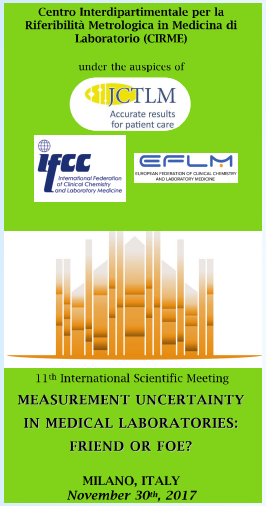

Defining uncertainty of reference measurement procedures: sources and performance criteria

Andrea Mosca

Centro per la Riferibilità metrologica in Medicina di Laboratorio

Dip. Fisiopatologia medico-chirurgica e dei trapianti

Università degli Studi di Milano

contents

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Bureau International des Poids et Mesures

Database of higher-order reference materials, measurement methods/procedures and services

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- Leaflet

ifcc International Federation of Clinical Chemistry and Laboratory Medicine

Analyte keyword search for reference materials, measurement methods/procedures and services

Type an analyte name in part or full, e.g. cholesterol

Refine search by analyte category All

Refine search by matrix category All

Please select your requirement :
- Higher-order reference materials
- Reference measurement methods/procedures
- Reference measurement services

Reset Search

Download entries as PDF

Please select your requirement :
- Higher-order reference materials
- Reference measurement methods/procedures
- Reference measurement services

Select an analyte category Download

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View a list of all entries Download

List of reference measurement methods/procedures for Enzymes

PDF description of measurement method/procedure contains limited information on methods/procedures. More complete information can be retrieved from the keyword search results for the reference measurement methods/procedures.

Analyte	Reference measurement method/procedure	Applicable matrice(s)	Measurement principle/technique	Reference(s)
alanine aminotransferase (ALT)	IFCC reference measurement procedure (37 °C) for ALT	lyophilized, fresh, or frozen human serum or plasma	Kinetic spectrophotometry	*Clin. Chem. Lab. Med.*, 2002, **40**, 718-724 *Clin. Chem. Lab. Med.*, 2002, **40**, 739-745
alkaline phosphatase (ALP)	IFCC reference measurement procedure (37 °C) for Alkaline Phosphatase	lyophilized, fresh or frozen blood serum, or calibration solution or other biological materials	kinetic spectrophotometry	*Clin. Chem. Lab. Med.*, 2011, **49**(9), 1439-1446; IFCC Primary Reference Procedures for the Measurement of Catalytic Activity Concentrations of Enzymes at 37 °C Part 9. Reference Procedure for the Measurement of Catalytic Concentration of Alkaline Phosphatase

Reference measurement procedures

Blood cell counting:	2
Drugs:	14
Electrolytes:	36
Enzymes:	7
Non-electrolyte metals:	15
Metabolites and substrates:	49
Non-peptide hormones:	30
Proteins:	23
Vitamins and micronutrients:	10
total:	186

Glucose in serum
Enzymatic: 2
ID/GC/MS: 3
ID/LC/MS/MS: 1

*What is in the JCTLM database

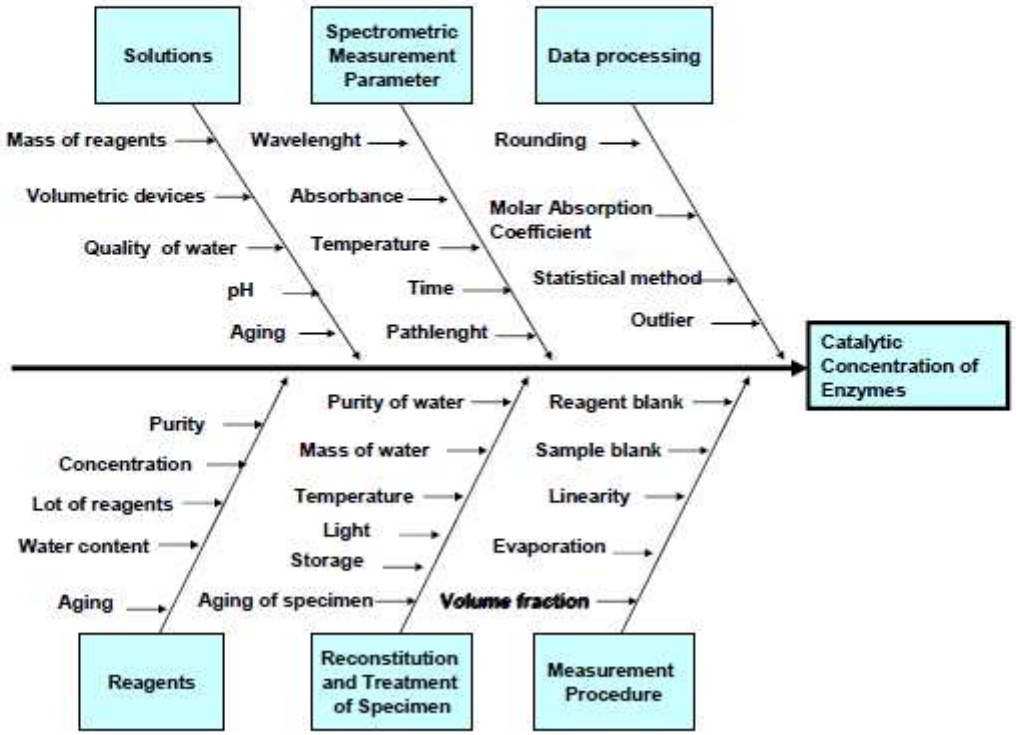
contents

The bottom-up approach according to Guide to the Expression of Uncertainty of Measurement (GUM) principles is based on a comprehensive categorization of the measurement in which each potential source of uncertainty is identified, quantified and combined to generate a combined uncertainty of the result using statistical propagation rules. This model has been fully endorsed by metrology institutions and suppliers of reference materials and is used in accredited reference laboratories that perform reference measurement procedures.

The top-down approach uses available laboratory test performance information, such as method validation, intra-laboratory and inter-laboratory data, to calculate estimates of the overall uncertainty associated with the result produced by a given measuring system. This model may be used by clinical laboratories to estimate measurement uncertainty.

I. Infusino, by courtesy

EXAMPLE: CAUSE AND EFFECT DIAGRAM OF THE MOST RELEVANT UNCERTAINTY SOURCES OF THE PRIMARY REFERENCE PROCEDURE FOR ENZYMES MEASUREMENT



CIRME

I. Infusino, by courtesy

The combined standard uncertainty (u_c) is:

$$u_c = \sqrt{(u^2_{cal} + u^2_{bias} + u^2_{imp})}$$

The appropriate coverage factor should be applied to give an *expanded uncertainty (U)*:

$$U = k \times u_c$$

The choice of the factor k is based on the desired level of confidence.
For an approximate level of confidence of 95 %, k is 2.

2002

Clin Chem Lab Med 2002; 40(7):718–724 © 2002 by Walter de Gruyter · Berlin · New York

IFCC 2002/5

IFCC Primary Reference Procedures for the Measurement of Catalytic Activity Concentrations of Enzymes at 37 °C

Part 4. Reference Procedure for the Measurement of Catalytic Concentration of Alanine Aminotransferase

Gerhard Schumann[1], Roberto Bonora[2], Ferruccio Ceriotti[3], G
Franck[5], F.-
Jørgen Jørg
Rainer Klau
Lessinger[4],
Mauro Pant
Schiele[13], H
and Lothar

The expanded (k=2) combined uncertainty (normally distributed) of the kinetic photometric measurement shall not exceed 1%. (This uncertainty does not include the uncertainty of the wave length adjustment.)

The expanded (k=2) combined uncertainty (normally distributed) of the volume fraction of sample shall be ≤1%.

EXAMPLE: CALCULATION OF COMBINED STANDARD UNCERTAINTY FOR ENZYME MEASUREMENT

Parameter	Declared uncertainty		Reference	Distribution of uncertainty	Type of uncertainty	Standard uncertainty	Coefficient of sensitivity	Pro		Relative standard uncertainty
wavelenght	0,1	nm	manufacturer's specification	rectangular	B	0,06	0,14	1	nm	0,01
absorbance	0,3	%	manufacturer's specification	rectangular	B	0,17	1	1	%	0,17
pH	0,05	pH	IFCC-document	rectangular	B	0,03	0,14	0,05	pH	0,08
temperature	0,1	°C	IFCC-document	rectangular	B	0,06	4,14	1	°C	0,24
reagent concentration	1,5	%	IFCC-document	rectangular	B	0,87	0,26	1	%	0,23
lot of reagent	1,5	%	IFCC-document	rectangular	B	0,87	1	1	%	0,87
volume fraction of sample	0,4	%	data basis	rectangular	B	0,22	1	1	%	0,22
time	0,03	%	experiment	rectangular	B	0,02	1	1	%	0,02
evaporation	0,1	%	experiment	rectangular	B	0,06	1	1	%	0,06
aging of specimen	0,5	%	IFCC-document	rectangular	B	0,29	1	1	%	0,29
linearity	0,6	%	experiment	normal	B	0,30	1	1	%	0,30
mean of the means	0,8	U/L	result of the RMV investigation	normal	A	0,40	1	1	U/L	0,40
							u combined			1,1
							U expanded (k=2)			2,3

$$[uc]^2 = u(wl)^2 + u(abs)^2 + u(pH)^2 + u(temp)^2 + u(reag)^2 + u(lot)^2 + u(vol)^2 + u(time)^2 + u(evap)^2 + u(aging)^2 + u(lin)^2 + u(mean)^2$$

$$= 0.01 + 0.17 + 0.08 + 0.24 + 0.23 + 0.87 + 0.22 + 0.02 + 0.06 + 0.29 + 0.30 + 0.40 = 1.3$$

$[uc] = \pm 1.14\ \%$ $\quad$ $U\ (k=2) = \pm 2.3\ \%$

(bottom-up)

CIRME

Università degli Studi di Milano

I. Infusino, by courtesy

2002

Clin Chem Lab Med 2002; 40(1):78–89 © 2002 by Walter de Gruyter · Berlin · New York

Approved IFCC Reference Method for the Measurement of HbA_{1c} in Human Blood

International Federation of Clinical Chemistry and Laboratory Medicine (IFCC)[1)2)]

Scientific Division
Working Group on HbA_{1c} Standar
Network of Reference Laboratorie

Prepared for publication[5),6)] *by*

Jan-Olof Jeppsson[1,7)], **Uwe Kobold**[2], **Finke**[2], **Wieland Hoelzel**[2], **Tadao Hosh**
Andrea Mosca[6], **Pierluigi Mauri**[7], **Rita**
Thienpont[9], **Masao Umemoto**[10] **and**

with a defined concentration of HbA_{1c}. The combined standard uncertainty u_{cal} for the target values of the calibrators calculated according to the GUM (21) is 0.63%. In the comparison studies of the Network of HbA_{1c} Reference Laboratories the average inter-laboratory CVs were about 2.0% (each sample was measured in duplicate on two occasions by each reference laboratory). If four reference laboratories participate in a value assignment exercise the uncertainty of the value assignment procedure u_{VA} is 1.0% (for 10 laboratories u_{VA} = 0.63%), and a combined standard uncertainty u_{total} (including the uncertainty of the primary calibrator) of about 1.2% can be attained for the target value assigned to a secondary reference material, calibrator or control material.

(top-down)

Clinica Chimica Acta 451 (2015) 305–309

Contents lists available at ScienceDirect

Clinica Chimica Acta

journal homepage: www.elsevier.com/locate/clinchim

Performance of glycated hemoglobin (HbA_{1c}) methods evaluated with EQAS studies using fresh blood samples: Still space for improvements

Andrea Mosca [a,*], Renata Paleari [a], Anna Carobene [b], Cas Weykamp [c,d], Ferruccio Ceriotti [b]

$$u_c = (u_{cal}^2 + u_{imp}^2 + u_{fix}^2)^{1/2}$$

HbA_{1c} mmol/mol	U_c mmol/mol	U_c %
37.4	0.57	**1.5**
62.0	0.91	**1.5**

Anal. Chem. **2004**, *76*, 1008−1014

2004

Development and Evaluation of a Candidate Reference Method for the Determination of Total Cortisol in Human Serum Using Isotope Dilution Liquid Chromatography/Mass Spectrometry and Liquid Chromatography/Tandem Mass Spectrometry

Susan S.-C. Tai* and Michael J. Welch

Analytical Chemistry Division, National Institute of Standards and Technology, Gaithersburg, Maryland 20899-8392

Table 5. Calculation of Expanded Uncertainties for Serum Cortisol by LC/MS-ESI and LC/MS/MS-ESI Measurements

uncertainty table	conc 1	conc 2	conc 3
LC/MS SD, μg/L	0.26	0.16	0.51
LC/MS/MS SD, μg/L	0.05	0.06	0.90
difference between methods, μg/L	0.21	0.11	0.06
purity, μg/L	0.17	0.33	0.50
volumetric, μg/L	0.83	1.66	2.48
combined SD uncertainty, μg/L	0.91	1.70	2.73
degrees of freedom	315	26298	157
k factor	2	2	2
expanded uncertainty[a], μg /L	1.83	3.40	5.46
mean, μg /L	83.3	165.5	248.1
relative expanded uncertainty, %	2.2	2.1	2.2

[a] Uncertainty of 95% confidence interval.

(mix)

2011

Clinical Chemistry 57:4
614–622 (2011)

Proposed Serum Cholesterol Reference Measurement Procedure by Gas Chromatography–Isotope Dilution Mass Spectrometry

Selvin H. Edwards,[1*] Mary M. Kimberly,[1] Susan D. Pyatt,[1] Shelton L. Stribling,[2]
Kara D. Dobbin,[2] and Gary L. Myers[1]

RESULTS: The mean percent bias between the AK and the GC-IDMS RMP was 1.6% for all samples examined. The mean percent bias from NIST's RMP was 0.5% for the SRMs. The total %CVs for SRM 1951b levels I and II were 0.61 and 0.73%, respectively. We found that none of the sterols investigated interfered with the cholesterol measurement.

No data on uncertainty !

Clinica Chimica Acta 413 (2012) 808–813

Contents lists available at SciVerse ScienceDirect

Clinica Chimica Acta

journal homepage: www.elsevier.com/locate/clinchim

2012

High accuracy analysis of glucose in human serum by isotope dilution liquid chromatography-tandem mass spectrometry

Yizhao Chen *, Qinde Liu, Sharon Yong, Tong Kooi Lee

Chemical Metrology Laboratory, Applied Sciences Group, Health Sciences Authority, Singapore

Results: All measurements had good precision with CVs of <1%. Results from GC–MS agreed very well with results from LC-MS/MS, with a difference of LC-MS/MS, were within the certified ranges 1.37% to 1.69% for the 4 levels of glucose, wh

Conclusions: The IDMS method based on LC-M tization steps and thus, greatly simplifies the

Table 2
Uncertainty budget and overall results for analysis of glucose in human serum, NIST SRM 965b.

	Level 1	Level 2	Level 3	Level 4
Uncertainty component				
M_X	0.48%	1.22%	2.01%	5.26%
M_Y	4.84%	2.49%	1.59%	0.63%
C_Z	3.26%	4.34%	2.86%	4.09%
Linear regression plot (R_M')	58.2%	46.6%	46.8%	50.9%
Measurement precision	7.42%	10.9%	5.02%	2.88%
Choice of method	12.3%	15.4%	6.27%	15.2%
Choice of ion pair	13.5%	19.1%	35.4%	21.1%
Obtained value (μg/g)	324.6	738.7	1143.1	2855.5
$U_{(X)}$ (μg/g)	5.1	10.1	19.3	40.4
% $U_{(X)}$	1.58%	1.37%	1.69%	1.41%
Cert. value (μg/g)	323.6	738.9	1159.0	2879.2
$U_{(X)}$ (μg/g)	4.7	10.4	16.6	35.2
% $U_{(X)}$	1.45%	1.40%	1.43%	1.22%
Deviation from certified value	0.31%	−0.03%	−1.38%	−0.82%

(top-down)

2015

analytical chemistry

Article

pubs.acs.org/ac

Candidate Reference Measurement Procedure for the Determination of (24*R*),25-Dihydroxyvitamin D3 in Human Serum Using Isotope-Dilution Liquid Chromatography–Tandem Mass Spectrometry

Susan S.-C. Tai* and Michael A. Nelson

Table 3. Estimation of Expanded Uncertainties for LC–MS/MS Measurement of Serum (24*R*),25(OH)$_2$D3

	conc 1	conc 2	conc 3
mean, ng/g	1.58	2.60	3.06
type A			
SD of mean, ng/g	0.003	0.015	0.008
type B			
0.8% uncertainty of purity of ref std, ng/g	0.013	0.021	0.024
0.1% uncertainty of weighing, ng/g	0.002	0.003	0.003
1% uncertainty of unidentified systematic biases, ng/g	0.016	0.026	0.031
combined standard uncertainty (u), ng/g	0.021	0.037	0.040
coverage factor (k)	2	2	2
expanded uncertainty (U)[a], ng/g	0.041	0.073	0.081
rel expanded uncertainty, %	2.6	2.8	2.6

[a]Uncertainty of 95% confidence interval.

(mix)

1. Introduction
2. U and RMP
3. Performance criteria
4. Conclusions

*contents

IFCC International Federation of Clinical Chemistry and Laboratory Medicine | JCTLM | **RELA - Homepage** External quality control for Reference Laboratories | RfB Referenzinstitut für Bioanalytik

Home -

Welcome

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Registration/ Accou

RELA in progress

order RELA 2017

enter RELA 2017 results

former RELA results

Choose year...

RELA - IFCC External Quality assessment scheme for Reference Laboratories in Laboratory Medicine

This site gives you all the information you will need for participating in the RELA scheme.

Time schedule for the annual surveys (may vary slightly)

Announcement: September 1
Deadline for ordering: September 30
Shipment of samples: October 15
Deadline for transmission of results: April 15 (following year)
Reporting results to participants: May 15
Publishing results on this website: June 15

Please refer to the navigation area on the left to (for instructions see our new RELA web manual)
- register or log in
- order the survey
- entering your results
- get the evaluation of past surveys

The whole RELA process is described in detail in the **IFCC-RELA-EQAS procedure manual**.

Offered measurands:
Metabolites and substrates (META): total cholesterol, total glycerol, creatinine, uric acid, urea, glucose, total bilirubine
Electrolytes (ELEC): sodium, potassium, chloride, calcium, lithium, magnesium
Enzymes (ENZY): ALT, AP, AST, CK, LDH, GGT, amylase
Glycated hemoglobins (GLYC): HbA1c
Proteins (PROT): total protein
Hormones (HORM): aldosterone, cortisol, progesterone, testosterone, estradiol-17ß, estriol, 17-OH-progesterone
Thyroid hormones (THYR): total thyroxine (TT4), total tri-iodthyronine (TT3), free thyroxine (ft4)
Therapeutic drugs (THER): digoxin, digitoxin, theophylline
Vitamins (VITA): 25-OH-vitamin D3

RELA 2016

- ALT
- Total
- HbA

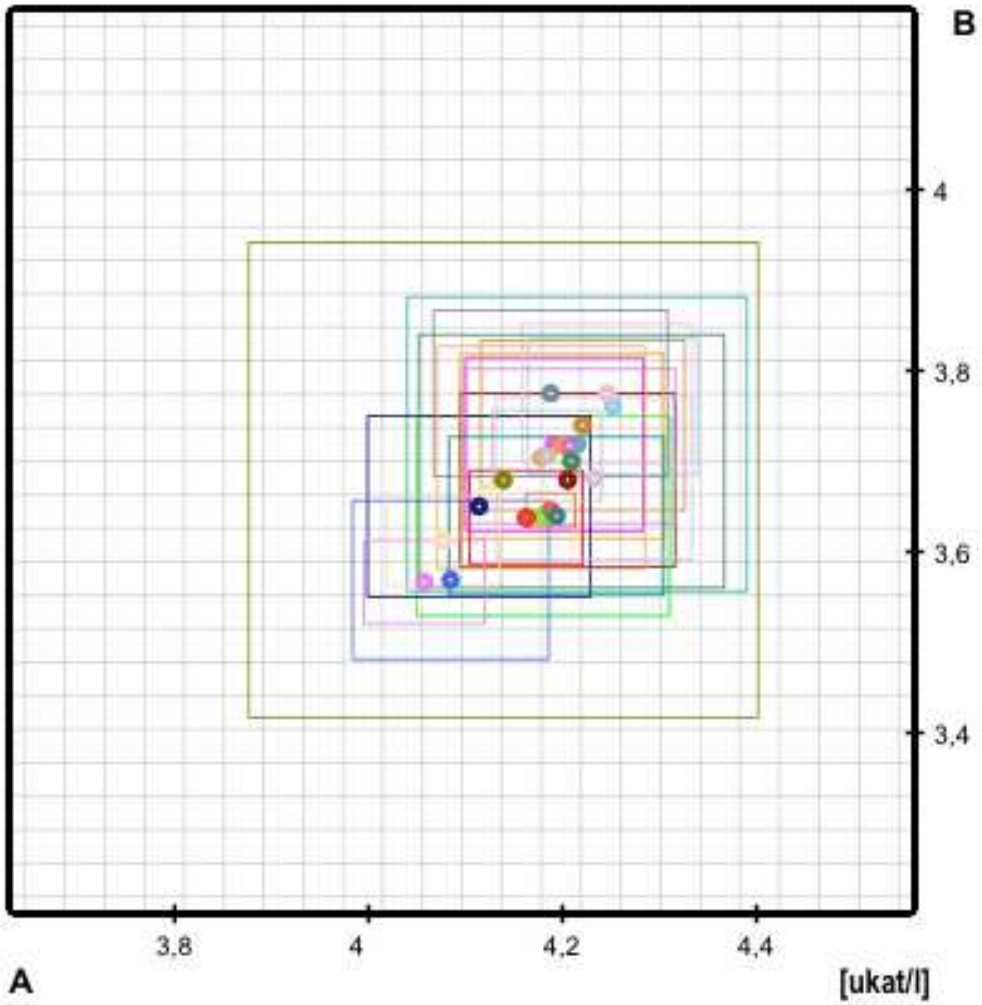
All or choose Lab ...

select lab analytes | full address

ALT | show result plot

with limits of equivalence

ALT



For highlighting a specific result please click on the corresponding result line.

Result lines printed in bold indicate JCTLM listed services.

Labcode	A	e.u. A	B	e.u. B	Method
3	4.191	0.092	3.718	0.096	Kinetic spectroscopy
12	4.206	0.111	3.679	0.096	Kinetic spectroscopy
27	4.22	0.106	3.74	0.094	Kinetic spectroscopy
41	4.18	0.13	3.64	0.11	Kinetic spectroscopy
47	4.252	0.088	3.76	0.075	Kinetic spectroscopy
48	4.215	0.176	3.718	0.162	Kinetic spectroscopy
51	4.123	0.087	3.666	0.081	Kinetic spectroscopy
54	4.188	0.121	3.774	0.093	Kinetic spectroscopy
55	4.113	0.115	3.651	0.099	Kinetic spectroscopy
61	4.199	0.105	3.717	0.102	Kinetic spectroscopy

✓ All or choose Lab ...
001 - Referenzinstitut für Bio , Dr. C. Ritter-Sket
003 - Medizinische Hochschule , Dr. D. Grote-Koska
005 - Roche Diagnostics GmbH , Herrn Gernot Brunny
006 - UOC Patologia Clinica , CIRME-Prof. Mauro Panteg
008 - Physikalisch-Technische , Dr. Henrion, Dr. Rienitz
011 - Ref4U, Laboratory of Tox , Dr. Katleen Van Uytfangh
012 - Fundacion Bioquimica Arg , Raul Girardi
018 - National Center for Clin , Prof. Wenxiang Chen
019 - Reference Material Insti , Eri Shimizu
023 - BioSystems, S.A. , Prof. D. Gella
024 - Children´ Hospital of Wi , Stanley F. Lo, Ph.D., DA
025 - Deputy Director , Dr. David Ducroq
027 - Instand e. V. , Dr. Patricia Kaiser
030 - Centers for Disease Cont , Julianne Cook Botelho, P
039 - Canadian EQA Laboratory , David W. Seccombe, MD, P
041 - Roche Diagnostics GmbH , Rolf Nagel
046 - Clinical Enzymology Refe , Francesca Canalias
047 - Beijing Aerospace Genera , Chen Baorong
048 - Biosino Bio-Technology a , Jiang lin
051 - Maccura Biotechnology Co , Sun Keqi
052 - Queen Beatrix Hospital , Cas Weykamp
054 - Shanghai Center for Clin , Ju Yi
055 - Reference Laboratory , Chi Shan
061 - Mindray Standardization , Wang Yingguo
063 - Beijing Leadman Biochemi , Chunlong Liu
065 - Clinical Laboratory of , Prof. Xianzhang Huang
073 - Department of clinical l , Runqing Mu
074 - Center of Laboratory Med , Dr. Huimin Wang
077 - Department of Laboratory , Rui Zhang
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104 - Department of Reference , Wang Xiaojian
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121 - Korea CDC, , Jeong-Ho Kim (Yonsei Uni
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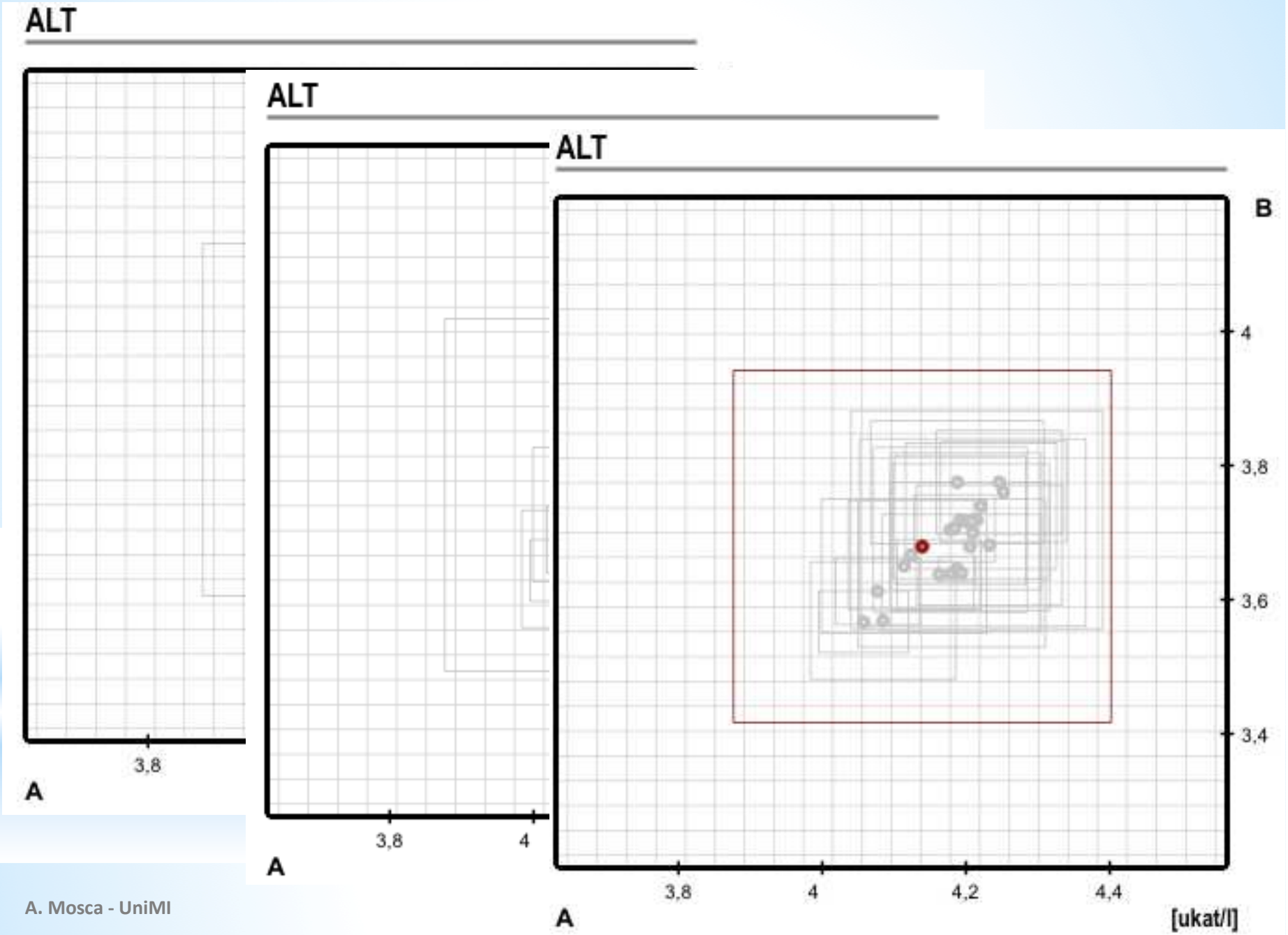
137 - JUSBIO SCIENCES (SHANGHA , huangyiqing
138 - Building C, No 38, Panor , Beijing Bio-top Co., LTD
139 - Beijing Wantai Derui Dia , Yang Yongchao
140 - Guangzhou KOFA Biotechno , Liao Wuyang
143 - Ningbo Ruiyuan Biotechno , Li Zhang
145 - Institut für Diabetestec , Dr. med. Guido Freckmann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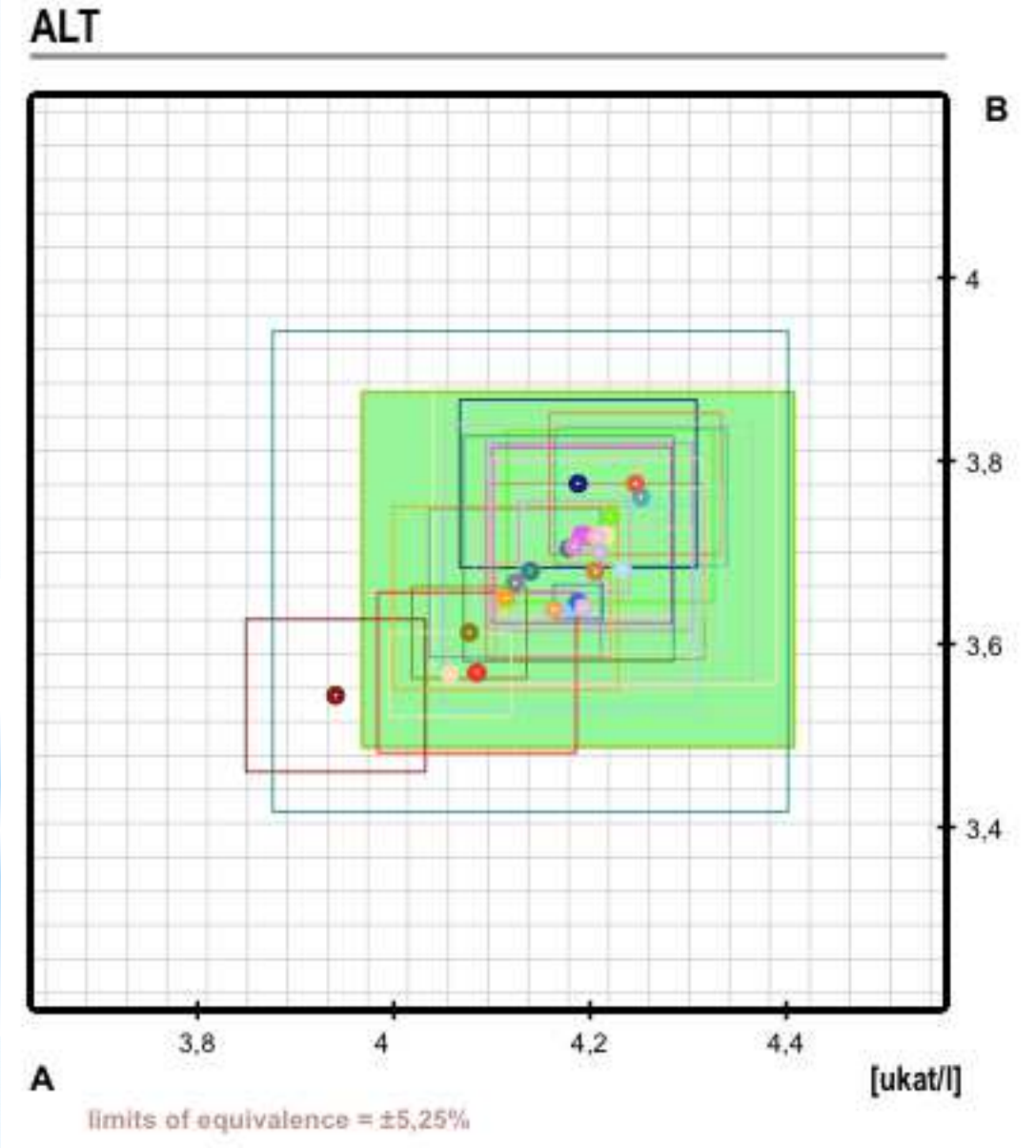
RfB Referenzinstitut für Bioanalytik

RELA 2016



TITLE: IFCC EXTERNAL QUALITY ASSESSMENT SCHEME FOR REFERENCE (CALIBRATION) LABORATORIES IN LABORATORY MEDICINE - PROCEDURES

IFCC – C-TLM

IFCC EXTER
SCHEME FOR
LABORATORIE

According to the decision to the SD Executive the limits of equivalence are currently set to 25 % of the performance limits for routine laboratories prescribed by the directive for External Quality Assurance for routine laboratories in Germany (valid from April 1, 2008).
In Table 1 all limits of equivalence for measurands offered in RELA ring surveys are listed. This list has to be supplemented as soon as new measurands are introduced.

Table 1(Part 1): Measurands and the corresponding Limits of Equivalence

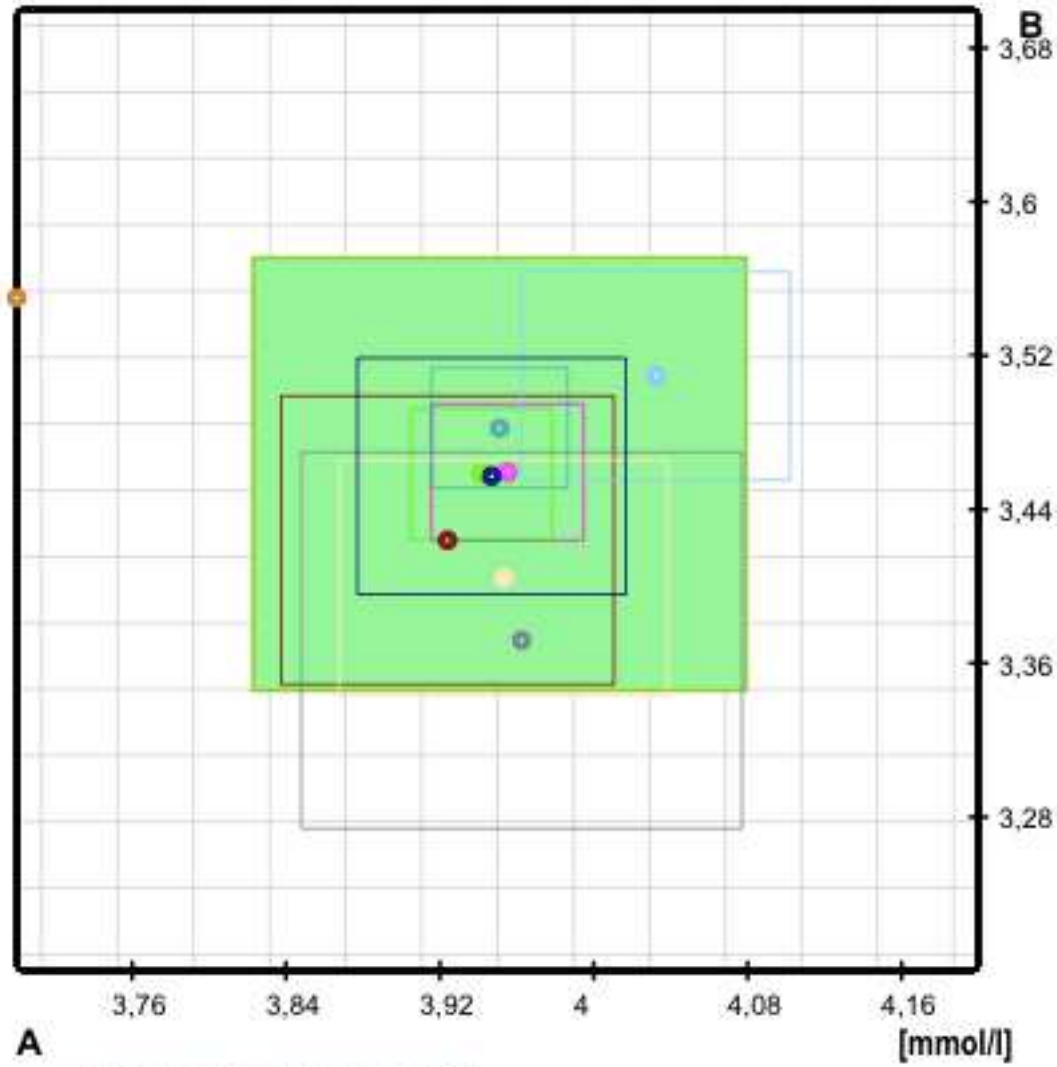
Group	Measurand	Limits of Equivalence [%]
Metabolites and Substrates (META)	Total Cholesterol	+/- 3.25
	Total Glycerol	+/- 4.0
	Creatinine	+/- 5.00
	Uric Acid	+/- 3.25
	Urea	+/- 5.00
	Glucose	+/- 3.75
	Total Bilirubine	+/- 5.50
Electrolytes (ELEC)	Sodium	+/- 1.25
	Potassium	+/- 2.00
	Chloride	+/- 2.00
	Calcium	+/- 2.50
	Lithium	+/- 3.00
	Magnesium	+/- 3.75
Enzymes (ENZY)	ALT	+/- 5.25
	AST	+/- 5.25
	CK	+/- 5.00
	LDH	+/- 4.50
	GGT	+/- 5.25
	Amylase	+/- 5.25
Glycated Hemoglobins (GLYC)	HbA1c	+/- 4.50
Proteins (PROT)	Total Protein	+/- 2.50

RELA 2016

- Total Cholesterol
- HbA

RELA 2016

Total cholesterol



limits of equivalence = ±3,25%

Cholesterol Reference Method Laboratory Network (CRMLN)

Survey Evaluation Report

Pool Series
PS0717

Survey Date: 7/31/2017
Report Date: 11/1/2017

Total cholesterol – AK
4 samples, in duplicate, over 2 different days

CRMLN Survey Evaluation Report

Total Cholesterol Abell-Kendall (TC-AK) Method

Pool Series: PS0717

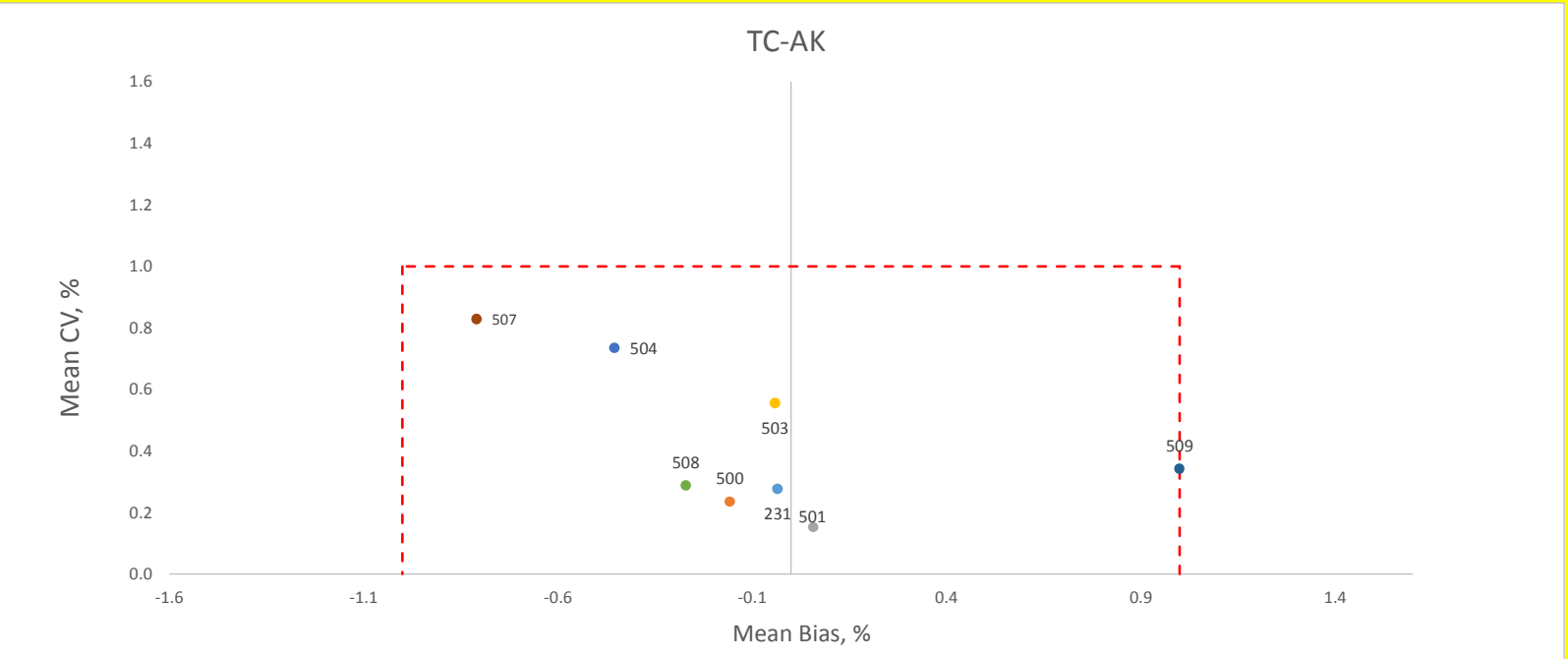
Lab #	Sample #	Mean, mg/dL	S.D., mg/dL	C.V., %	Bias vs. Overall Laboratory Mean, %	Bias vs. CDC, %	Mean CV,%	Mean Bias,%
231	1	169.45	0.29	0.2	0.3	0.3	0.3	0.0
	2	174.30	0.78	0.4	0.3	-0.1		
	3	185.95	0.75	0.4	-0.2	0.3		
	4	238.03	0.21	0.1	-0.1	-0.6		
500	1	169.26	0.45	0.3	0.1	0.2	0.2	-0.2
	2	173.47	0.23	0.1	-0.2	-0.6		
	3	186.33	0.50	0.3	0.0	0.5		
	4	237.76	0.64	0.3	-0.3	-0.7		
501	1	168.90	0.34	0.2	-0.1	0.0	0.2	0.1
	2	173.86	0.17	0.1	0.0	-0.4		
	3	186.78	0.27	0.1	0.3	0.7		
	4	239.22	0.41	0.2	0.4	-0.1		
[illegible]	1	169.36	0.77	0.5	[illegible]	[illegible]	0.6	0.0

Overall	1	169.01	0.74	0.4	-	0.0	0.4	-0.1
	2	173.84	0.60	0.3	-	-0.4		
	3	186.26	0.88	0.5	-	0.5		
	4	238.36	1.07	0.5	-	-0.5		

Sample	Target Value, mg/dL
1	168.97
2	174.49
3	185.42
4	239.46

Performance Criteria, %	
Overall Bias	±1.0
CV	

Summary of Laboratory Performance



Dashed lines represent analytical performance limits

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- Total
- HbA_{1c}

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External quality control for Reference Laboratories

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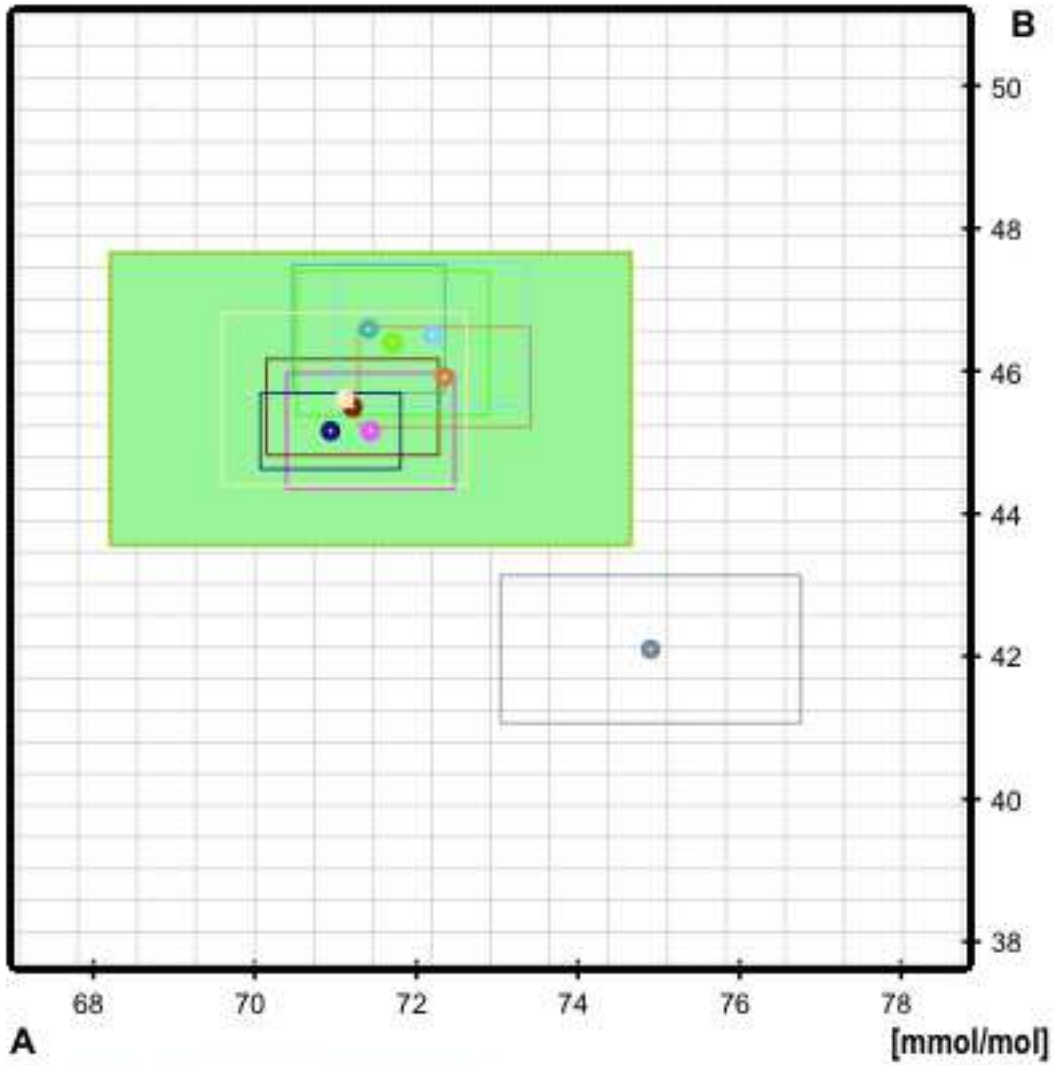
HbA1c



limits of equivalence = ±4,50%

Network on HbA_{1c} Standardization

2016

REPORT

Intercomparison Studies

Shanghai-1 and Shanghai-2

of the

IFCC Network on Standardisation of HbA_{1c}

Design

The design of the studies is essentially the same as in the past years and covers the following issues:

a. Re-approval network laboratories
b. Approval candidate network laboratories
c. Long-term verification of network stability: reproducibility of previous samples
d. Long-term verification of network stability: reproducibility calibrators and approval of new calibrators
e. Relation IFCC Reference Method and Designated Comparison Methods
f. Value assignment and Expanded Uncertainty Intercomparison Samples

Samples

The design includes different types of samples in the Shanghai studies:

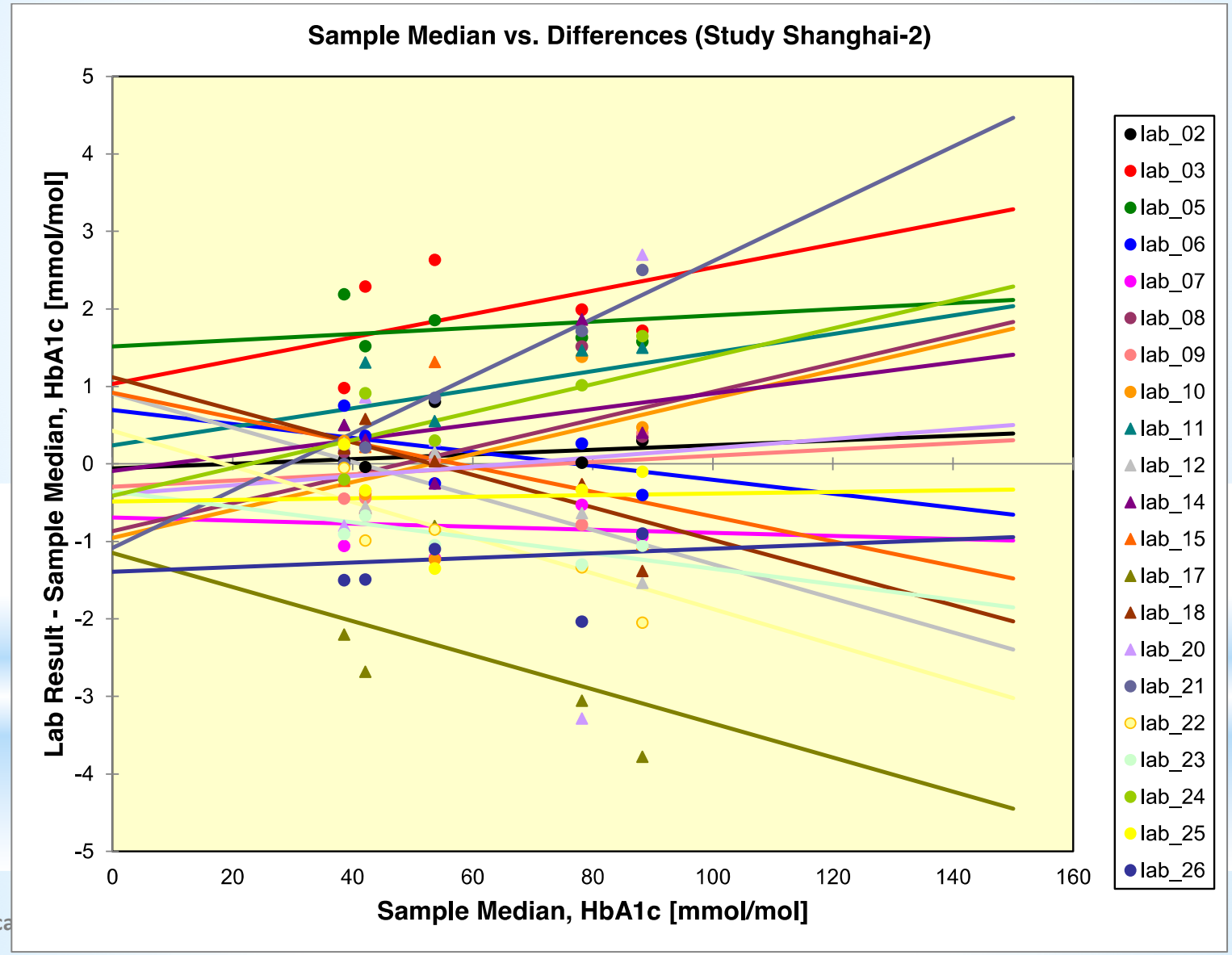
- Five intercomparison samples in the Shanghai-1 study (labels Shanghai 1 to Shanghai 5) and five intercomparison samples in the Shanghai-2 study (labels Shanghai 6 to Shanghai 10)
- Three control samples: LTPC-1 in both the Shanghai-1 and 2 study, Berlin 8 in the Shanghai-1 study and Milano 1 in the Shanghai-2 study.
- Six calibrators to be used as calibrators in both the Shanghai-1 and Shanghai-2 study (labels pcal 2012-A to 2012-F)
- Two old calibrators to check stability, LTCC-1 in the Shanghai-1 study; CalCheck 58 (pcal 2011-D) in the Shanghai-2 study.
- Six new calibrators to check/approve the new lot calibrators (pcal 2016-A, C and E in the Shanghai-1 study and pcal 2016-B, D and F in the Shanghai-2 study)

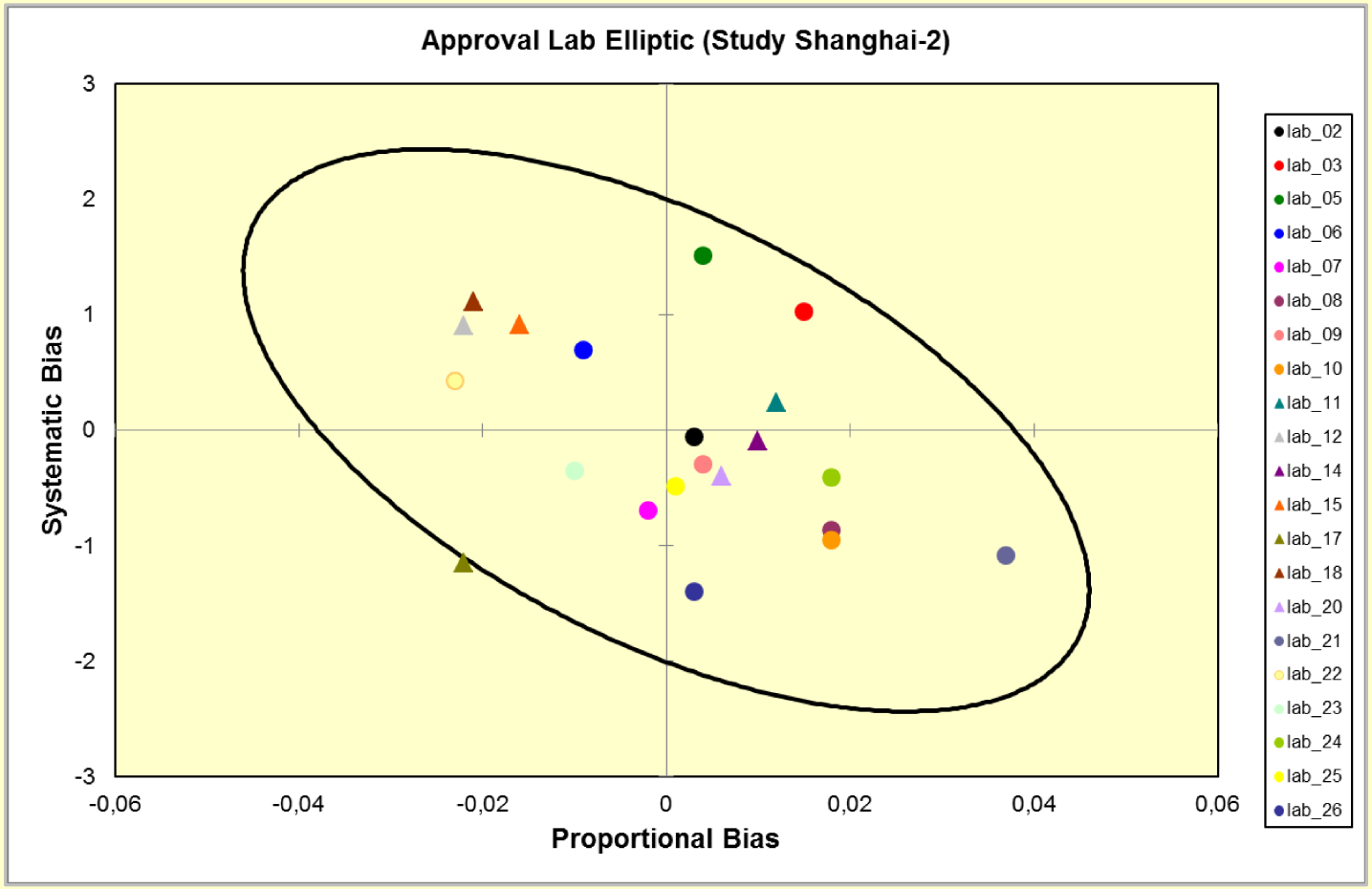
Ad a. Re-approval of approved network laboratories

To keep the status of approved network laboratory, network laboratories must participate in the intercomparison study of the network. A lab loses its status when it fails in two consecutive studies, when it does not submit results in two consecutive studies or in case it fails in one study and did not submit results for the second one.

For pass or failure of a lab the data of all intercomparison samples are examined together. The differences between the results of a lab and the overall median are plotted against the overall median of the network labs and from the linear relation the slope (proportional bias) and the intercept (systematic bias) are calculated. Slope and intercept together determine a criterion: when a lab has a higher value than this criterion it fails.

HbA_{1c}
5 samples, in duplicate, over 2 different days





Combined Statistical Test Critical Value 10.6
0,1
6,9
7,1
0,9
1,5
1,9
0,2
2,1
1,7
2,5
0,7
1,8
11,2
2,9
0,3
6,7
2,8
1,5
1,7
0,5
4,4

Accred Qual Assur (2006)
DOI 10.1007/s00769-006-0113-0

GENERAL PAPER

Andrea Konnert
Sabine Arends
Stefan Schubert
Christoph Berding
Cas Weykamp
Carla Siebelder

Uncertainty calculation for calibrators of the IFCC HbA1c standardization network

Table 1 Uncertainty components and sensitivity coefficients of primary calibrators

Uncertainty component	Sensitivity coefficient $\partial f / \partial x_i$
$\bar{c}_{hb(A0)}$	$\dfrac{w^j_{hb(A1c)} \cdot \bar{c}_{hb(A1c)} \cdot (i_{A0/A1c} - 100) \cdot w^j_{hb(A0)}}{\bar{c}^2_{hb}}$
$\bar{c}_{hb(A1c)}$	$-\dfrac{w^j_{hb(A0)} \cdot \bar{c}_{hb(A0)} (i_{A0/A1c} - 100) \cdot w^j_{hb(A1c)}}{\bar{c}^2_{hb}}$
$w^j_{hb(A1c)}$	$\dfrac{w^j_{hb(A1c)} \cdot \bar{c}_{hb(A1c)} \cdot (i_{A0/A1c} - 100) \cdot \bar{c}_{hb(A0)}}{\bar{c}^2_{hb}}$
$w^j_{hb(A0)}$	$-\dfrac{w^j_{hb(A0)} \cdot \bar{c}_{hb(A0)} \cdot (i_{A0/A1c} - 100) \cdot \bar{c}_{hb(A1c)}}{\bar{c}^2_{hb}}$
$i_{A0/A1c}$	$-\dfrac{w^j_{hb(A1c)} \cdot \bar{c}_{hb(A1c)}}{\bar{c}_{hb}}$

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Uncertainty due to measurement

After appropriate data analysis of the measured data points, the means of the measured results become the assigned values of the secondary calibrators. The uncertainty component due to the measurement error of the reference method is calculated considering the nested measurement design (laboratory, digestion, repetition) for each sample. The between-laboratory, between-digest, and within-digest variances enter the calculation of the uncertainty component of the secondary calibrators in the following way:

$$u(c_{\mathrm{scal}})_{\mathrm{meas}} = \sqrt{\frac{1}{L}u^2_{b.-lab} + \frac{1}{L \cdot D}u^2_{b.-dig} + \frac{1}{L \cdot D \cdot R}u^2_{w.-dig}},$$

where L denotes the number of laboratories, D the number of digests and R the number of repetitions (see also

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Table 3 Uncertainty contributions, bias and 95% confidence intervals for the secondary calibrators from the Orlando 2 study according to GUM

Secondary calibrator	Uncertainty measurement (%)	Uncertainty calibration (%)	Combined uncertainty (%)	Bias (%)	Lower limit ($k=2$) (%)	Assigned value (%)	Upper limit ($k=2$ + bias) (%)
Orlando 6	0.034	0.018	0.038	0.019	6.32	6.40	6.50
Orlando 7	0.027	0.011	0.029	0.019	3.90	3.96	4.04
Orlando 8	0.037	0.025	0.045	0.018	8.39	8.48	8.59
Orlando 9	0.042	0.018	0.046	0.019	5.62	5.71	5.82
Orlando 10	0.017	0.010	0.019	0.019	3.44	3.48	3.54

1. Introduction
2. U and RMP
3. Performance criteria
4. Conclusions

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Analyte	Lab	Sample	mean	e.u.	e.u.,%
ALT	77	A	4.187	0.0026	0.06
	77	B	3.645	0.0018	0.05
	137	A	4.14	0.262	6.33
	137	B	3.68	0.262	7.12
Cholesterol	39	A	3.951	0.0035	0.09
	39	B	3.482	0.031	0.89
	119	A	3.963	0.115	2.90
	119	B	3.372	0.098	2.91
HbA1c	121	A	70.94	0.886	1.25
	121	B	45.15	0.542	1.20
	139	A	74.9	1.85	1.85
	139	B	42.1	1.04	2.47

Conclusions

* Too many RMPs (?)
* The expression of U is not always present in RMPs
* Few networks have taken into account the U issue
* Performance criteria are also heterogeneous

Future perspectives

* Need to update the RMPs
* Need for eliminate the old ones
* Need to define consensus documents

Acknowledgments

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