How to use the best of your QA data

Dubrovnik Course in Zagreb 2015

Gunnar Nordin

EQUALIS

The topics

- Evaluate your QC results!
  Be interested. Discuss them at the lab and with friends.

- Why are my, and not others, results out of limits?

  “The EQA material is not commutable”
  “The assigned target value is not correct”
  “The EQA material is not stable”

- There are too many ways to express “accuracy”

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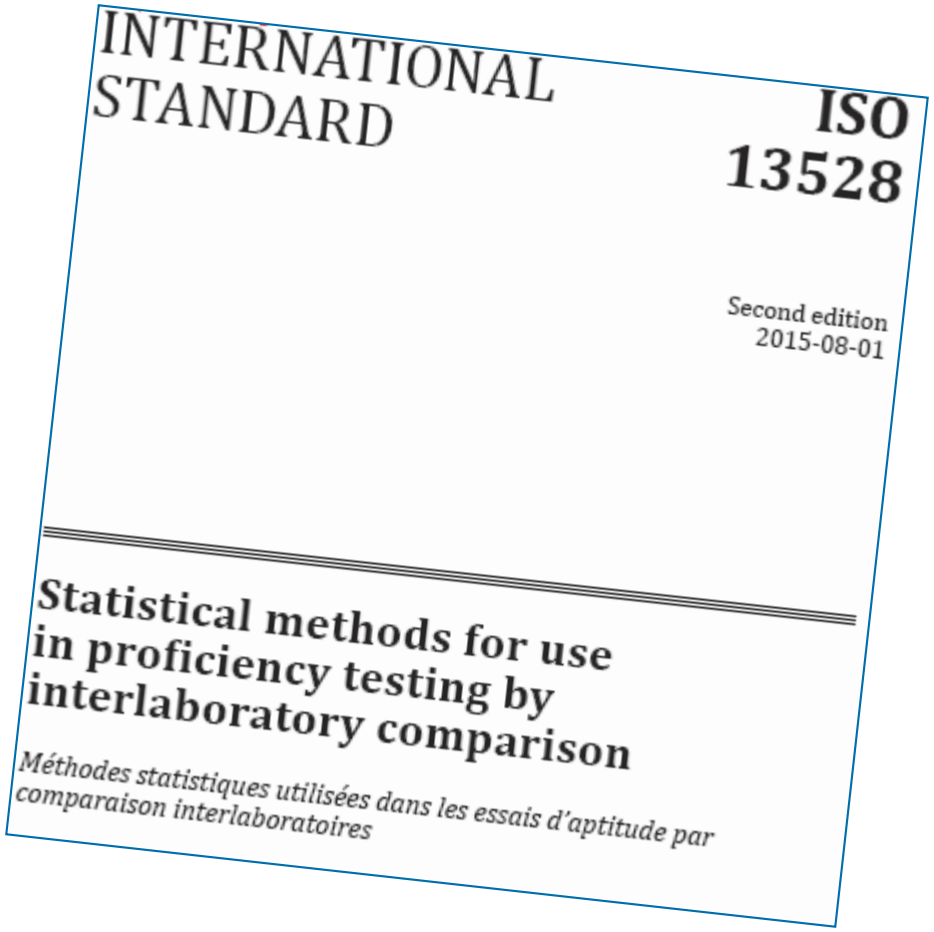
Standard for the evaluation of a participant in an EQA scheme


INTERNATIONAL STANDARD

ISO 13528

Second edition
2015-08-01

Statistical methods for use in proficiency testing by interlaboratory comparison

Méthodes statistiques utilisées dans les essais d'aptitude par comparaison interlaboratoires

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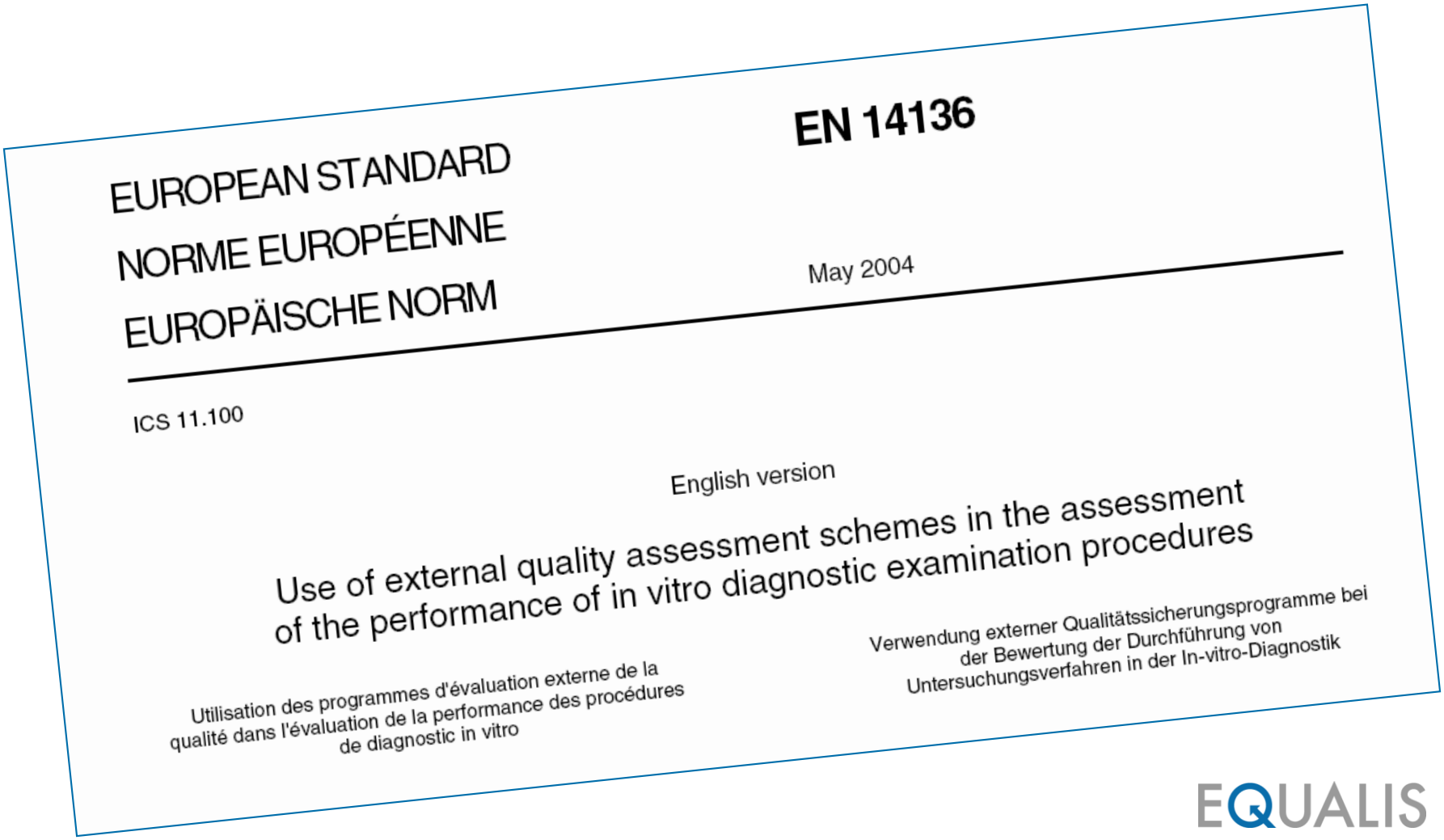
Standard for assessment of IVD procedures



EUROPEAN STANDARD

NORME EUROPÉENNE

EUROPÄISCHE NORM

EN 14136

May 2004

ICS 11.100

English version

Use of external quality assessment schemes in the assessment of the performance of in vitro diagnostic examination procedures

Utilisation des programmes d'évaluation externe de la qualité dans l'évaluation de la performance des procédures de diagnostic in vitro

Verwendung externer Qualitätssicherungsprogramme bei der Bewertung der Durchführung von Untersuchungsverfahren in der In-vitro-Diagnostik

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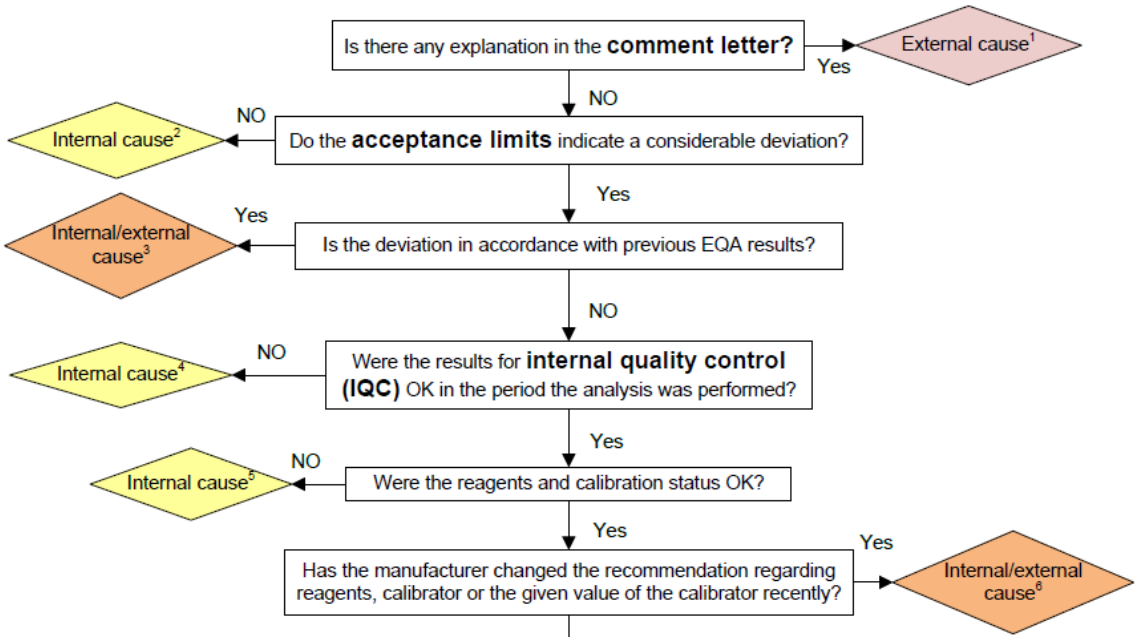
A flowshart for deviating EQA-results

NKK
Norsk Klinisk-kjemisk Kvalitetssikring

FLOWCHART FOR HANDLING DEVIATING EQA-RESULT

Gunn B B Kristensen, Kristine Solem and Pål Rustad
NKK, Norsk Klinisk-kjemisk Kvalitetssikring
e-mail:gunn.kristensen@noklus.no



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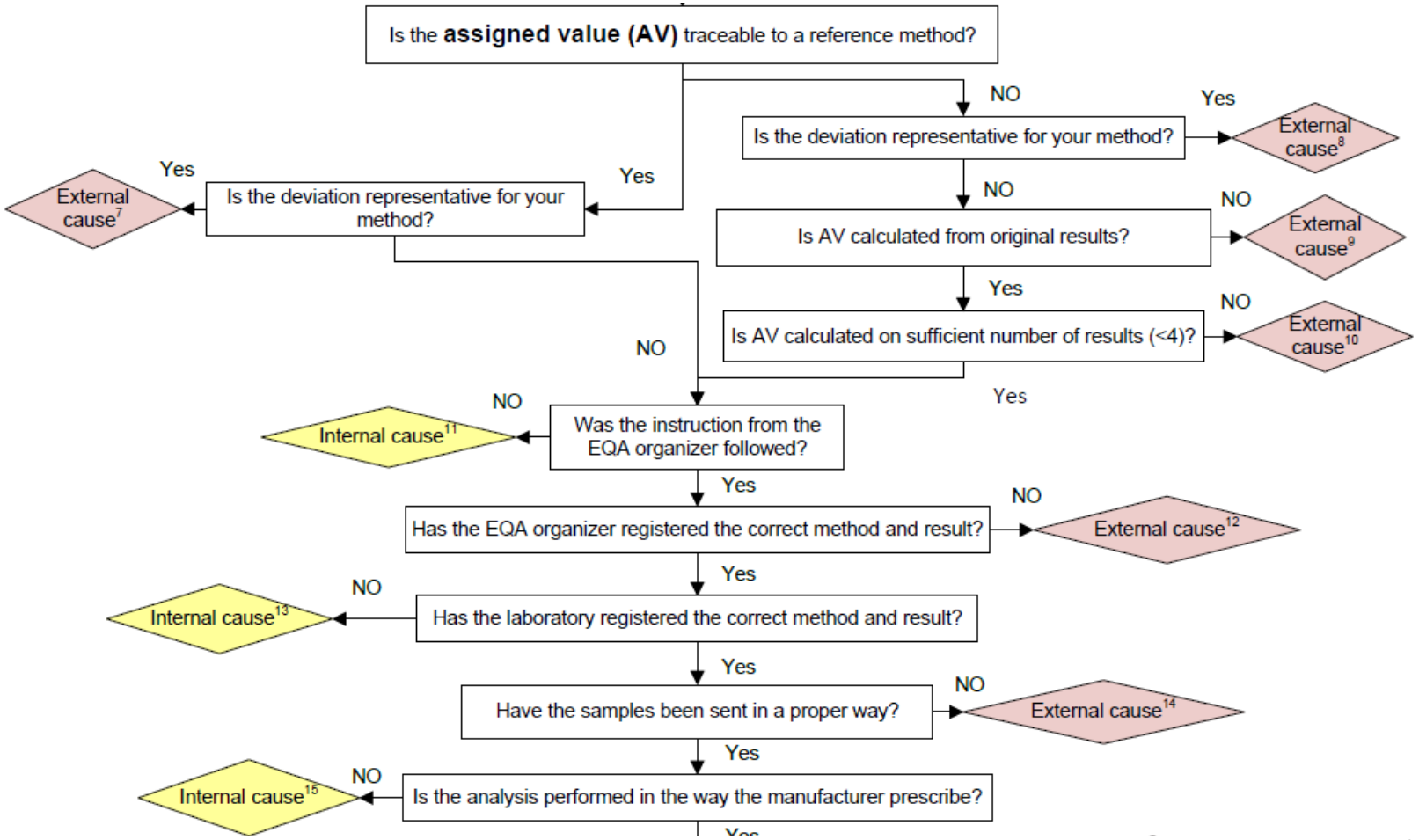
A flowshart for deviating EQA-results



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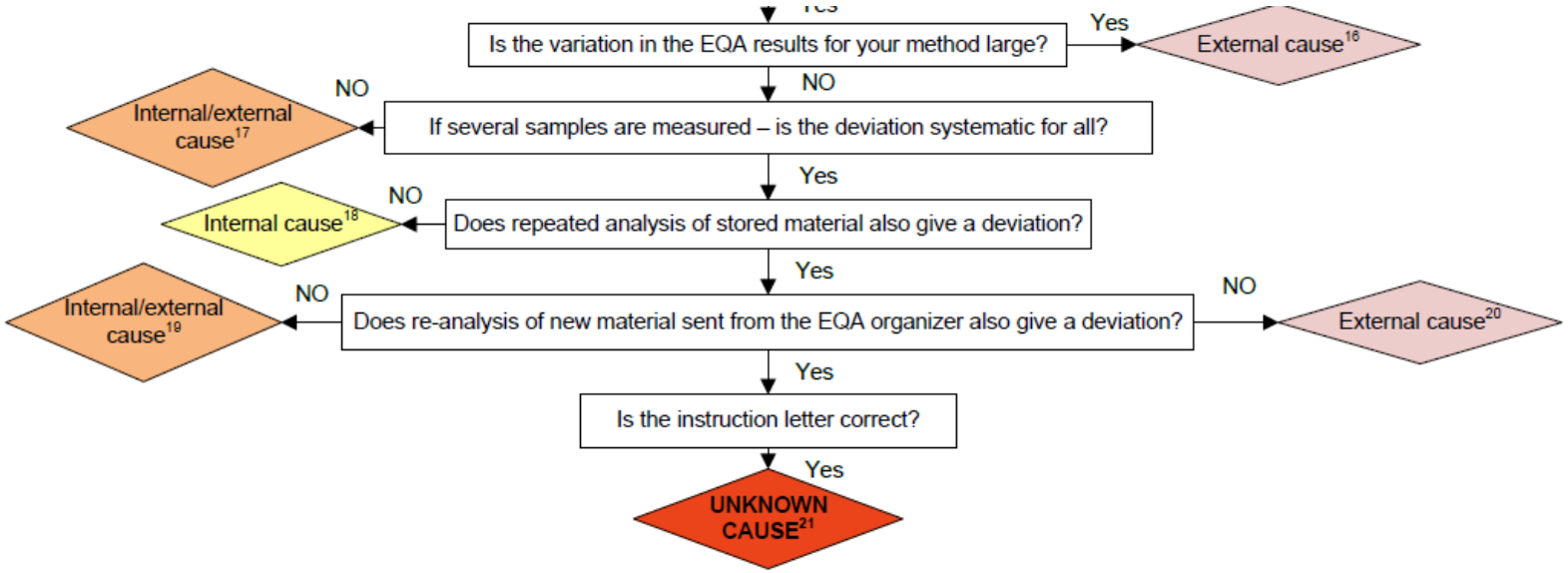
A flowshart for deviating EQA-results



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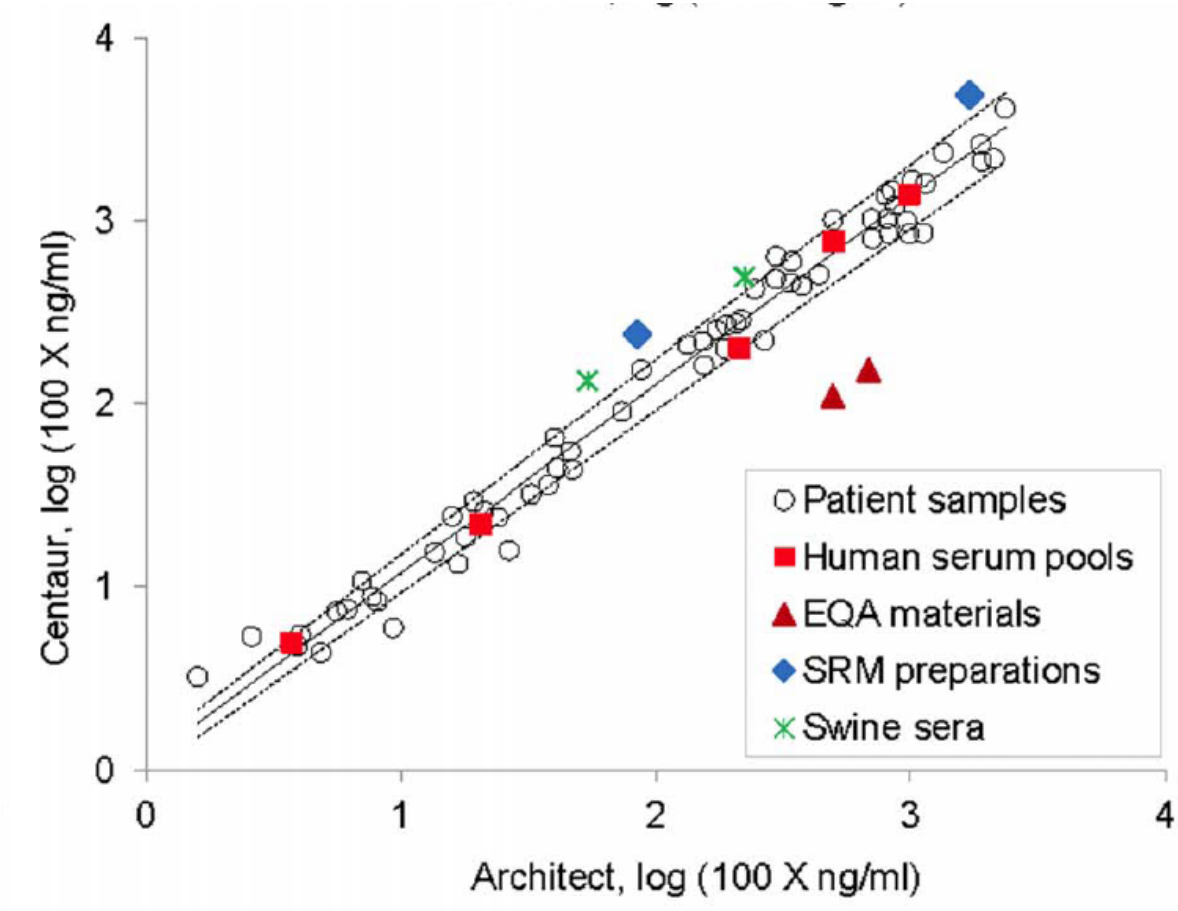
EQA material should be commutable



Zhang et al, Commutability of Possible External Quality Assessment Materials for Cardiac Troponin Measurement, 2014

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EQA material should be stable

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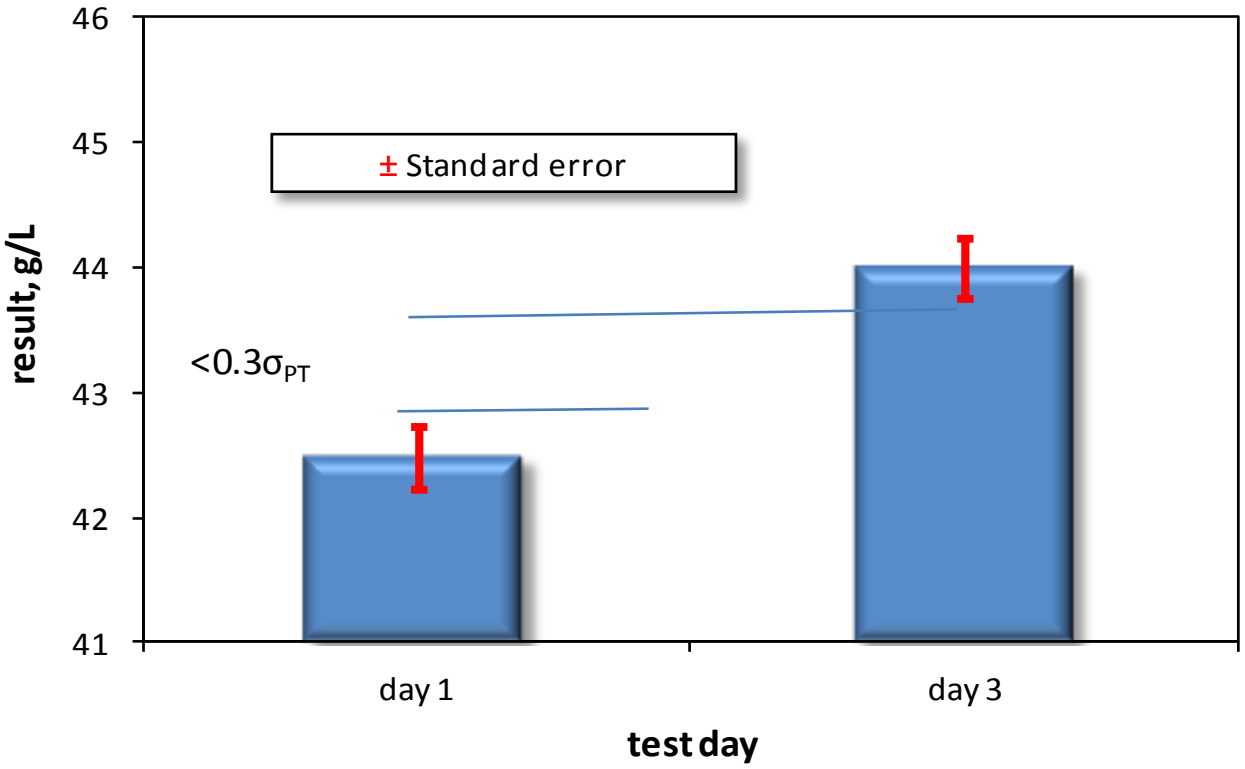
ISO 13528:2015

$$|\bar{y}_1 - \bar{y}_2| \leq 0{,}3\sigma_{pt} + 2\sqrt{u(\bar{y}_1)^2 + u(\bar{y}_2)^2}$$

Stability tested by repeated measurments at one site at the day of distribution and at the last day for the round.



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The target value for a EQA material should be a true value

1. Target value known by formulation
2. Target value from by reference measurement procedure
3. Target value by ’expert laboratory methods’
4. Target value by consensus mean

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The consensus value is often not a true value

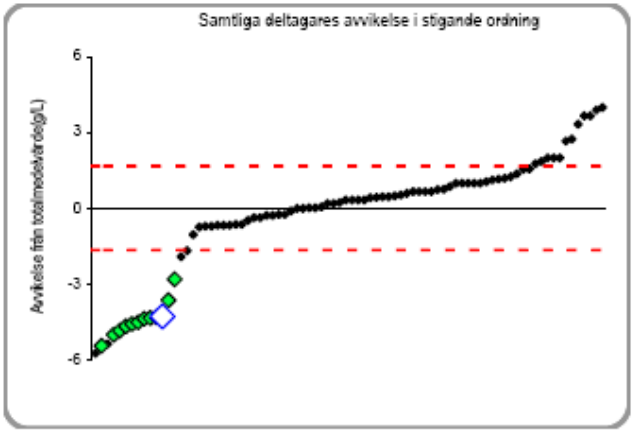
Instrument: Vitros 5,1 FS--VVI01

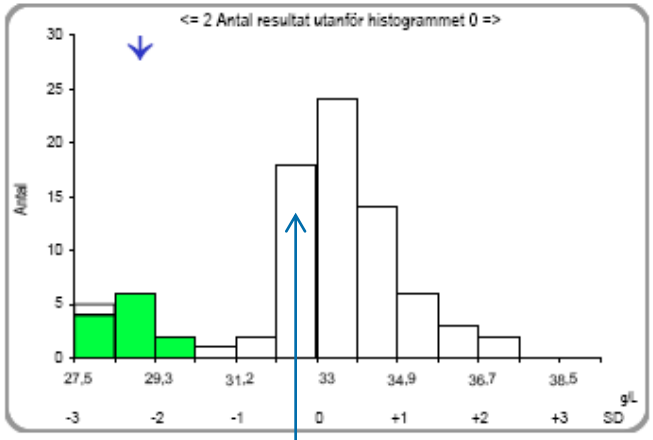
P-Albumin (g/L)

Kvalitetsmål (%): +/- 5

Egen rapportgrupp: Ortho

		Egen rapportgrupp (13)		Samtliga (85)	
Eget resultat:	28,73	Medelvärde:	28,5	Medelvärde:	33,0
		SD:	0,67	SD:	1,84
Åsatt värde:	-	CV%:	2,3	CV%:	5,6
		Egen avvikelse		Egen avvikelse	
		Absolut (enheter):	+0,27	Absolut (enheter):	-4,28
		Relativ (%):	+0,9	Relativ (%):	-13,0
		Antal SD	+0,40	Antal SD	-2,33
		Medelavvikelse%:	+1,12	Medelavvikelse%:	-8,4
		(senaste 9 omgångarna)		(senaste 9 omgångarna)	





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Consensus value

”Mean of method mean” (MOMM)

Mean of the major and homogenous method group mean values

Deviating method groups are excluded

Small method groups are excluded

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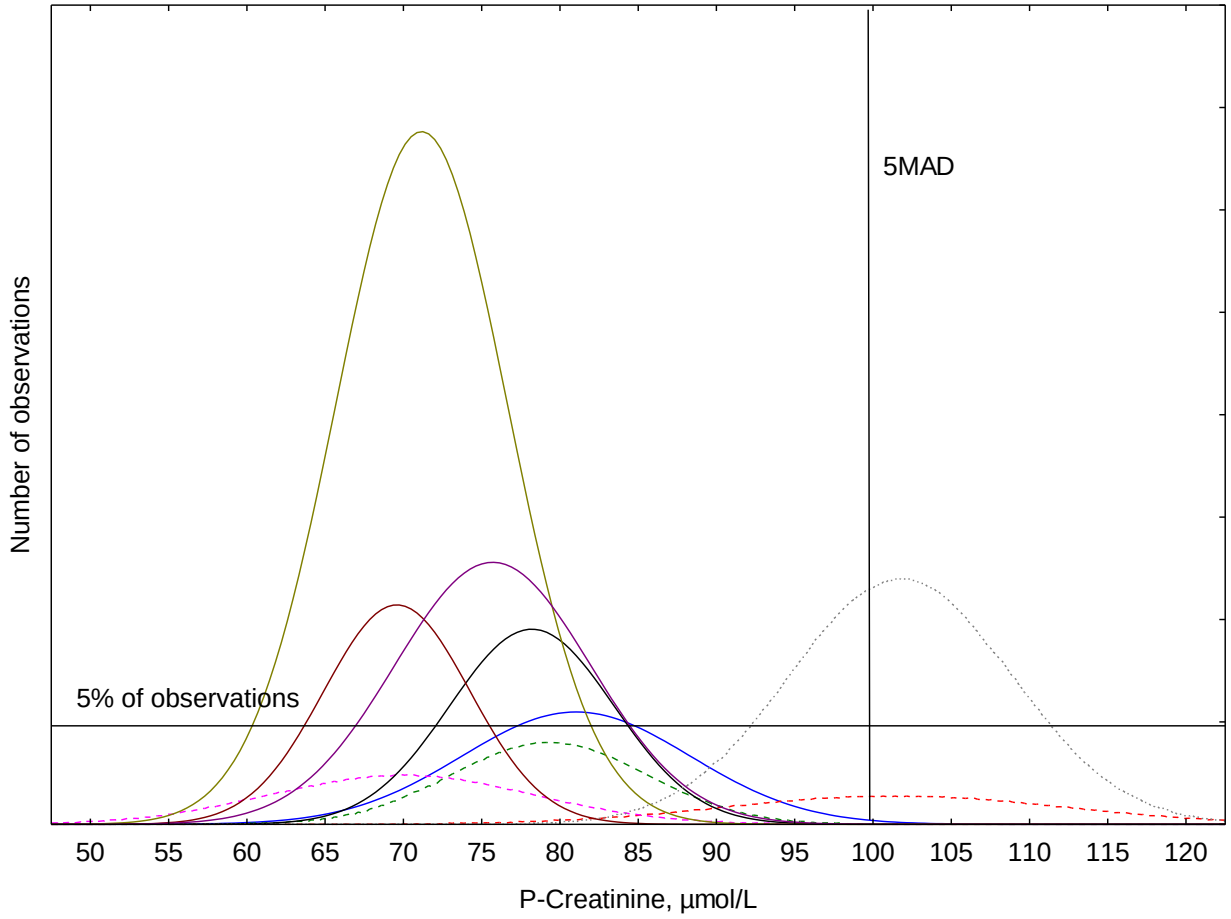
”Mean of method mean” (MOMM)



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”Mean of method mean” (MOMM)

Do you think MOMM is a more realiable target value than the consensus mean?

Yes ?

No ?

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Uncertainty is clearly defined

2.26 (3.9)
measurement uncertainty
uncertainty of measurement
uncertainty

non-negative parameter characterizing the dispersion of the **quantity values** being attributed to a **measurand**, based on the information used

NOTE 1 Measurement uncertainty includes components arising from systematic effects, such as components associated with **corrections** and the assigned quantity values of **measurement standards**, as well as the **definitional uncertainty**. Sometimes estimated systematic effects are not corrected for but, instead, associated measurement uncertainty components are incorporated.

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What is accuracy?

2.13 (3.5)
measurement accuracy
accuracy of measurement
accuracy

closeness of agreement between a **measured quantity value** and a **true quantity value** of a **measurand**

NOTE 1 The concept 'measurement accuracy' is not a **quantity** and is not given a **numerical quantity value**. A **measurement** is said to be more accurate when it offers a smaller **measurement error**.

"more" or "less" are results on an ordinal scale

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Is it possible to measure accuracy?

Yes

No

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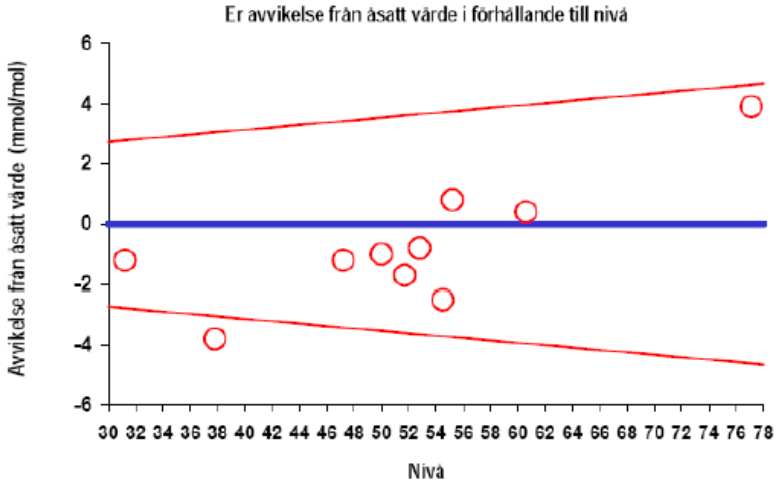
One type of measure of accuracy

Fraction of results within quality specifications

Förslag till tolkning av resultat från externkontroll

Mål för noggrannhet: Figuren till höger visar avvikelse från åsatt värde för 10 utskick för en deltagare i Equalis kvalitetssäkrings-program för HbA1c. Ett (1) resultat ligger utanför den rödmarkerade gränsen för



A pragmatic approach for POCT HbA1c in Sweden:

Max 2 of 10 results outside the limits

gränserna som maximalt kan accepteras:

- För upp till 3 kontrollresultat: Alla måste vara inom gränserna för kvalitetsmålet.
- För 4 – 9 kontrollresultat: Maximalt ett (1) resultat utanför gränserna för kvalitetsmålet.
- För 10 – 11 kontrollresultat: Max två (2) resultat utanför gränserna för kvalitetsmålet.

I figuren ovan är ett (1) av 10 resultat utanför kvalitetsmålsgränsen, vilket alltså kan accepteras.
Mål för systematisk avvikelse: För de 6 senaste utskicken får genomsnittsavvikelsen inte vara utanför ± 1,5 mmol/mol. Värdet beräknas i resultatrapporten från Equalis.

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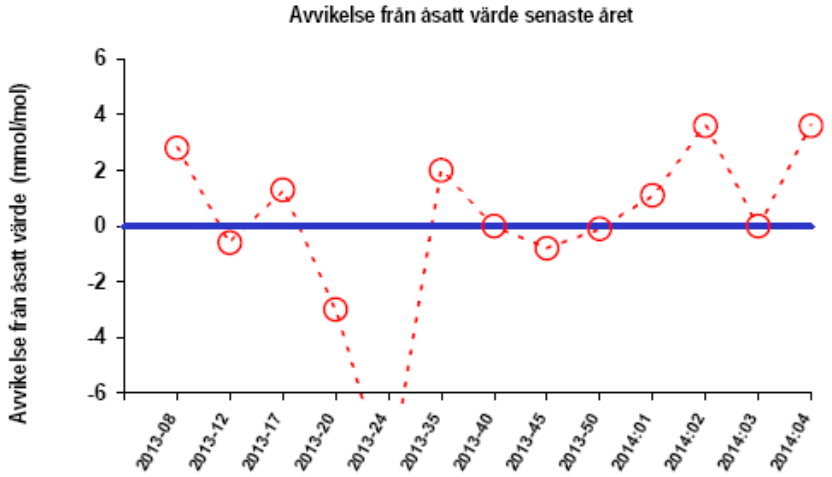
Accuracy and bias reported to participants in Equalis HbA1c scheme

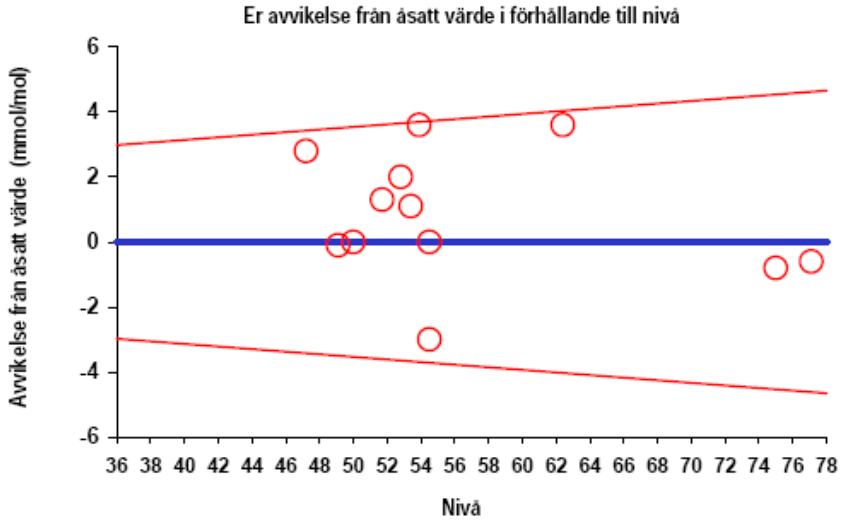
Resultat tidigare omgångar:



Er genomsnittliga avvikelse från åsatt värde de senaste 6 Equalis utskicken:

1,23 mmol/mol

För optimal kvalitet bör genomsnitts avvikelsen vara < +/- 1,5 mmol/mol



Accuracy as ”fraction of values within” denoted ”P_{30}” for accuracy of eGFR

TABLE III
CRITERIA FOR BIAS, PRECISION AND ACCURACY

Criterion	Metric	Definition
Bias	Median difference	Measured GFR - estimated GFR
	Median percentage difference	(Measured GFR - estimated GFR)/measured GFR
Precision	SD difference	
	IQR difference	IQR of (measured GFR - estimated GFR)
	IQR % difference	IQR of [(measured GFR - estimated GFR)/measured GFR] × 100
Accuracy	Median absolute difference	Median of the absolute value of estimated GFR - measured GFR
	P_{30}	Percentage of estimates within 30% of measured GFR
	RMSE	Square root of mean (log measured GFR - log estimated GFR)^2

Root mean square error (RMSE) measures precision when bias is 0 (development data set). Interquartile range (IQR) is the width of the 25th to 75th percentile.
P_{30} = percentage of estimated GFR within 30% of measured GFR; SD = standard deviation.

Stevens, 2008

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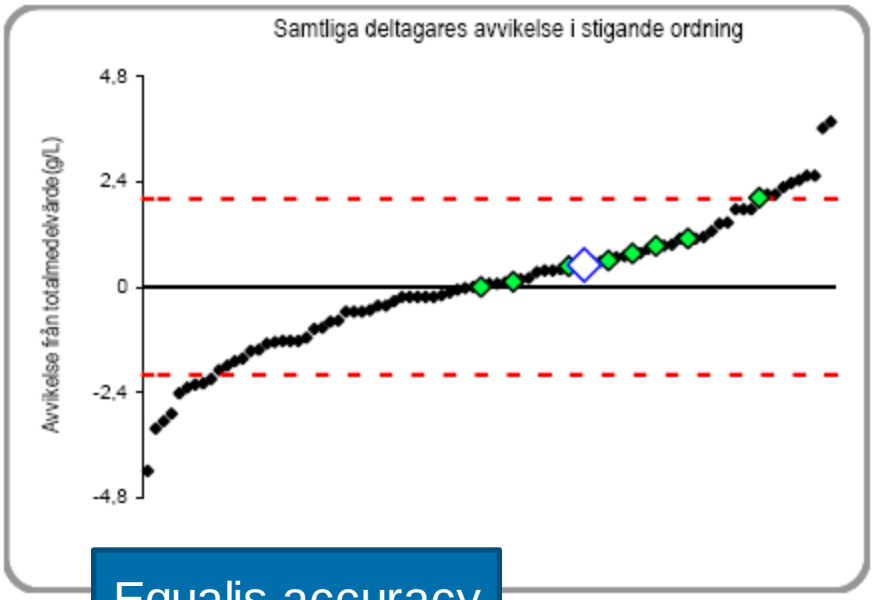
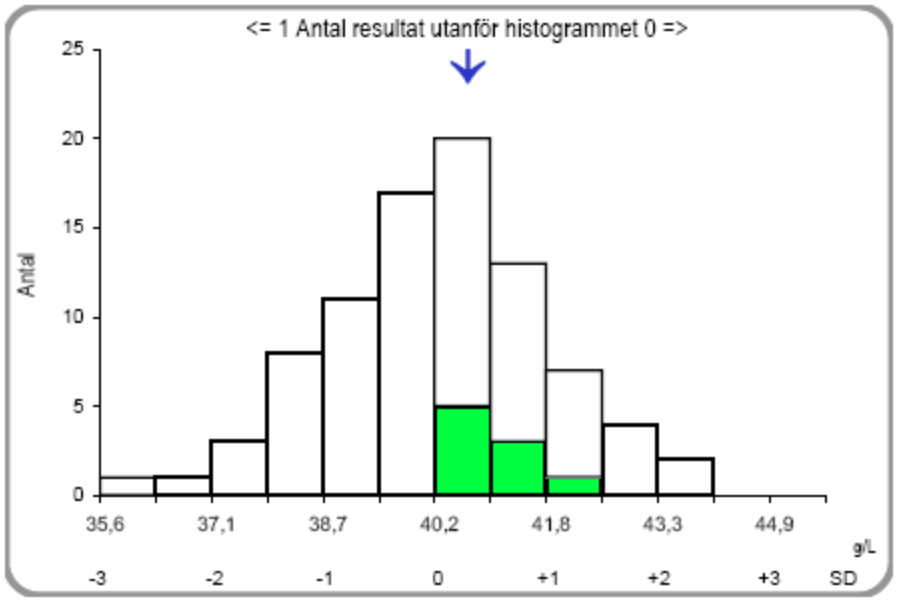
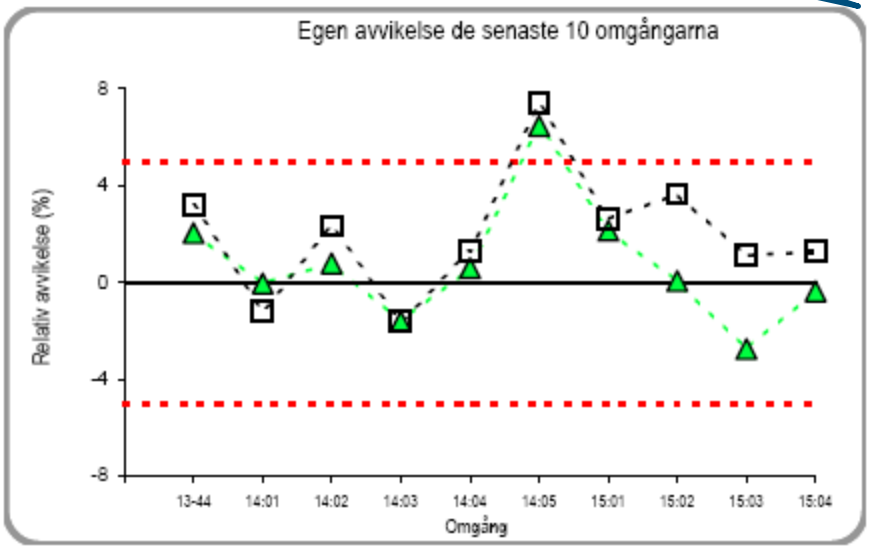
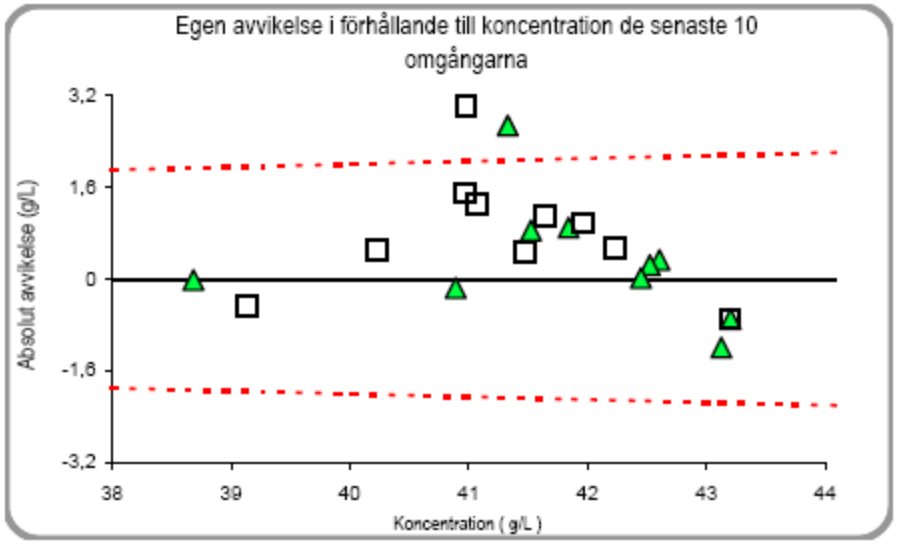


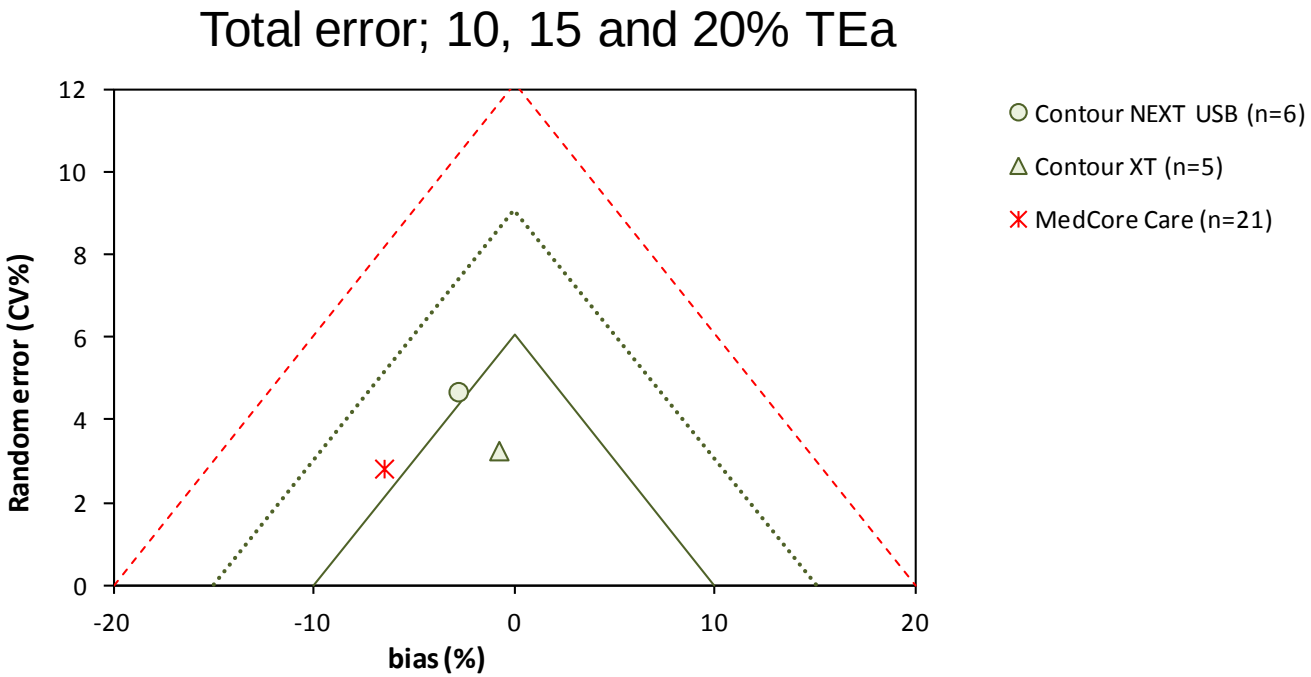


Equalis accuracy graphs





Accuracy described as ”total error”
the simple model TEa = bias(%) + 1.65 x CV



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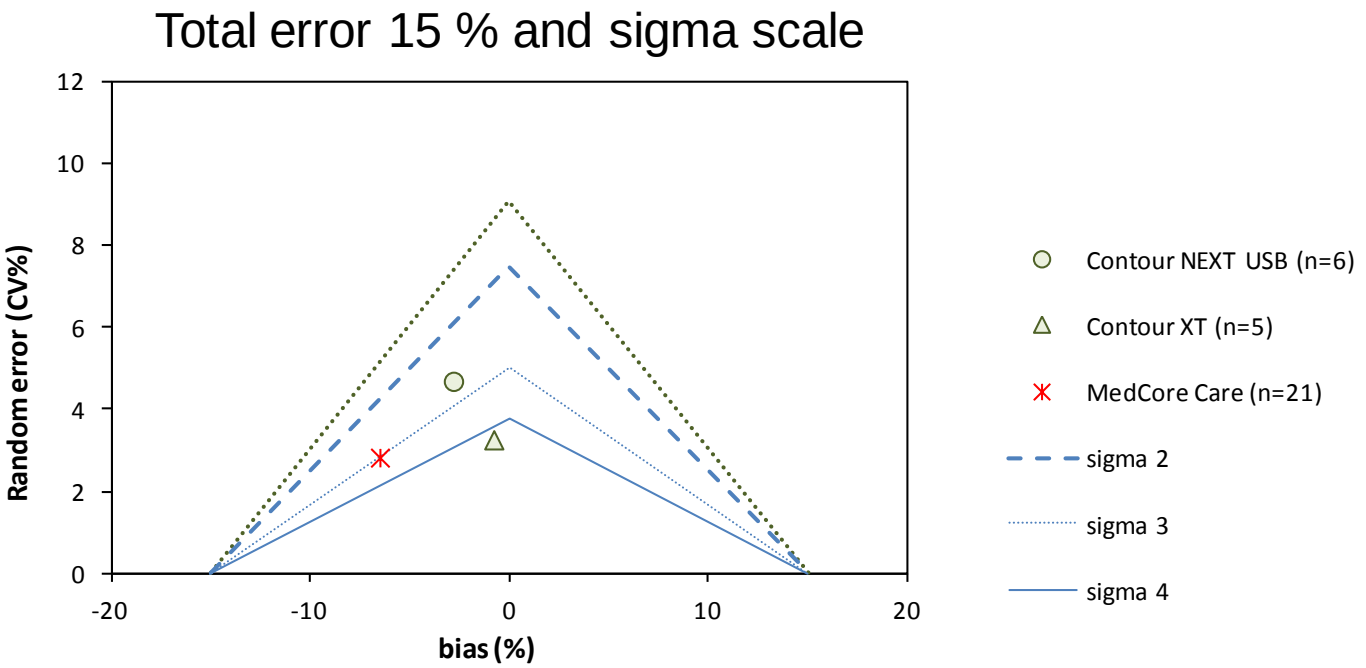
Accuracy described on the ”six sigma” scale



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Accuracy (or total error?) with the root mean square concept (RiliBÄK)

Table 1 Selected examples for maximum permissible errors as given in [1] and corresponding maximum allowable rms deviation of measurement for n = 15.

Analyte in serum/plasma except *	$\frac{\varepsilon_s}{\bar{x}}$ (%)	$\frac{\varepsilon_\delta}{x_0}$ (%)	$2\frac{\varepsilon_s}{\bar{x}} + \frac{\varepsilon_\delta}{x_0}$ (%)	$\frac{\sqrt{\frac{n-1}{n}\varepsilon_s^2 + \varepsilon_\delta^2}}{x_0}$ (%)
Albumin	6.0	11.0	23.0	12.4
α-Fetoprotein	10.0	14.0	34.0	17.0
Bilirubin	7.0	12.0	26.0	13.8
Calcium	3.0	5.0	11.0	5.8
Cholesterol	4.0	6.0	14.0	7.1
Glucose	5.0	6.0	16.0	7.7
hCG	12.0	14.0	38.0	18.1
Hemoglobin*	2.0	2.0	6.0	2.8
Lactat-Dehydrogenase	5.0	8.0	18.0	9.3
Natrium	1.8	2.5	6.1	3.1

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Accuracy described as ”long term uncertainty measurement” (LTUM)

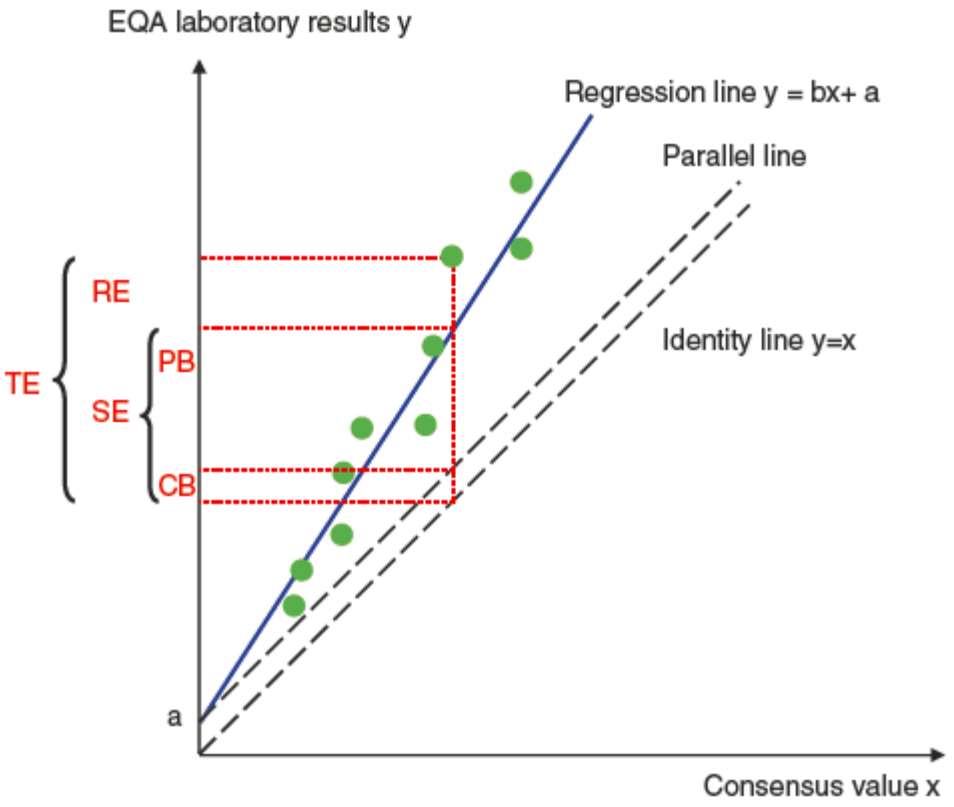

Figure 1: Linear regression model for the assessment of UM: y=bx+a. CB, constant bias; PB, proportional bias; RE, random error; SE, systematic error; TE, total error.

Matar et al, 2015

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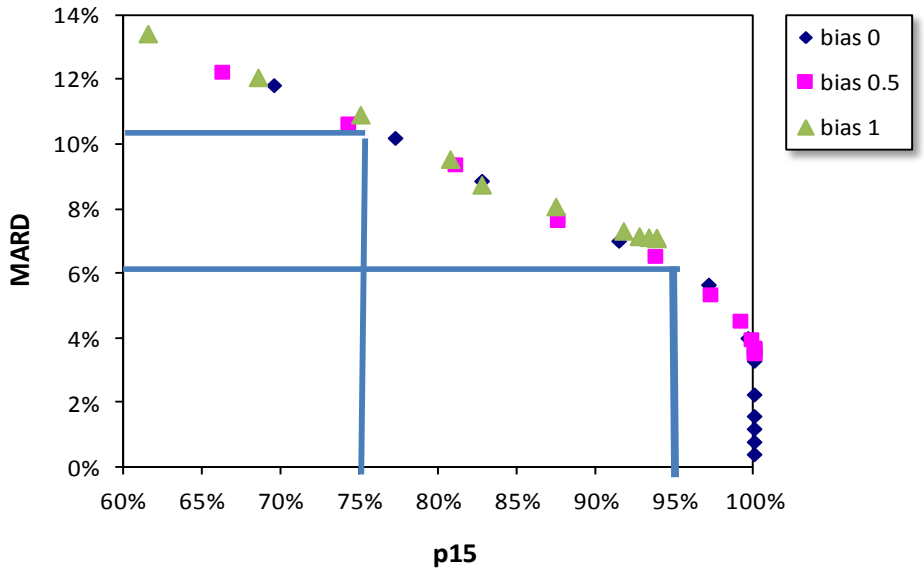
mean absolute relative deviation (MARD) – a new accuracy metric

Much used to describe performance of continous glucose measurment (CGM)

In case of no bias MARD ≈ 0,8 x CV

No additional information compared with “p15”



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Alternative expressions for accuracy

1. Something that can only be good or bad?
2. A fraction of results within performance specification?
3. The “total error”
4. The root mean square of bias and precision
5. The long term uncertainty measurement (LTUM)
6. The mean absolute relative deviation (MARD)

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Thank you for listening

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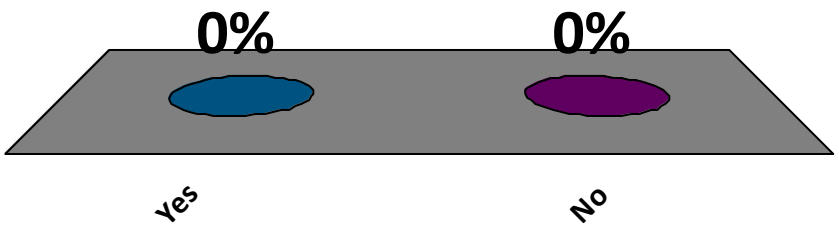
Do you think MOMM is a more realiable target value than the consensus mean?

A. Yes

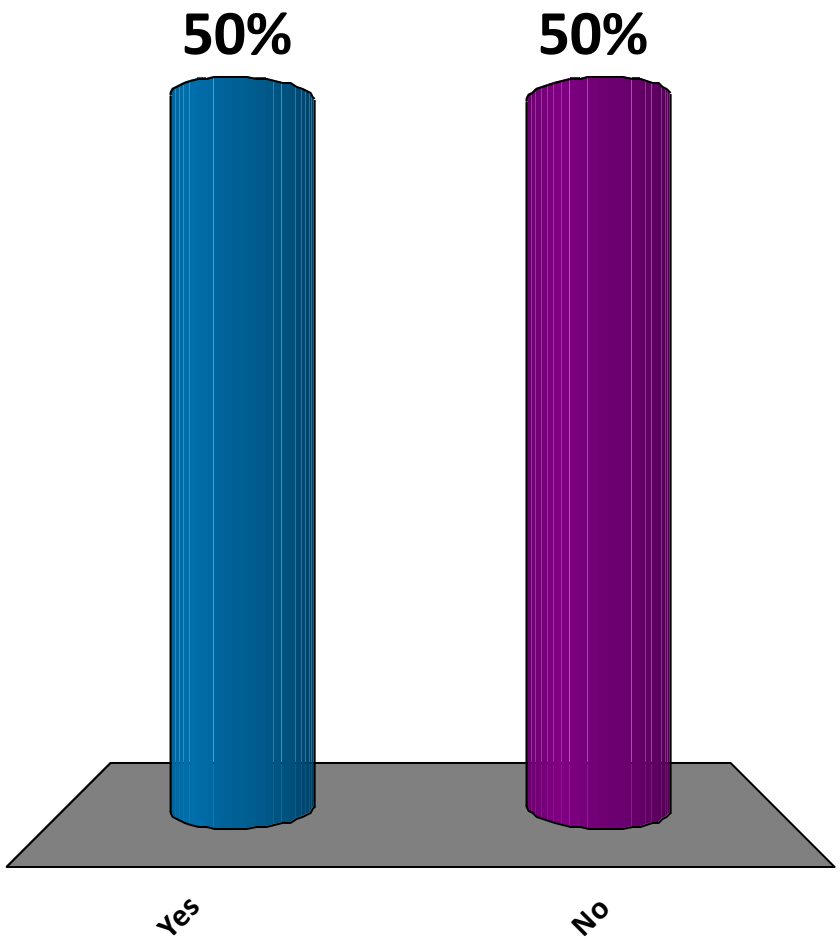
B. No



Is it possible to measure accuracy?

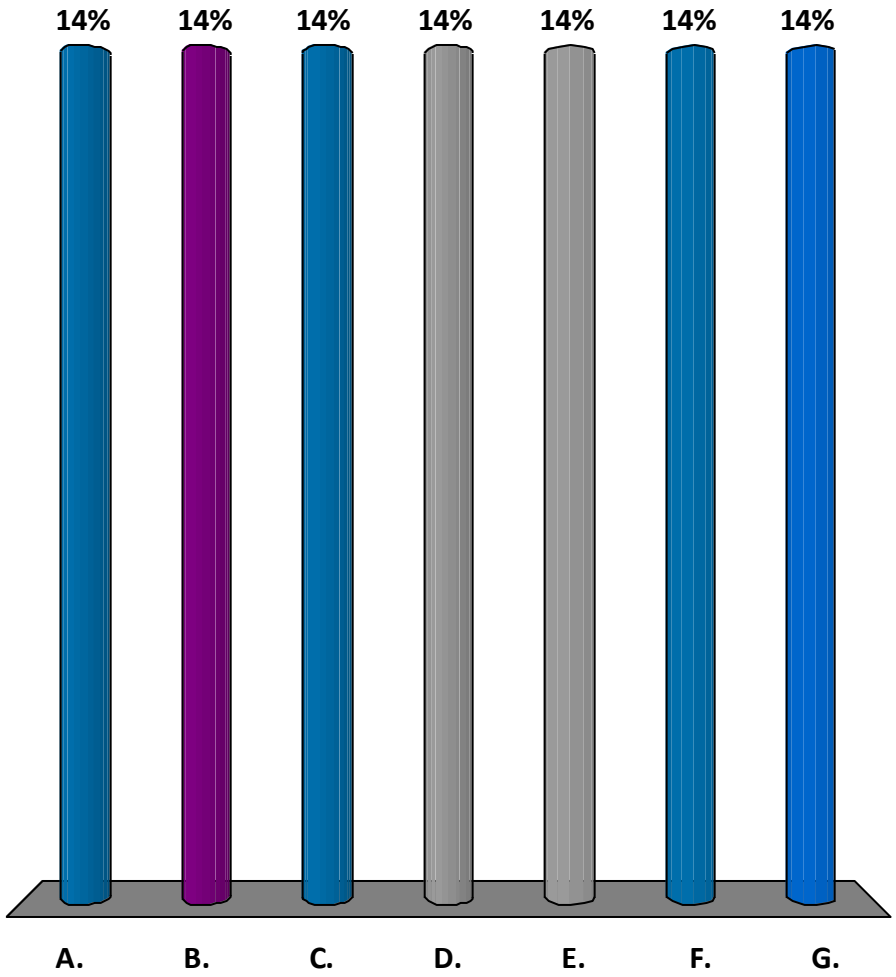
A. Yes

B. No



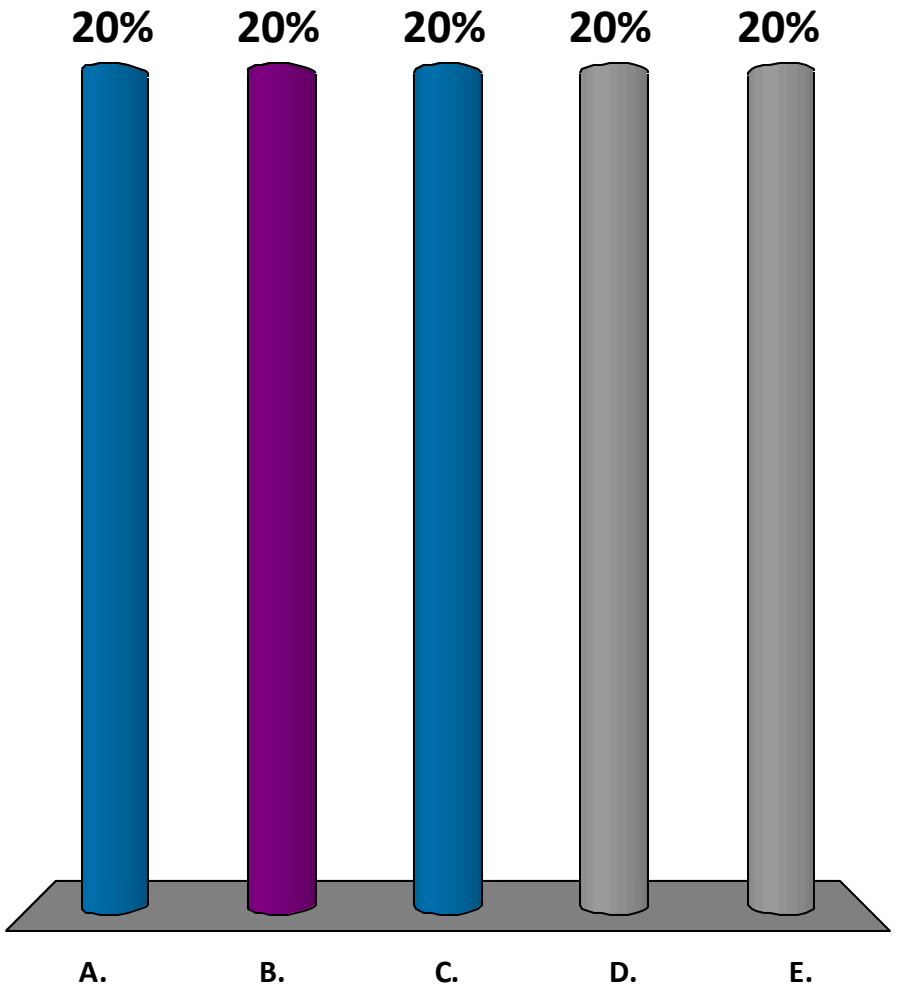
Which expression for accuracy do you prefer?

A. Something that can only be good or bad?
B. A fraction of results within performance specification?
C. The “total error”
D. The root mean square of bias and precision
E. The long term uncertainty measurement (LTUM)
F. The mean absolute relative deviation (MARD)
G. The question is wrong, beacuse these terms do cover different concepts and should be given different names



How should target values be assigned to commutable EQA materials?

A. Reference method values
B. Value transfer from certified reference materials
C. Consensus mean from all participants
D. Mean of method mean (MOMM)
E. Method group mean values should be used



Some words on results that are not quantitative

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What is a ”qualitative test” ?

1. Semi quantitative test
2. Classification test
3. Binary test
4. Test with results ”yes/no”
5. Test with results on an ordinal scale

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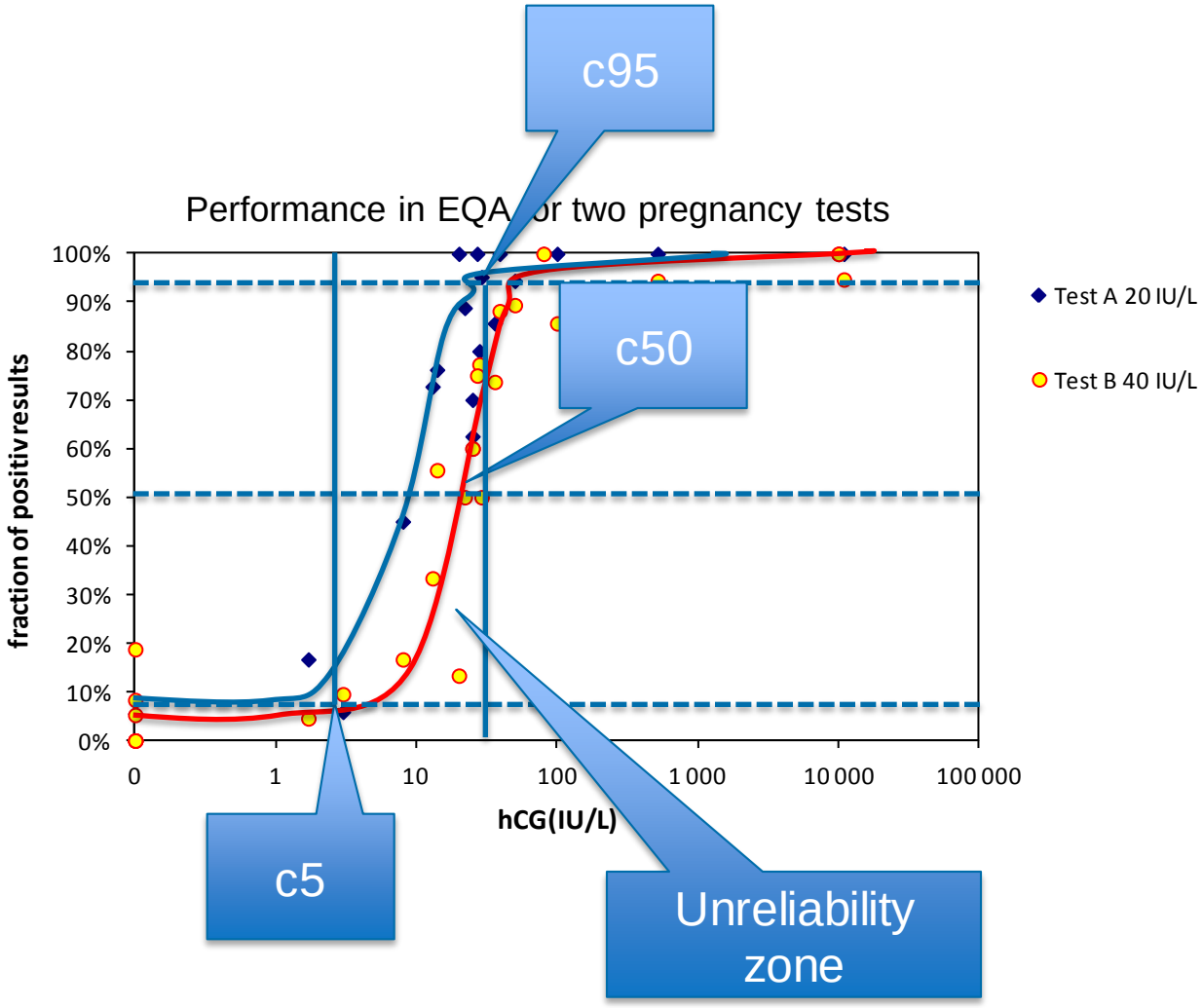
Performance characterstics for pregnancy tests



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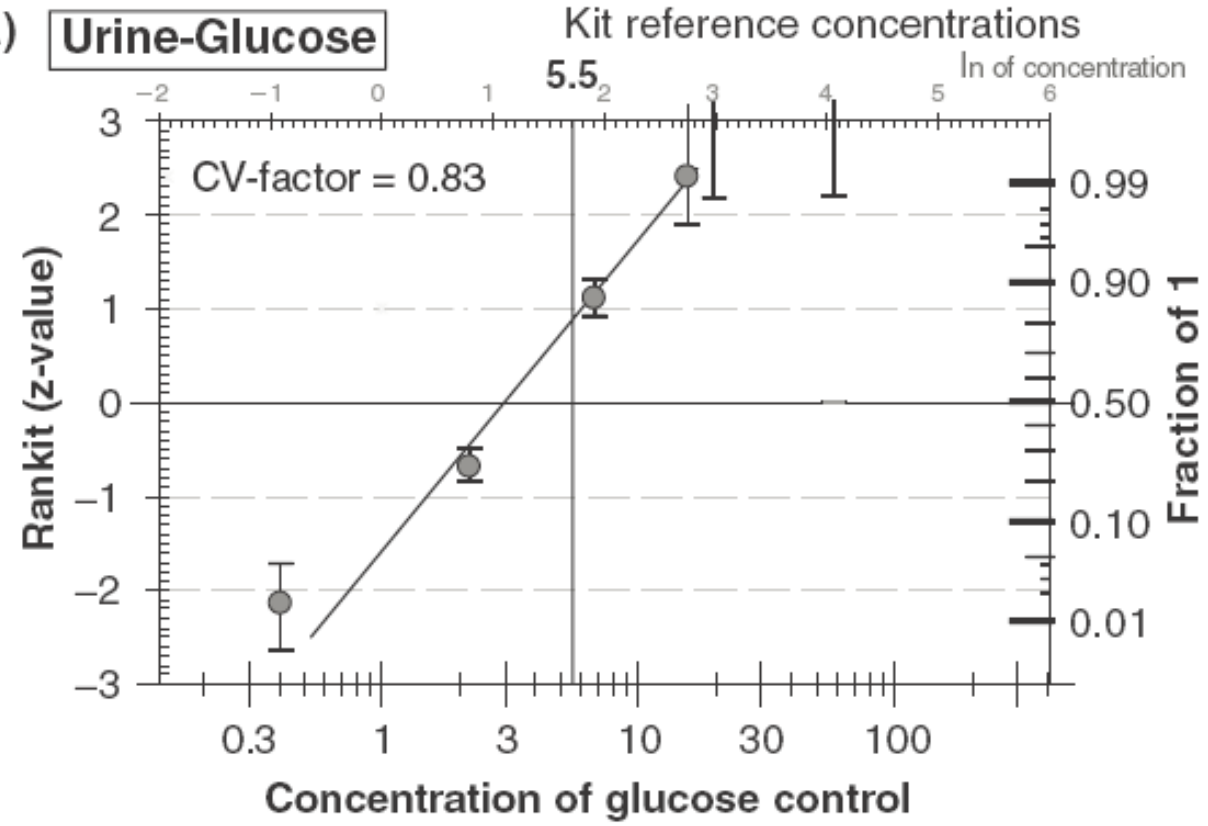
How to draw the line….



Hyltoft Petersen, P., et al. (2008) Scand J Clin Lab Invest 68(4): 298-311.

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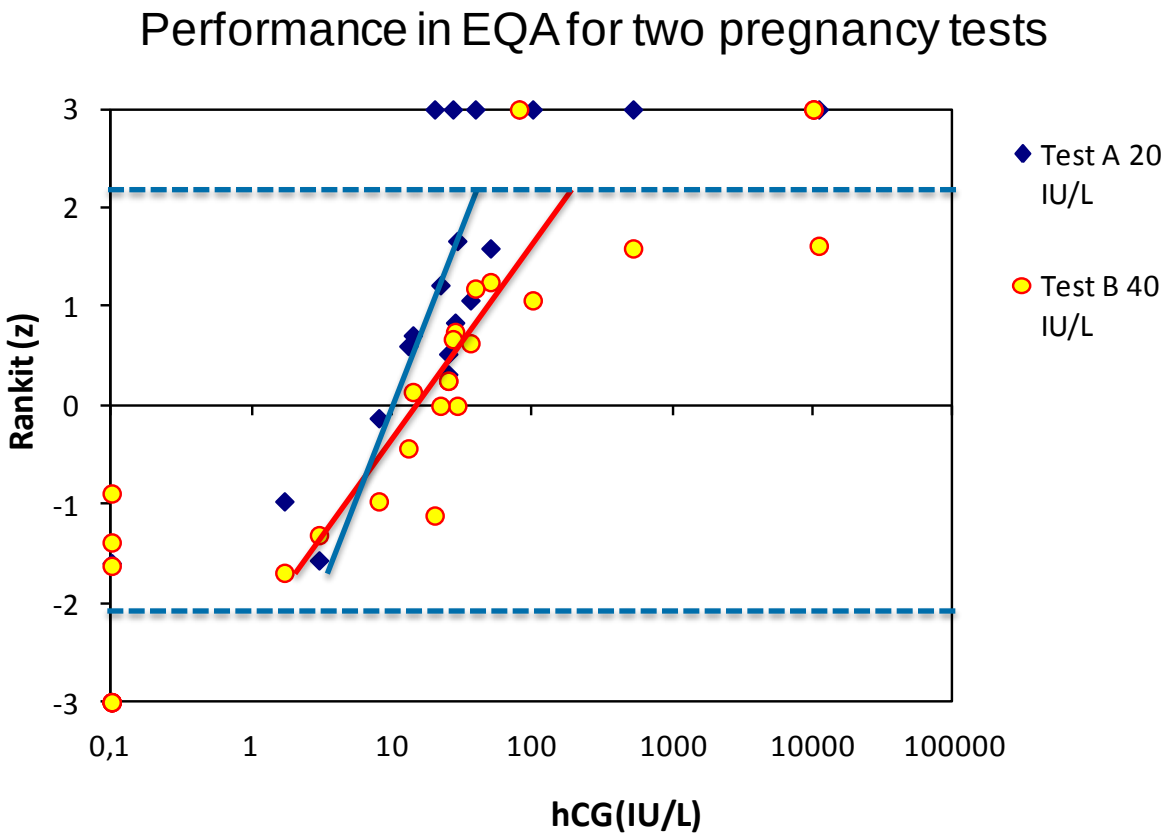
How to draw the line….



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Proposal 2: c5, c50 an c95

For ordinal binary test with a quantitative back ground scale assays should be characterized with the three quantities:

“c5”, ”c50” and ”c95”.

The manufacturer should declare the c50 value for the assay, and describe the metrological traceability

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Internal quality assessment for ordinal tests

<c5	c5 – c95	>c95
False pos	-	True pos
True neg	-	False neg

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External quality assessment for ordnal tests

<c5	c5 – c95	>c95
False pos	True pos ?	True pos
True neg	True neg ?	False neg

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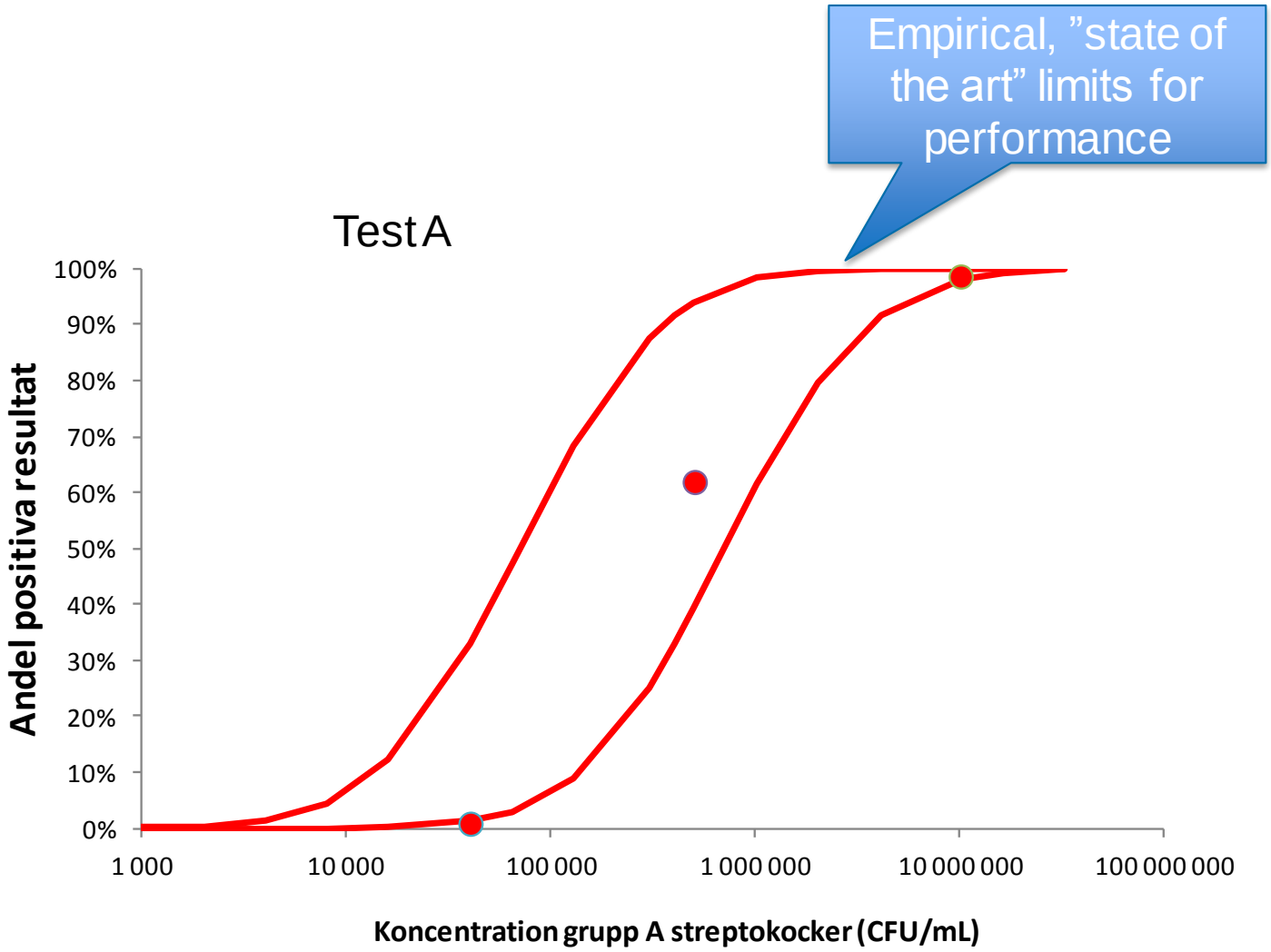
Empirical, ”state of the art” limits for performance
Test A
Andel positiva resultat
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
1 000
10 000
100 000
1 000 000
10 000 000
100 000 000
Koncentration grupp A streptokocker (CFU/mL)

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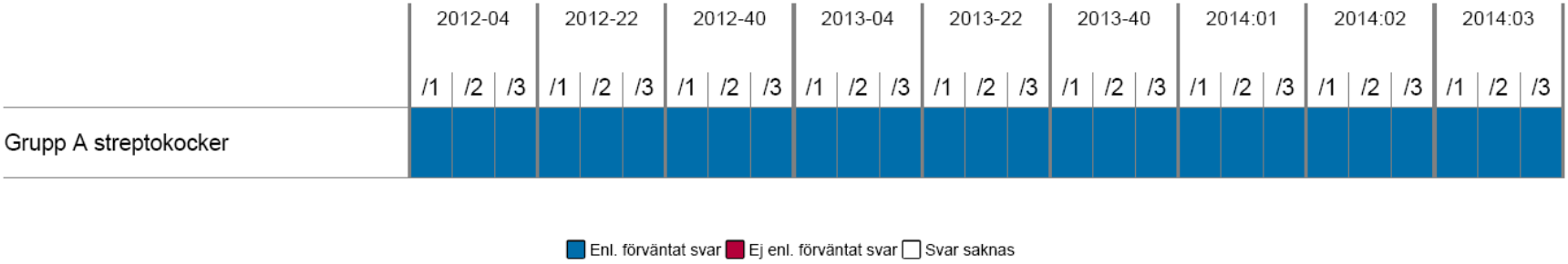
How do we report EQA results on ordinal scale

Oversikt

Prov	Komponent	n	Andel med förväntat svar (%)	Förväntat svar	Eget resultat
/1	Grupp A streptokocker	766	99.1	Negativ	Negativ
/2	Grupp A streptokocker	764	100	Negativ el. Positiv	Positiv
/3	Grupp A streptokocker	764	97.5	Positiv	Positiv

Historik



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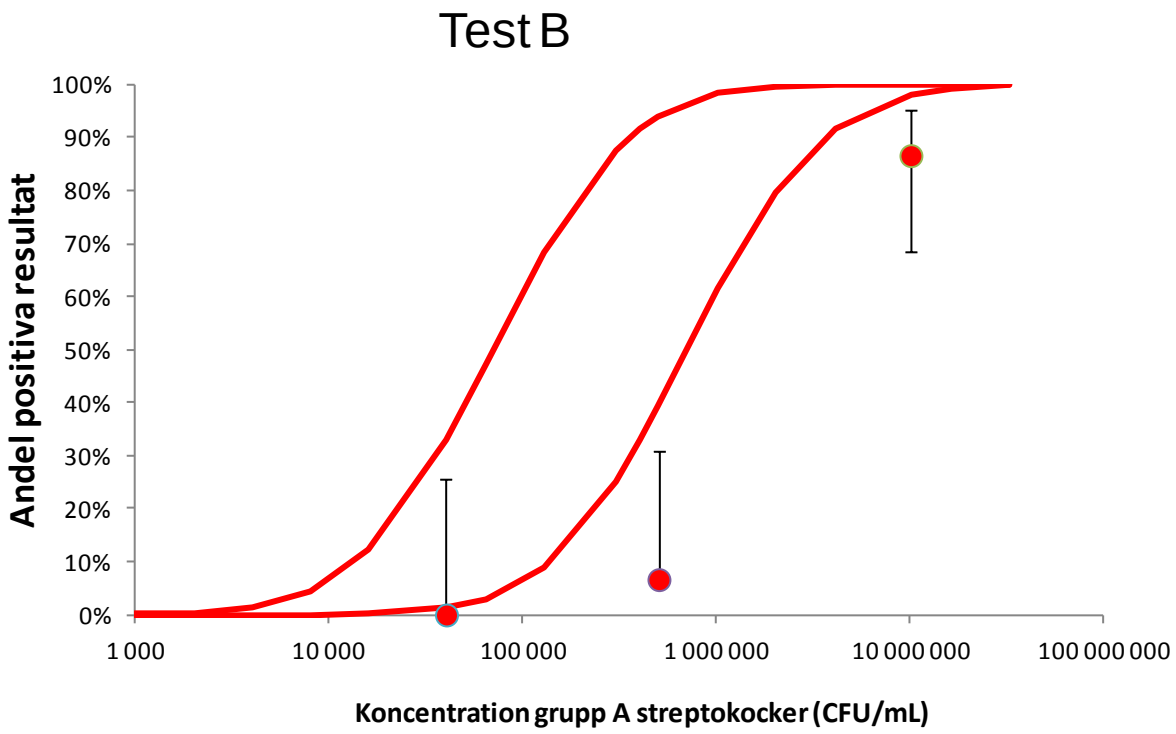
Tests with deviating performance can be revealed



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Take a home message

All QC results must be evaluated and discussed.

If deviating QC results are not related the performance of the method, it might be due to properties of the material used. Some examples are:

Non commutable material
Incorrect target value for the material
Unstable material

The measure of method performance varies. Unfortunately there are today many different measures for “accuracy”. We need to agree on a common use of the concept accuracy.

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