-1} [$U=k\cdot u_c$ (k=2)]

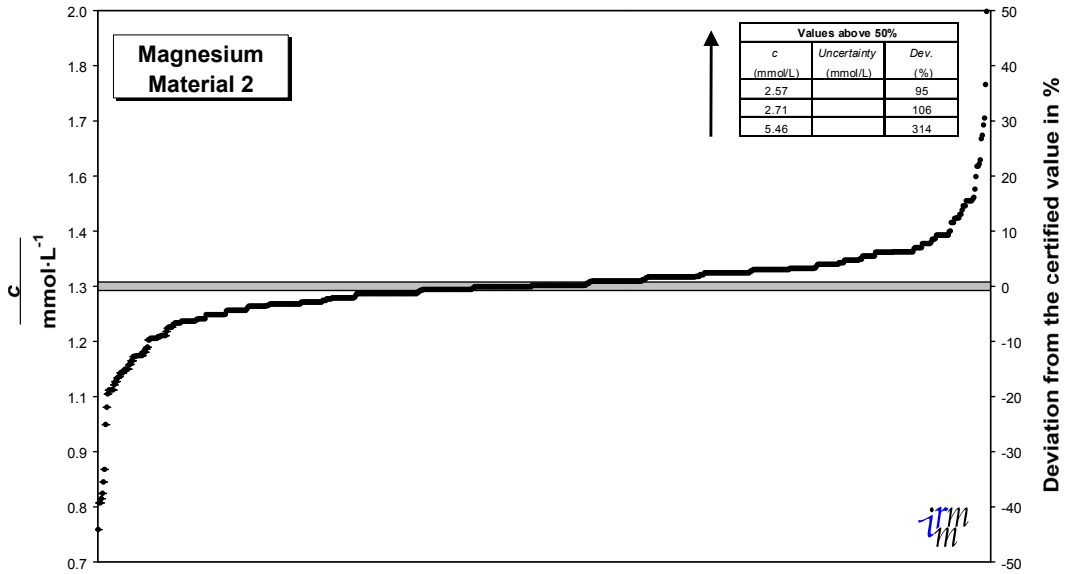


Results from all participants (992 laboratories)

Fig. 3

IMEP- 17: Trace and minor constituents in human serum

Certified value : 1.318 ± 0.010 mmol·L^{-1} [$U=k\cdot u_c$ (k=2)]

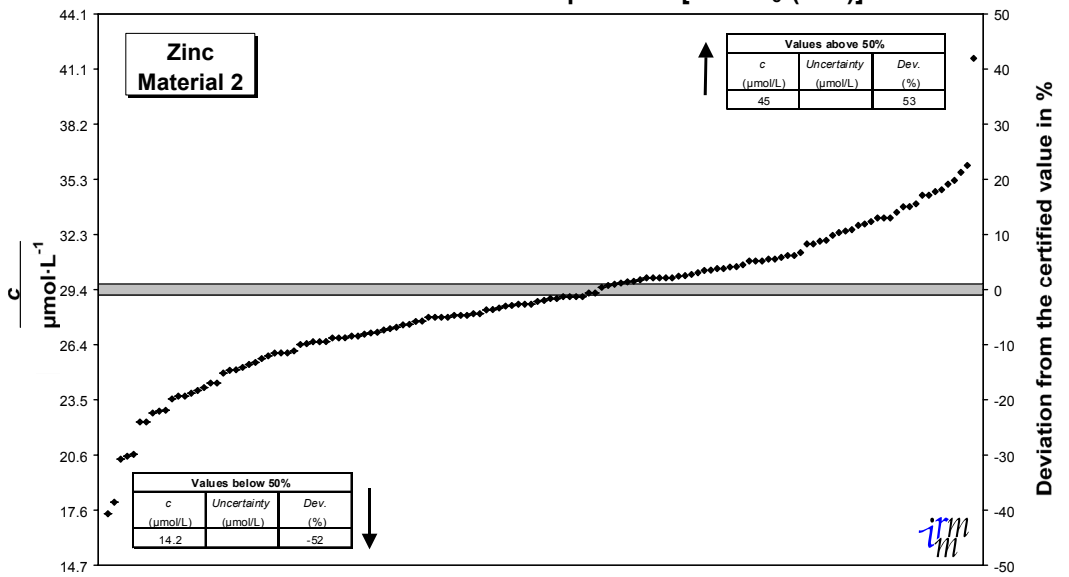


Results from all participants (835 laboratories)

Fig. 4

IMEP- 17: Trace and minor constituents in human serum

Certified value : 29.38 ± 0.29 µmol·L^{-1} [$U=k\cdot u_c$ (k=2)]



Results from all participants (138 laboratories)

Fig. 5

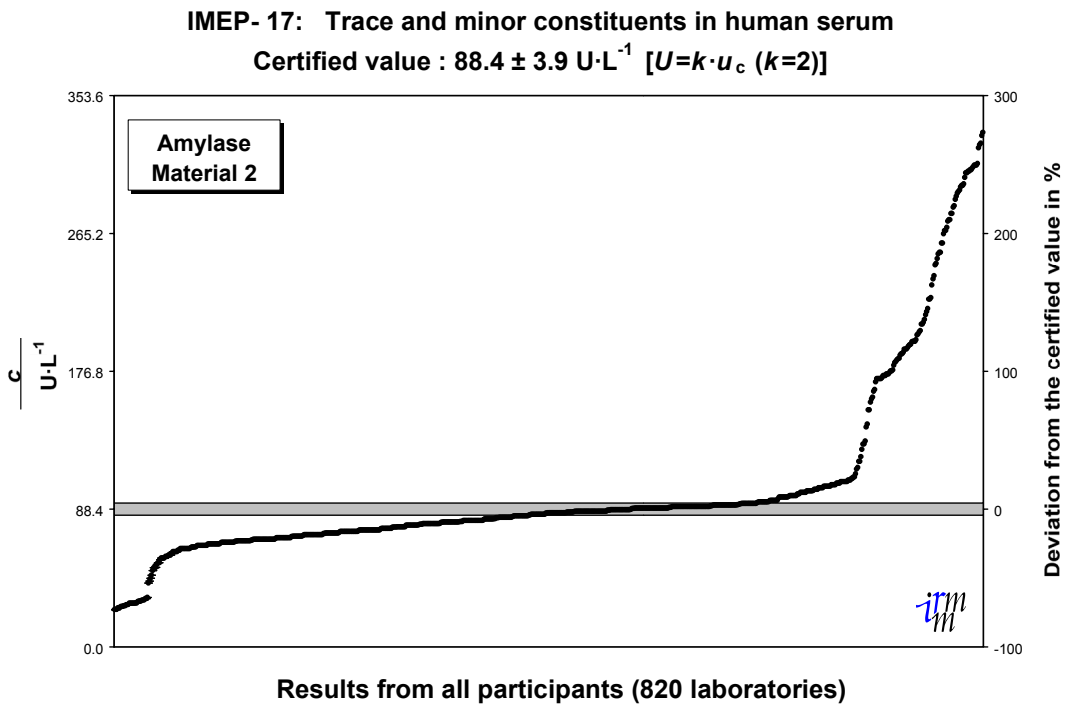

IMEP- 17: Trace and minor constituents in human serum
Certified value : 88.4 ± 3.9 U·L-1 [U=k·uc (k=2)]
Amylase
Material 2
353.6
265.2
176.8
88.4
0.0
300
200
100
0
-100
c
U·L-1
Deviation from the certified value in %
Results from all participants (820 laboratories)

Fig. 6

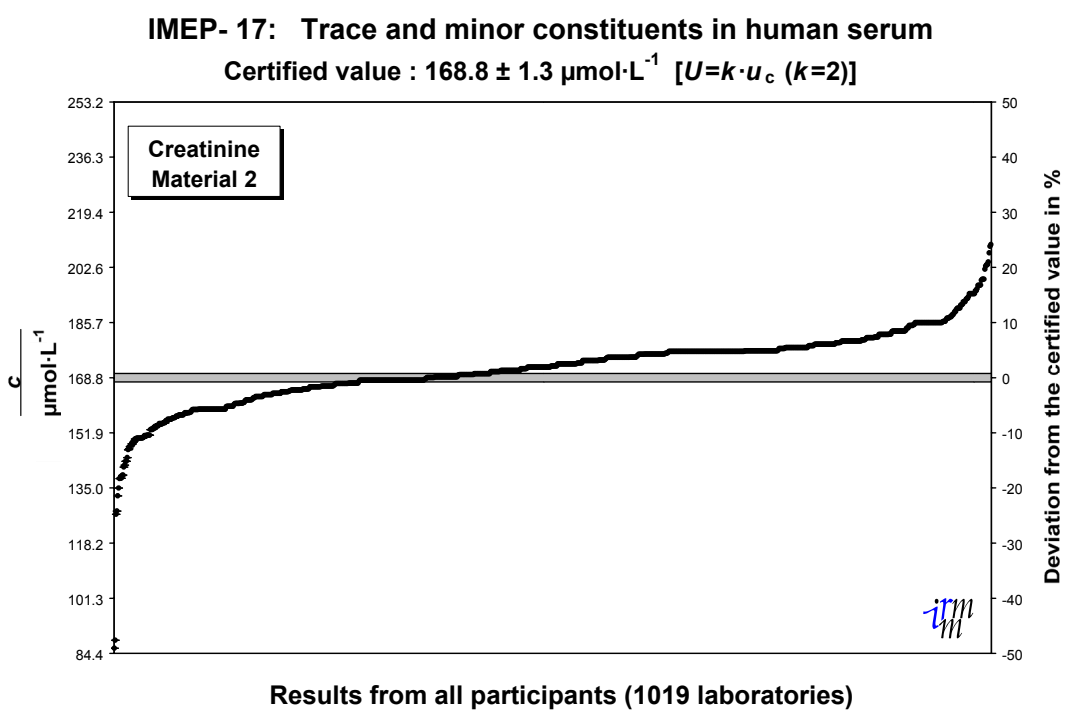
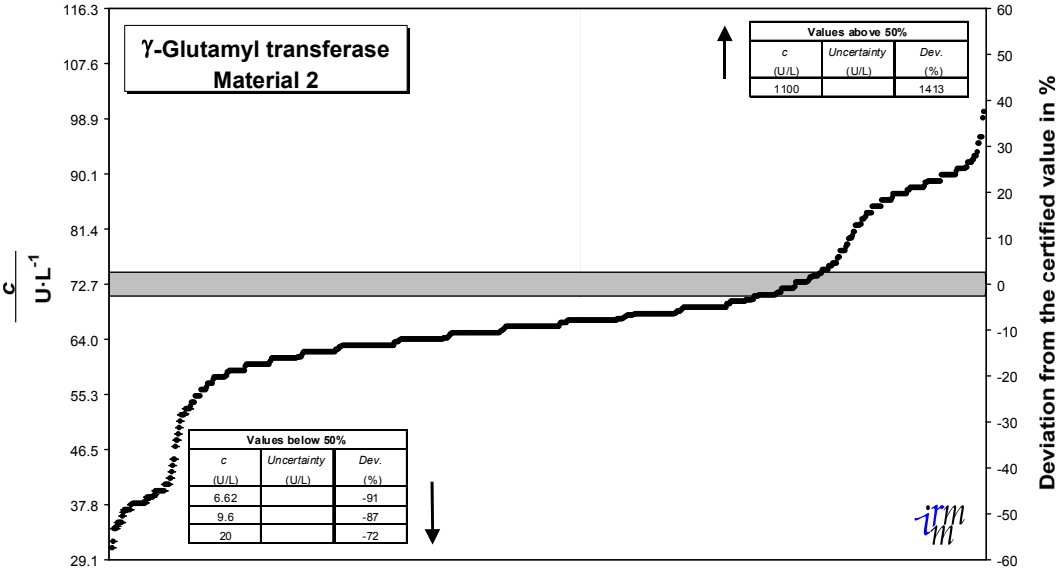

IMEP- 17: Trace and minor constituents in human serum
Certified value : 168.8 ± 1.3 µmol·L-1 [U=k·uc (k=2)]
Creatinine
Material 2
253.2
236.3
219.4
202.6
185.7
168.8
151.9
135.0
118.2
101.3
84.4
50
40
30
20
10
0
-10
-20
-30
-40
-50
c
µmol·L-1
Deviation from the certified value in %
Results from all participants (1019 laboratories)

Fig. 7

IMEP- 17: Trace and minor constituents in human serum

Certified value : 72.7 ± 1.9 U·L^{-1} [$U=k\cdot u_c$ (k=2)]

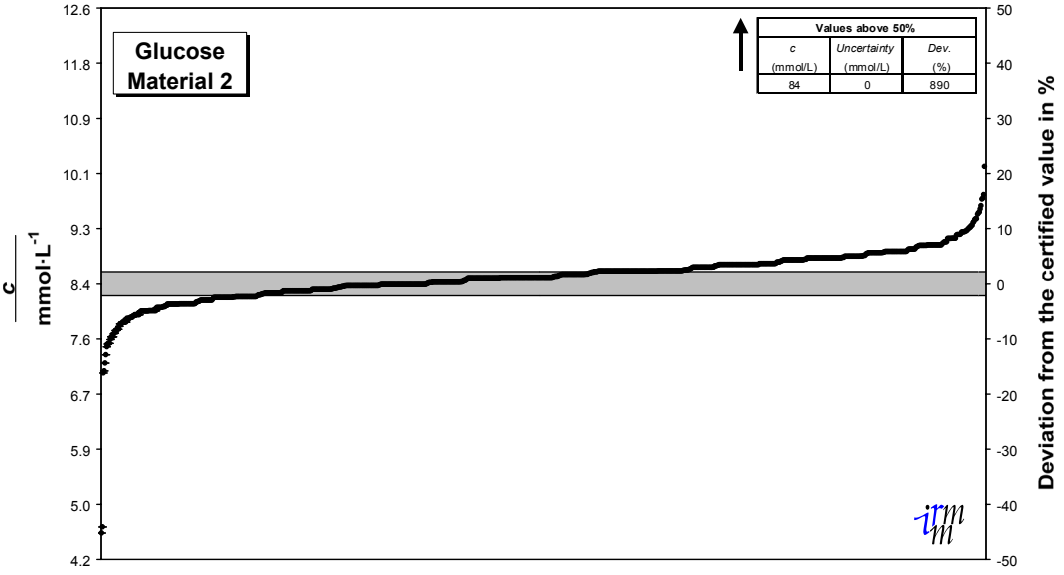


Results from all participants (928 laboratories)

Fig. 8

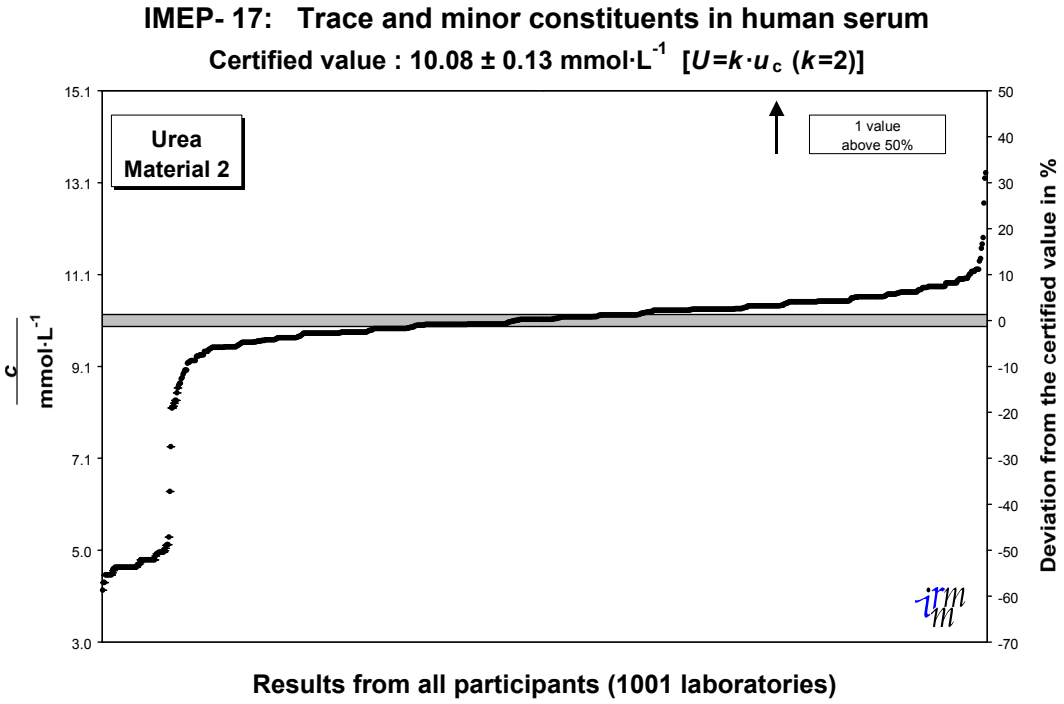
IMEP- 17: Trace and minor constituents in human serum

Certified value : 8.41 ± 0.18 mmol·L^{-1} [$U=k\cdot u_c$ (k=2)]



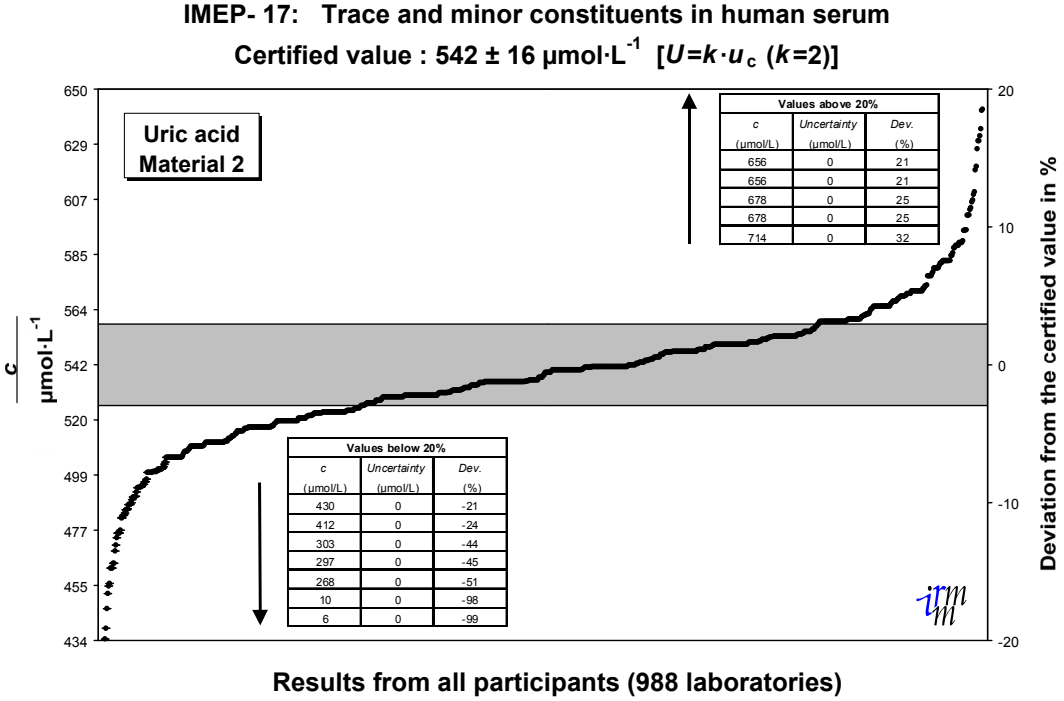
Results from all participants (1007 laboratories)

Fig. 9



It is common in the United States to report and express results of urea assays as Urea-N. It is suspected that all but two US participants did so, although, only a few of them actually stated this in their report form. It is likely that also some thirty participants from China, Germany, Italy, Poland, Turkey, Mexico and Austria also reported results as Urea-N. The lower part of the figure reflects this way of reporting results.

Fig. 10

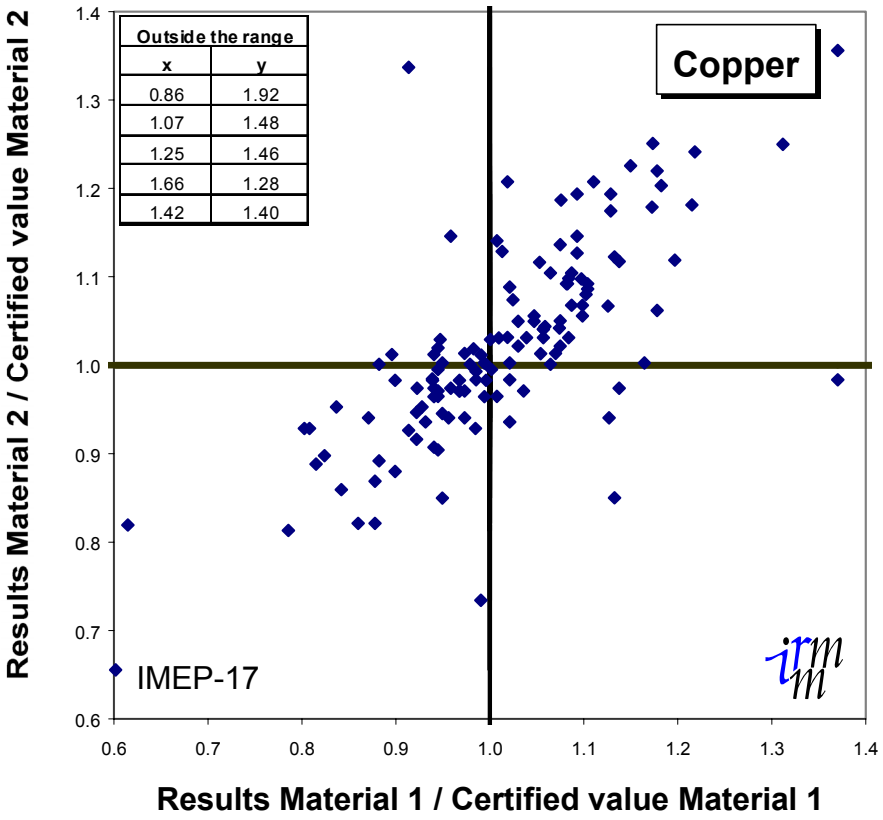


IMEP-17
Participants' results.
Youden graphs

Fig. 11

Certified value Material 1 : 17,57 ± 0,10 µmol·L^{-1} [$U=k\cdot u_c$ (k=2)]

Certified value Material 2 : 16,48 ± 0,12 µmol·L^{-1} [$U=k\cdot u_c$ (k=2)]

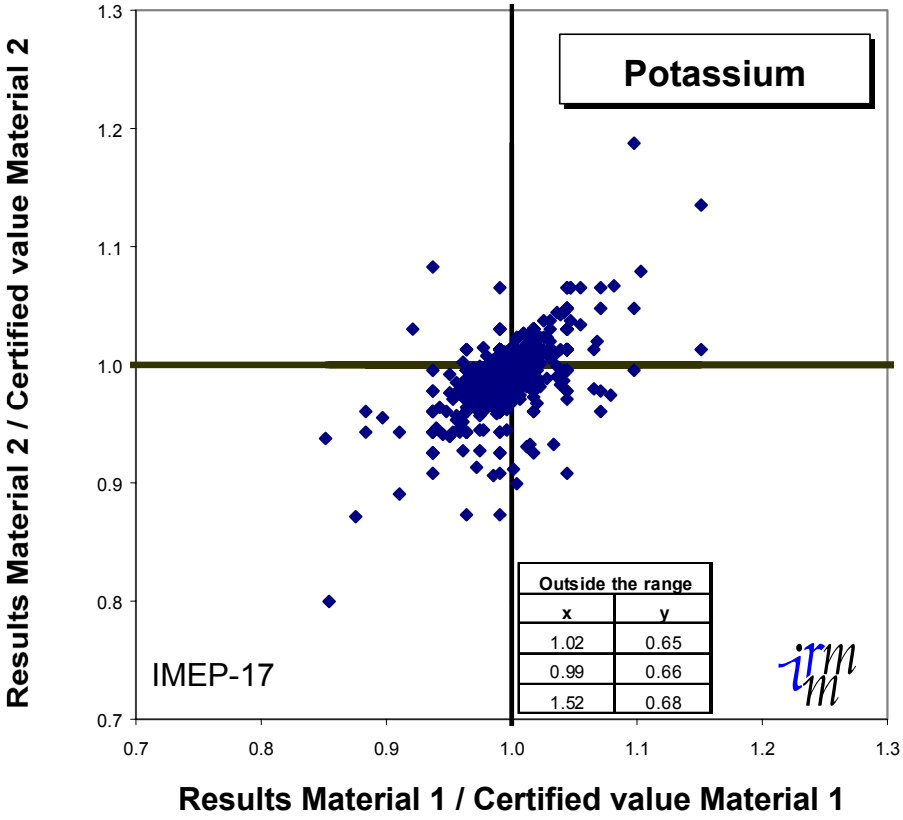


Results of all laboratories measuring copper in both materials (135 laboratories)

Fig. 12

Certified value Material 1 : 3.735 ± 0.021 mmol·L^{-1} [$U=k\cdot u_c$ (k=2)]

Certified value Material 2 : 5.727 ± 0.031 mmol·L^{-1} [$U=k\cdot u_c$ (k=2)]

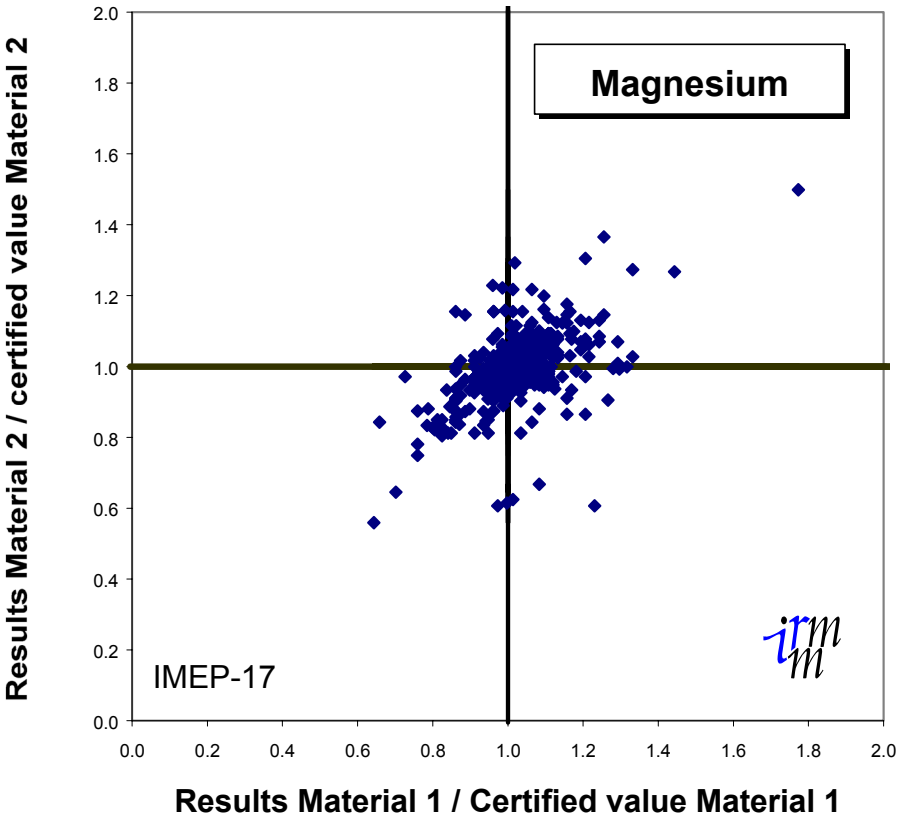


Results of all laboratories measuring potassium in both materials (985 laboratories)

Fig. 13

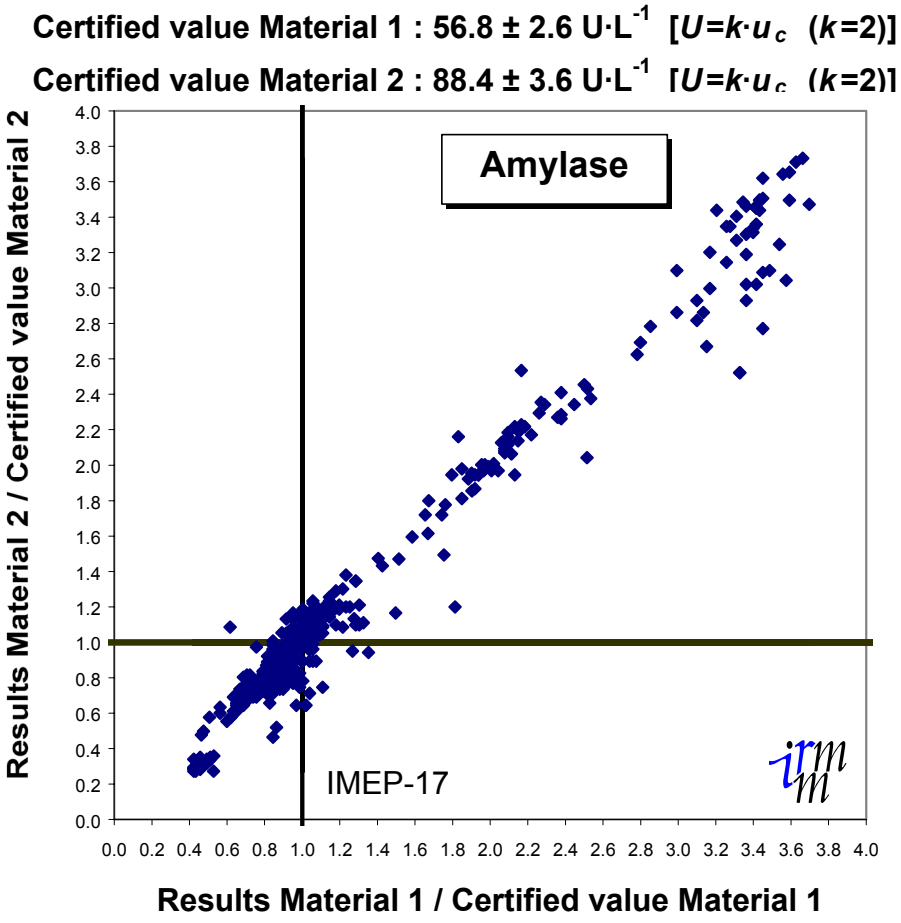
Certified value Material 1 : 0.812 3 ± 0.005 6 mmol·L^{-1} [$U=k\cdot u_c$ (k=2)]

Certified value Material 2 : 1.318 ± 0.010 mmol·L^{-1} [$U=k\cdot u_c$ (k=2)]



Results of all laboratories measuring magnesium in both materials (827 laboratories)

Fig. 14

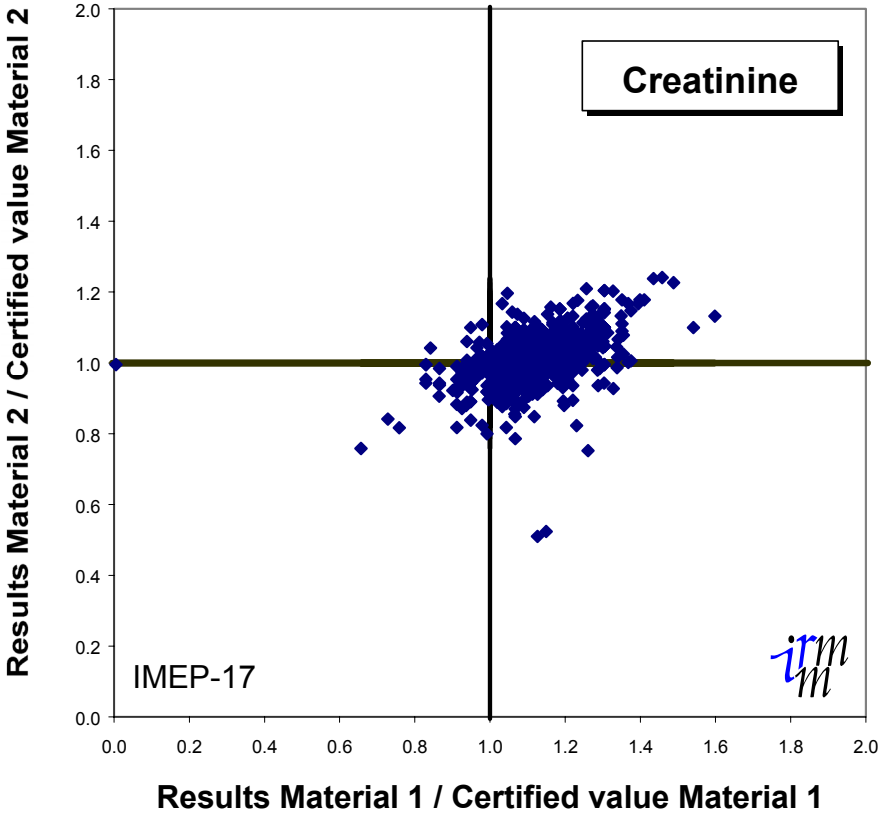


Results of all laboratories measuring amylase in both materials (809 laboratories)

Fig. 15

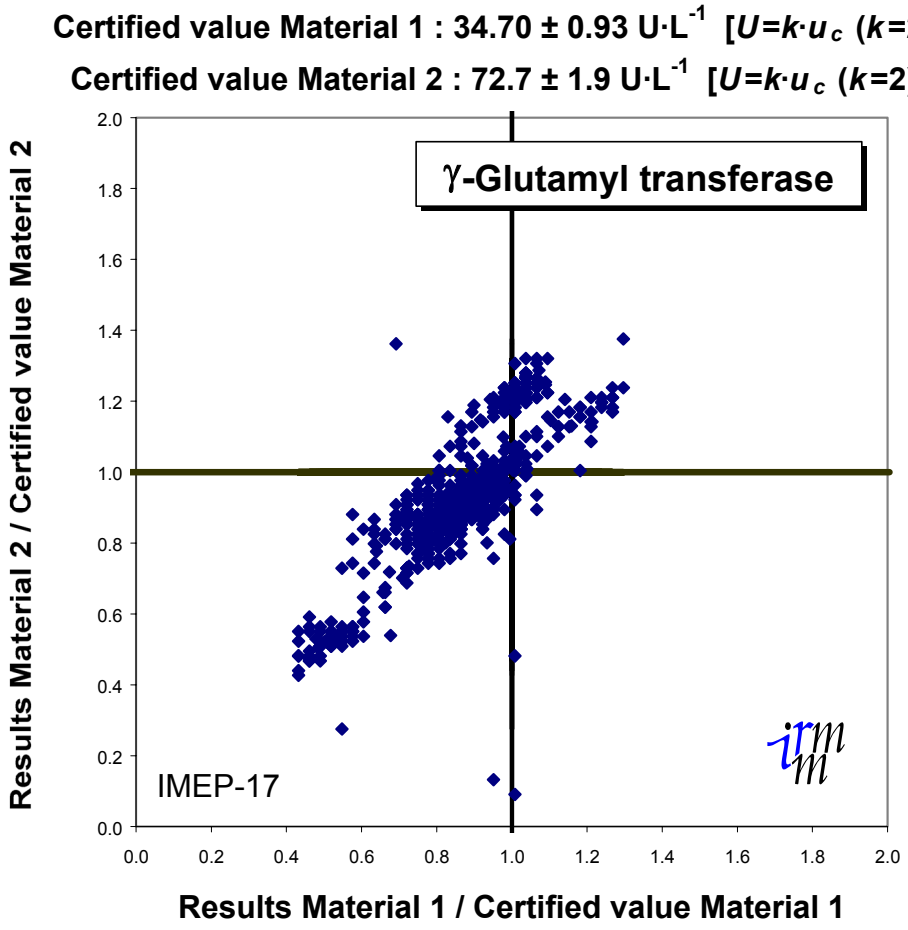
Certified value Material 1 : 74.57 ± 0.57 µmol·L^{-1} [$U=k\cdot u_c$ (k=2)]

Certified value Material 2 : 168.8 ± 1.3 µmol·L^{-1} [$U=k\cdot u_c$ (k=2)]



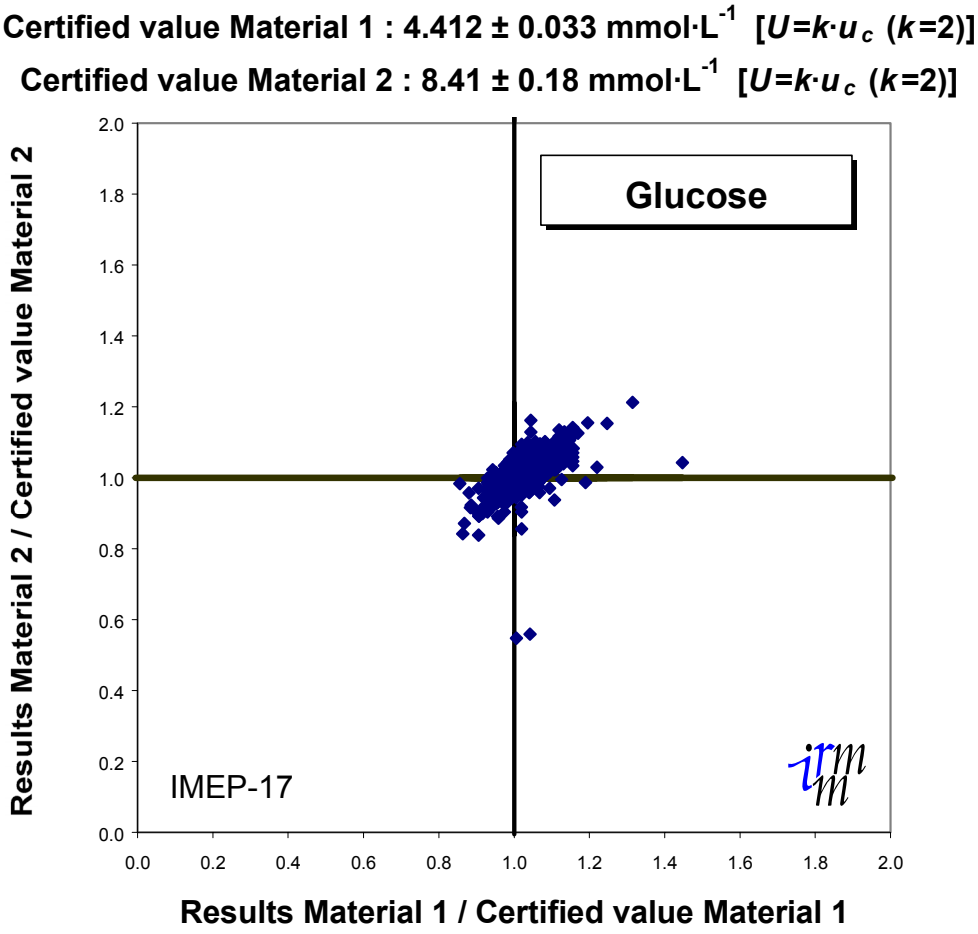
Results of all laboratories measuring creatinine in both materials (1015 laboratories)

Fig. 16



Results of all laboratories measuring glutamyl transferase in both materials (919 laboratories)

Fig. 17

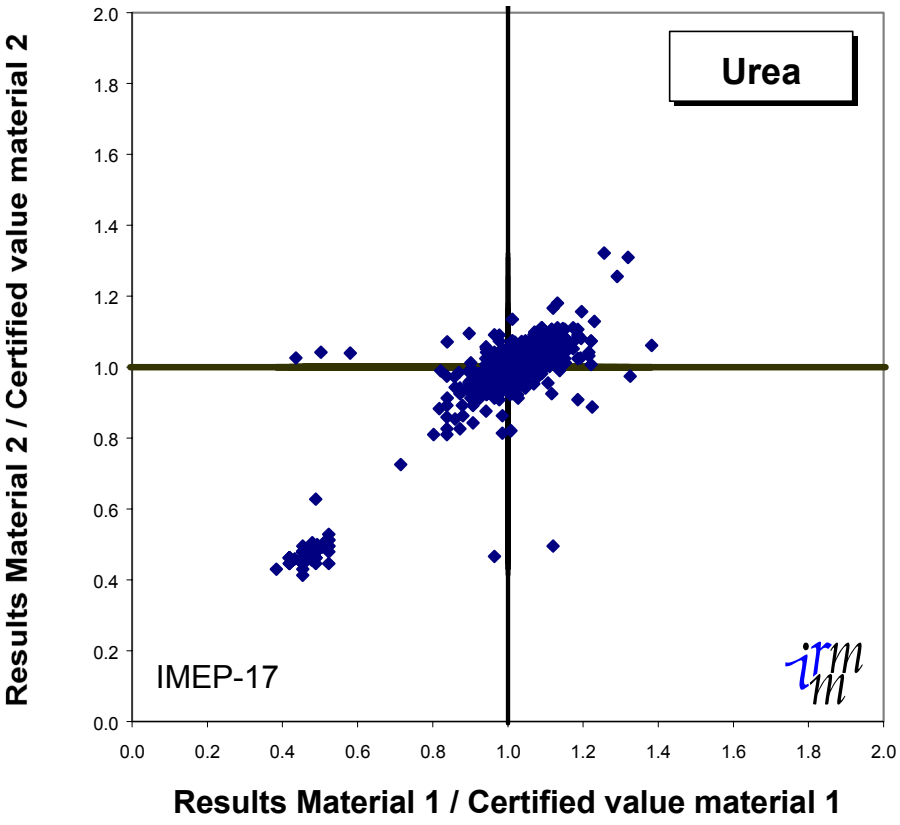


Results of all laboratories measuring glucose in both materials (1002 laboratories)

Fig. 18

Certified value Material 1 : 4.772 ± 0.049 mmol·L^{-1} [$U=k\cdot u_c$ (k=2)]

Certified value Material 2 : 10.08 ± 0.13 mmol·L^{-1} [$U=k\cdot u_c$ (k=2)]

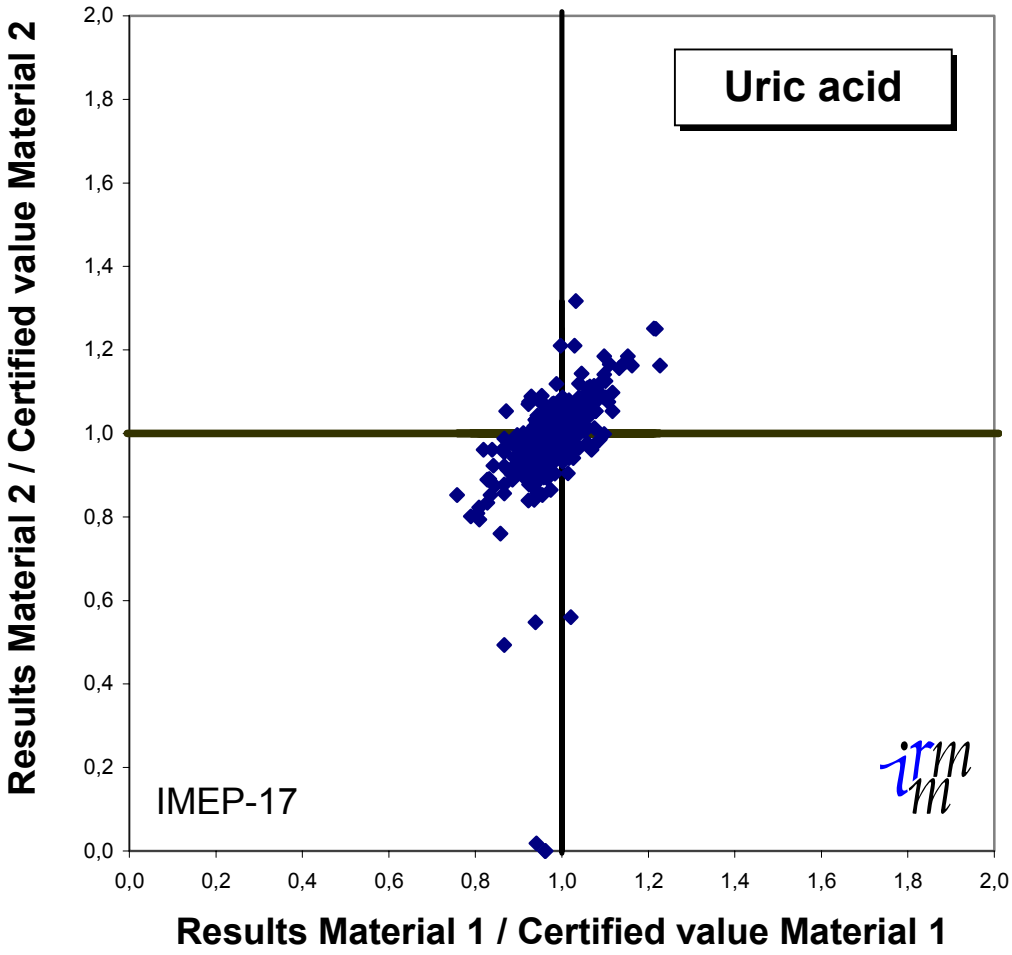


Results of all laboratories measuring urea in both materials (996 laboratories)

Fig. 19

Certified value Material 1: 308.9 ± 5.7 µmol·L^{-1} [$U = k \cdot u_c$ (k=2)]

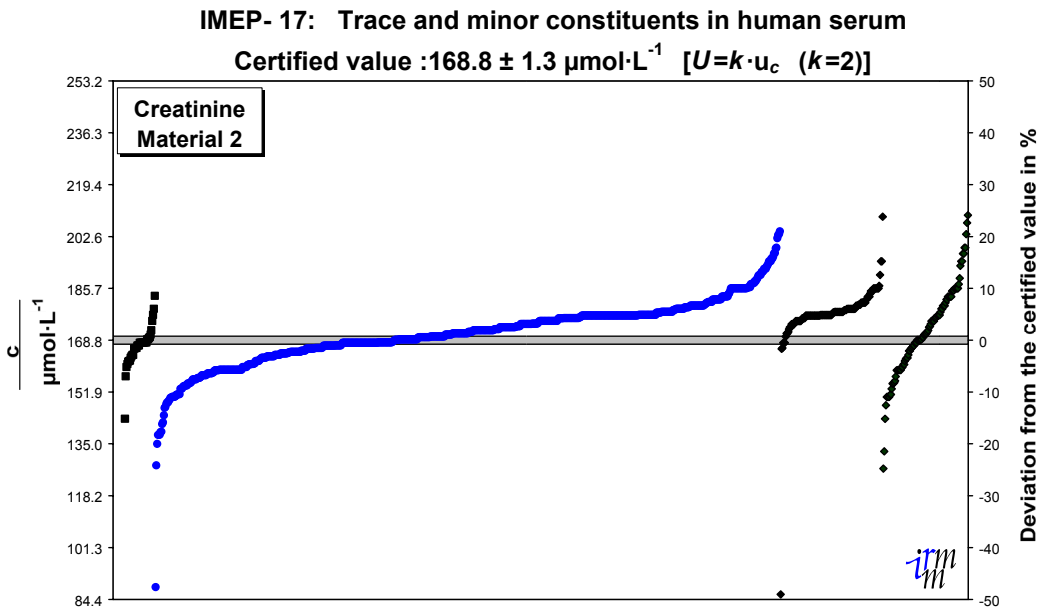
Certified value Material 2: 542 ± 16 µmol·L^{-1} [$U = k \cdot u_c$ (k=2)]



Results of all laboratories measuring uric acid in both materials (985 laboratories)

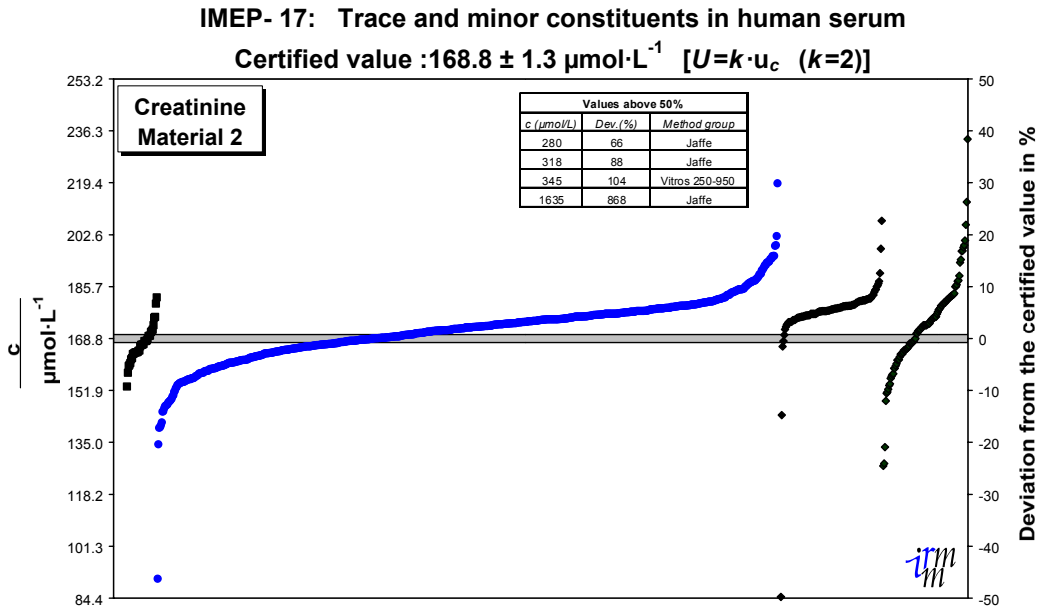
IMEP-17
Participants' results.
Graphs by method group/ specific method and component

Fig. 20



All 1019 results (based on one single replicate) arranged in method groups: Photometry, enzymatic; Photometry, Jaffe; Vitros 250-950 and Other/No info

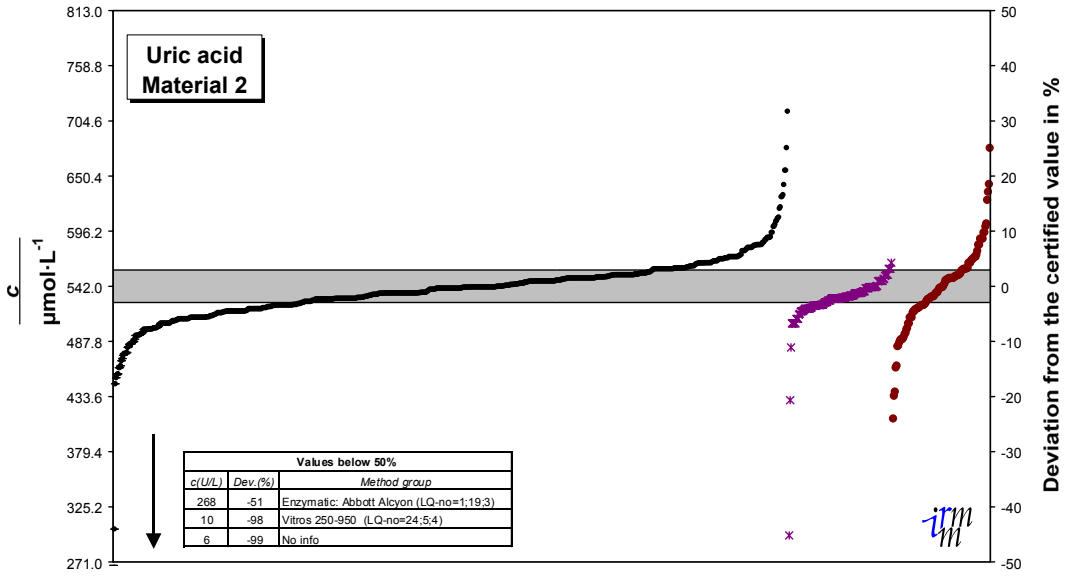
Fig. 21



Averaged results (based on all replicates reported by 1019 laboratories) in method groups: Photometry, enzymatic; Photometry, Jaffe; Vitros 250-950 and Other/No info

Fig. 22

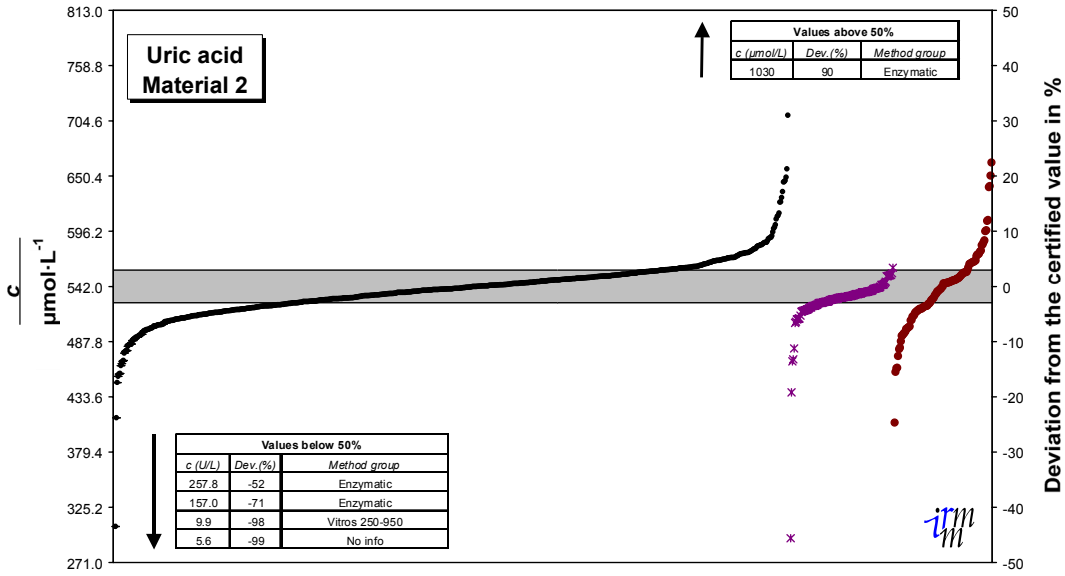
IMEP- 17: Trace and minor constituents in human serum
Certified value : 542 ± 16 µmol·L^{-1} [$U=k\cdot u_c$ (k=2)]



All 988 results (based on one single replicate) arranged in method groups: Photometry- Enzymatic, Vitros 250-950 and Other/No info

Fig. 23

IMEP- 17: Trace and minor constituents in human serum
Certified value : 542 ± 16 µmol·L^{-1} [$U=k\cdot u_c$ (k=2)]

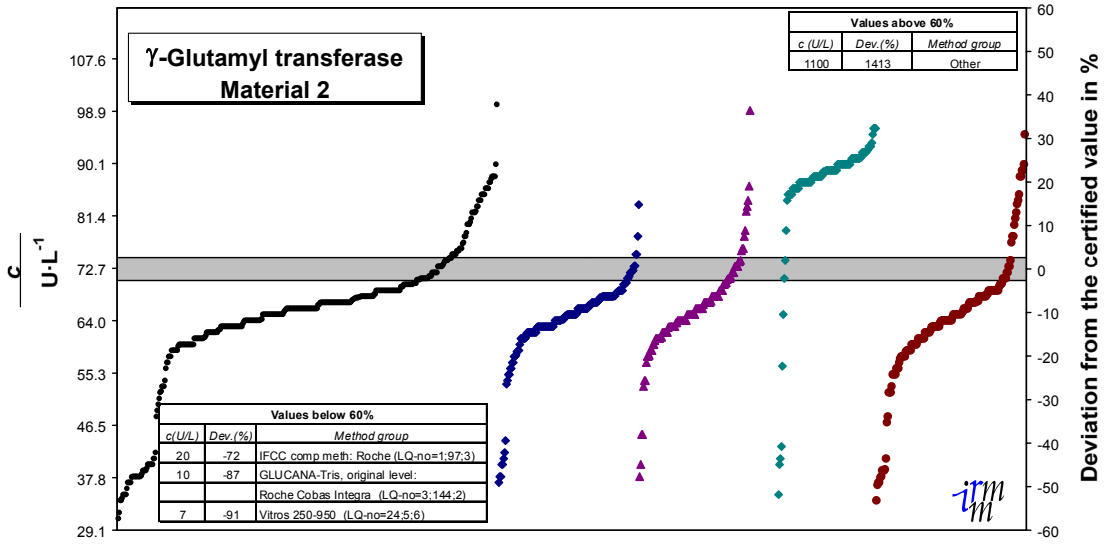


Averaged results (based on all replicates reported by 988 laboratories) in method groups: Photometry- Enzymatic, Vitros 250-950 and Other/No info

Fig. 24

IMEP- 17: Trace and minor constituents in human serum

Certified value : 72.7 ± 1.9 U·L^{-1} [$U=k\cdot u_c$ (k=2)]

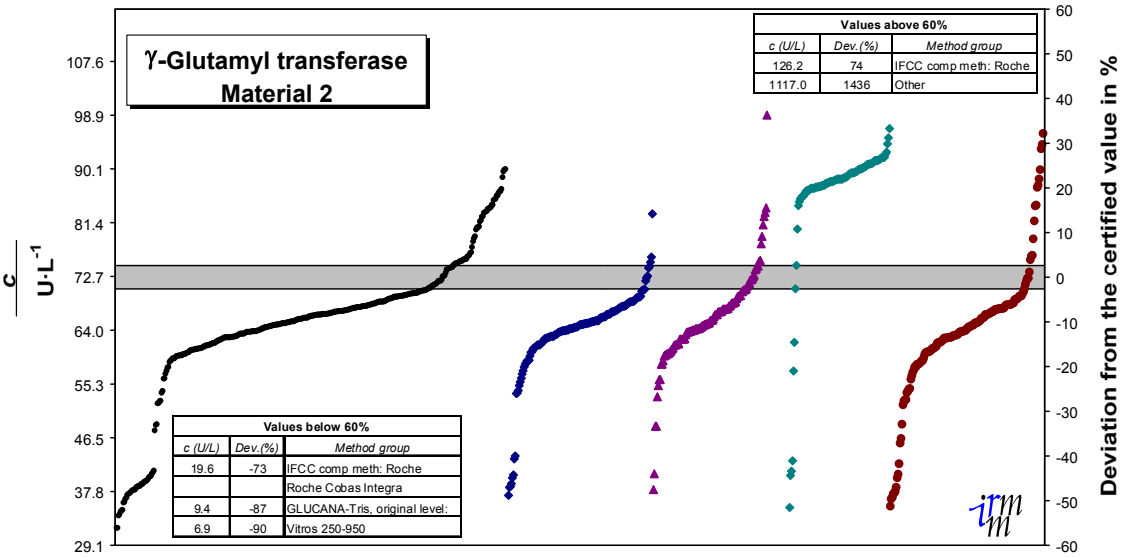


All 928 results (based on one single replicate) arranged in method groups: IFCC comparable methods; GLUCANA-Tris, original level; GLUNA, original level; Vitros 250-950 and Other/No info

Fig. 25

IMEP- 17: Trace and minor constituents in human serum

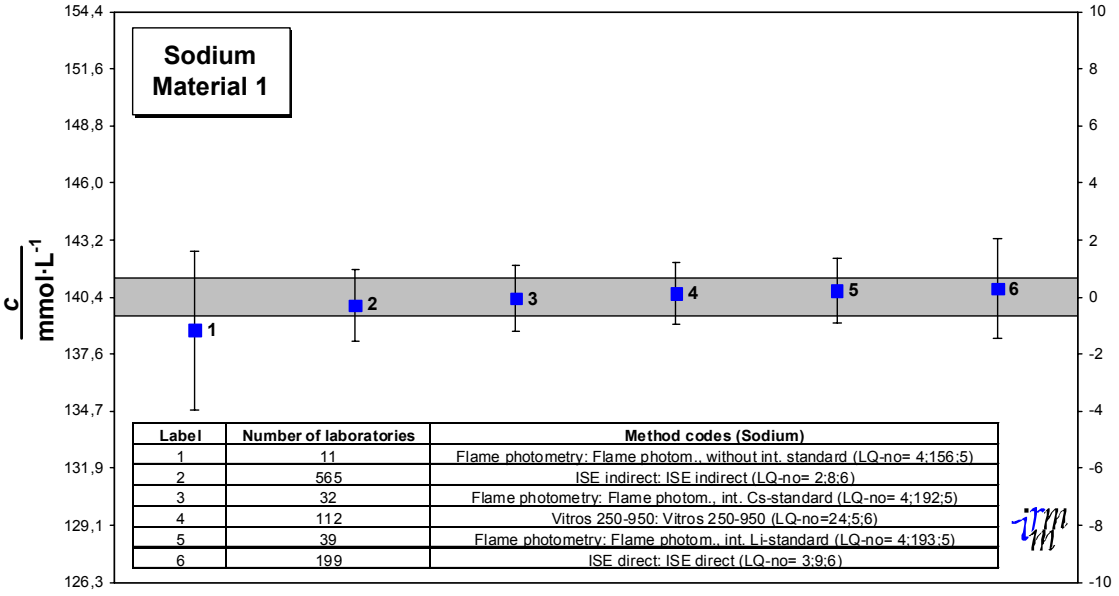
Certified value : 72.7 ± 1.9 U·L^{-1} [$U=k\cdot u_c$ (k=2)]



Averaged results (based on all replicates reported by 928 laboratories) arranged in method groups: IFCC comparable methods; GLUCANA-Tris, original level; GLUNA, original level; Vitros 250-950 and Other/No info

Fig. 26

IMEP- 17: Trace and minor constituents in human serum
Certified value : 140.36 ± 0.95 mmol·L^{-1} [$U = k \cdot u_c$ (k=2)]

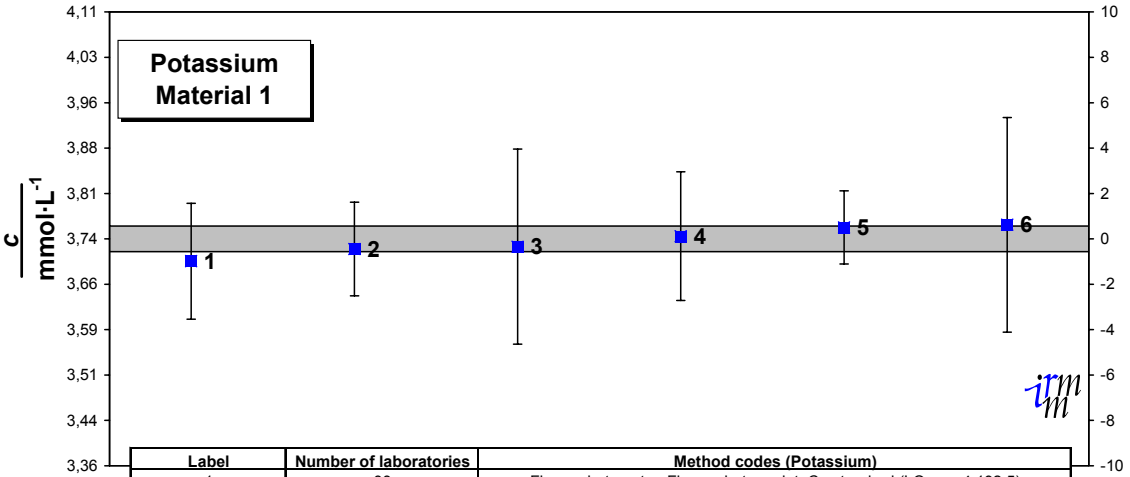


Label	Number of laboratories	Method codes (Sodium)
1	11	Flame photometry: Flame photom., without int. standard (LQ-no= 4;156;5)
2	565	ISE indirect: ISE indirect (LQ-no= 2;8;6)
3	32	Flame photometry: Flame photom., int. Cs-standard (LQ-no= 4;192;5)
4	112	Vitros 250-950: Vitros 250-950 (LQ-no=24;5;6)
5	39	Flame photometry: Flame photom., int. Li-standard (LQ-no= 4;193;5)
6	199	ISE direct: ISE direct (LQ-no= 3;9;6)

Average and standard deviation of all replicate results for specific methods

Fig. 27

IMEP- 17: Trace and minor constituents in human serum
Certified value :3.735 ± 0.021 mmol·L^{-1} [$U = k \cdot u_c$ (k=2)]



Label	Number of laboratories	Method codes (Potassium)
1	33	Flame photometry: Flame photom., int. Cs-standard (LQ-no= 4;192;5)
2	568	ISE indirect: ISE indirect (LQ-no= 2;8;6)
3	11	Flame photometry: Flame photom., without int. standard (LQ-no= 4;156;5)
4	39	Flame photometry: Flame photom., int. Li-standard (LQ-no= 4;193;5)
5	116	Vitros 250-950: Vitros 250-950 (LQ-no=24;5;6)
6	197	ISE direct: ISE direct (LQ-no= 3;9;6)

Average and standard deviation of all replicates for specific methods

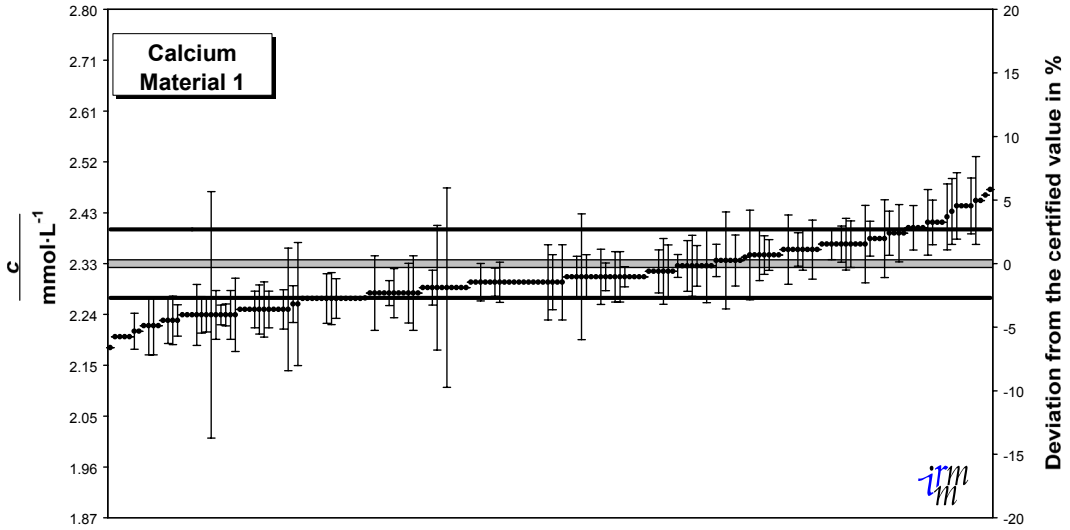
Remark: In clinical chemistry, the term 'indirect potentiometry' is sometimes used to indicate that the sample is pre-treated, e.g. diluted before the potential is measured. [28]. The term is not used in analytical chemistry textbooks.

IMEP-17
Participants' results. Country/regional graphs by component including quality specifications

Fig. 28

IMEP- 17: Trace and minor constituents in human serum

Certified value : 2.334 2 ± 0.006 9 mmol·L^{-1} [$U=k\cdot u_c$ (k=2)]



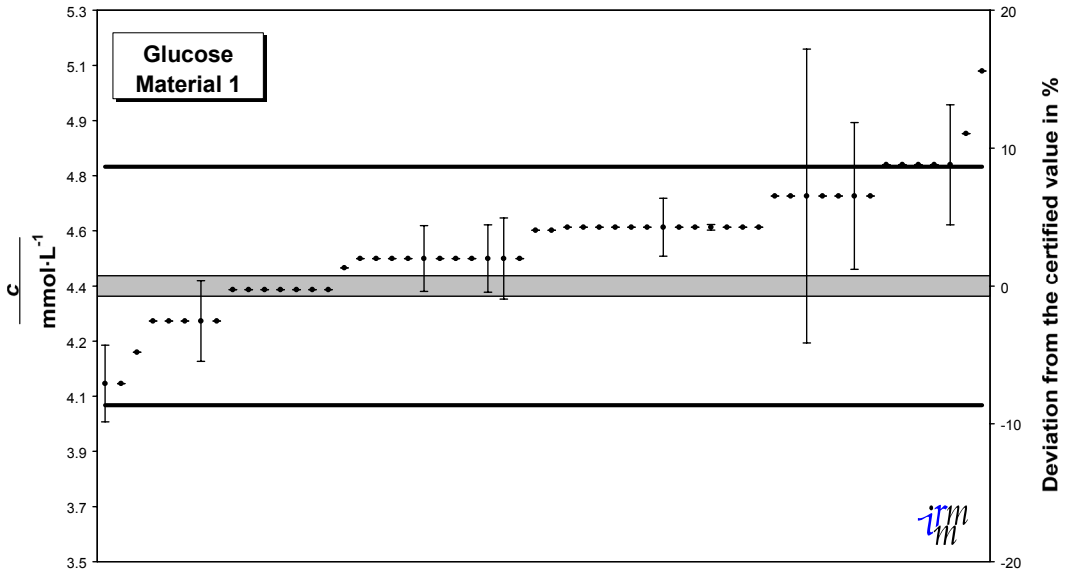
Results from participants from Nordic countries; Denmark, Finland, Iceland, Norway and Sweden (184 laboratories)

'Desirable total error' (———) based on biological variation

Fig. 29

IMEP- 17: Trace and minor constituents in human serum

Certified value : 4.412 ± 0.033 mmol·L^{-1} [$U=k\cdot u_c$ (k=2)]



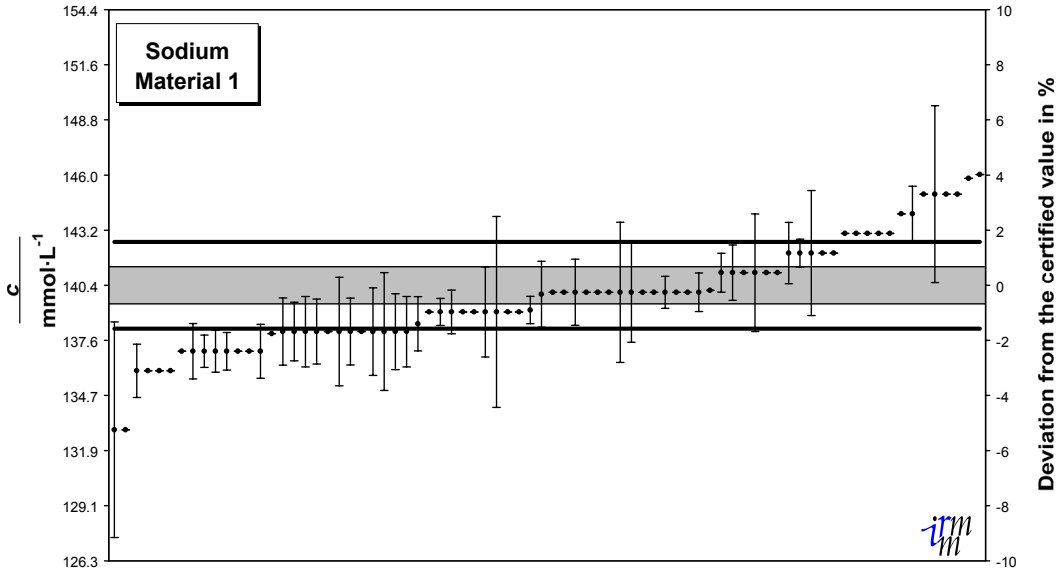
Results from participants from Australia and New Zealand (56 laboratories)

'Desirable total error' (———) based on biological variation

Fig. 30

IMEP- 17: Trace and minor constituents in human serum

Certified value : 140.36 ± 0.95 mmol·L^{-1} [$U=k\cdot u_c$ (k=2)]



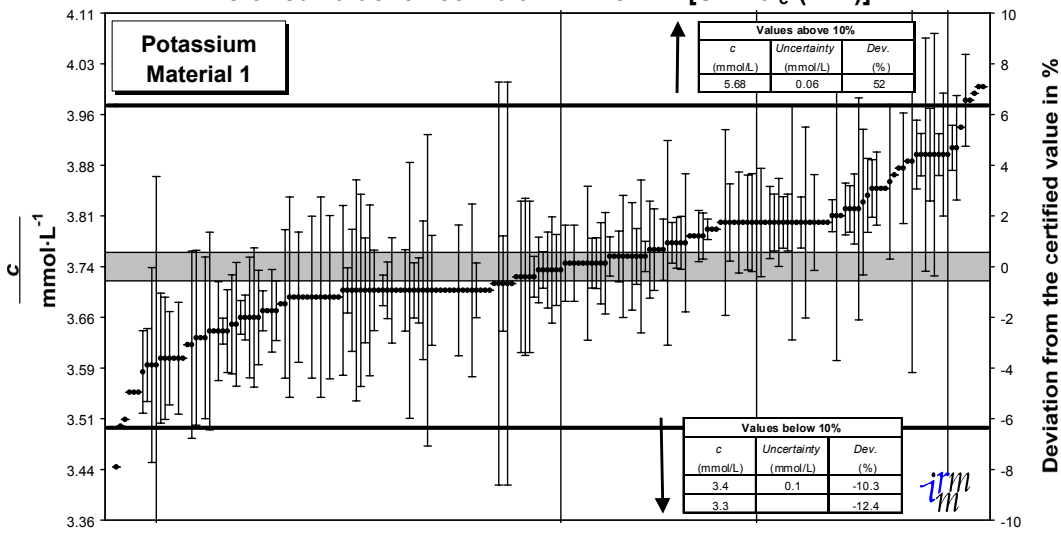
Results from participants from North America; Canada and USA (78 laboratories)

'Desirable total error' (———) based on biological variation

Fig. 31

IMEP- 17: Trace and minor constituents in human serum

Certified value :3.735 ± 0.021 mmol·L^{-1} [$U=k\cdot u_c$ (k=2)]



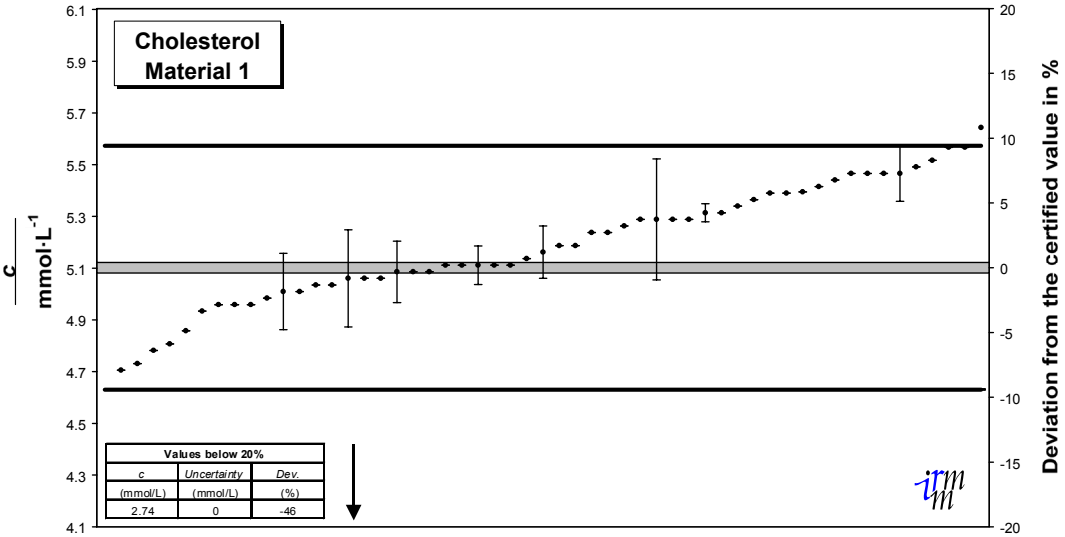
Results from participants from EU Candidate Countries; Bulgaria, Cyprus, Czech Republic, Estonia, Hungary, Poland, Romania, Slovak Republic, Slovenia and Turkey (199 laboratories)-

'Desirable total error' (———) based on biological variation

Fig. 32

IMEP- 17: Trace and minor constituents in human serum

Certified value : 5.111 ± 0.021 mmol·L^{-1} [$U=k\cdot u_c$ (k=2)]



Results from participants from South and Central America;
Argentina and Mexico (55 laboratories)
'Desirable total error' (———) based on biological variation

Annex 2 - Forms, letters and documents

The following official documents are an integral part of IMEP-17. They constitute the information sent to regional coordinators and participants. The documents can be found at the back of the report.

- IRMM Letter IM/L/70/01 of 4 December 2001. Invitation to EQA scheme organisations and contacts.
- Appendix 1 to Letter IM/L/70/01. Information for regional co-ordinators and participating laboratories about the test materials' properties.
- Appendix 2 to Letter IM/L/70/01. Tasks and guidelines for EQAS organisations and individuals acting as national/regional co-ordinators in IMEP-17.
- Appendix 3 to Letter IM/L/70/01. Reply form for invited EQAS organisations/co-ordinators.
- Appendix 4. Result report form
- Certificate, IMEP-17 Certified reference values - Material 1, IM/L/062/02, IRMM, Belgium, September 2002.
- Certificate, IMEP-17 Certified reference values - Material 2, IM/L/063/02, IRMM, Belgium, September 2002.

Annex 3 - References

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