Commutability
of Control Materials for EQAS

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In Vitro Diagnostica Directive

European Union

“.... the traceability of values assigned to calibrators and control materials must be assured through available reference measurement procedures and/or reference materials of higher order ...”

Implementation of the Traceability Concept

by

- Diagnostic Kit Manufacturers
- External Quality Assessment Schemes

Implementation of the Concept of Traceability in German EQA (1987)

- **On the basis of the German Law for Calibration and the Directives of the Federal Medical Association whenever available Reference Method Values must be used as target values in EQA since 1987.**

- **Considerable improvement in standardization and comparability of test results has been achieved.**

DGKL Reference Procedures

DGKL
Deutsche Vereinte Gesellschaft
für Klinische Chemie und Laboratoriumsmedizin e.V.

- **Electrolytes:**
  - Calcium
  - Chloride
  - Lithium
  - Magnesium
  - Potassium
  - Sodium

- **Metabolites and Substrates:**
  - Cholesterol
  - Creatinine
  - Glucose
  - Total Glycerol
  - Uric Acid
  - Urea
  - Bilirubine
  - Lactate

- **Enzymes;**
  - AST
  - ALT
  - CK
  - GGT
  - AMYLASE
  - AP

- **Hormones:**
  - Aldosterone
  - Cortisol
  - Estradiol-17ß
  - Estriol
  - Progesterone
  - 17-Hydroxy-progesterone
  - Testosterone
  - Thyroxine
  - Tri-Iodothyronine

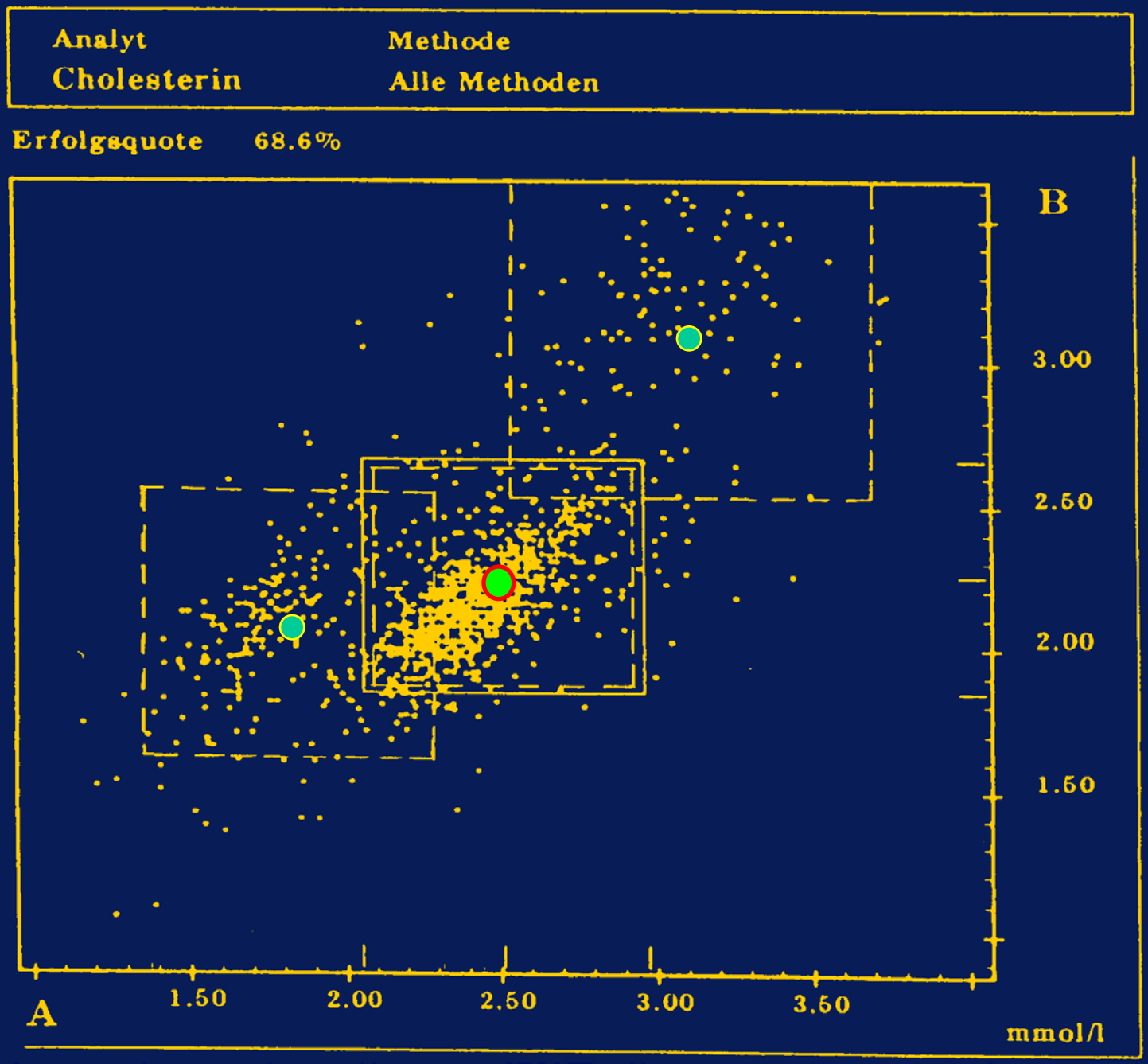
- **Drugs:**
  - Theophylline
  - Digoxin
  - Digitoxin

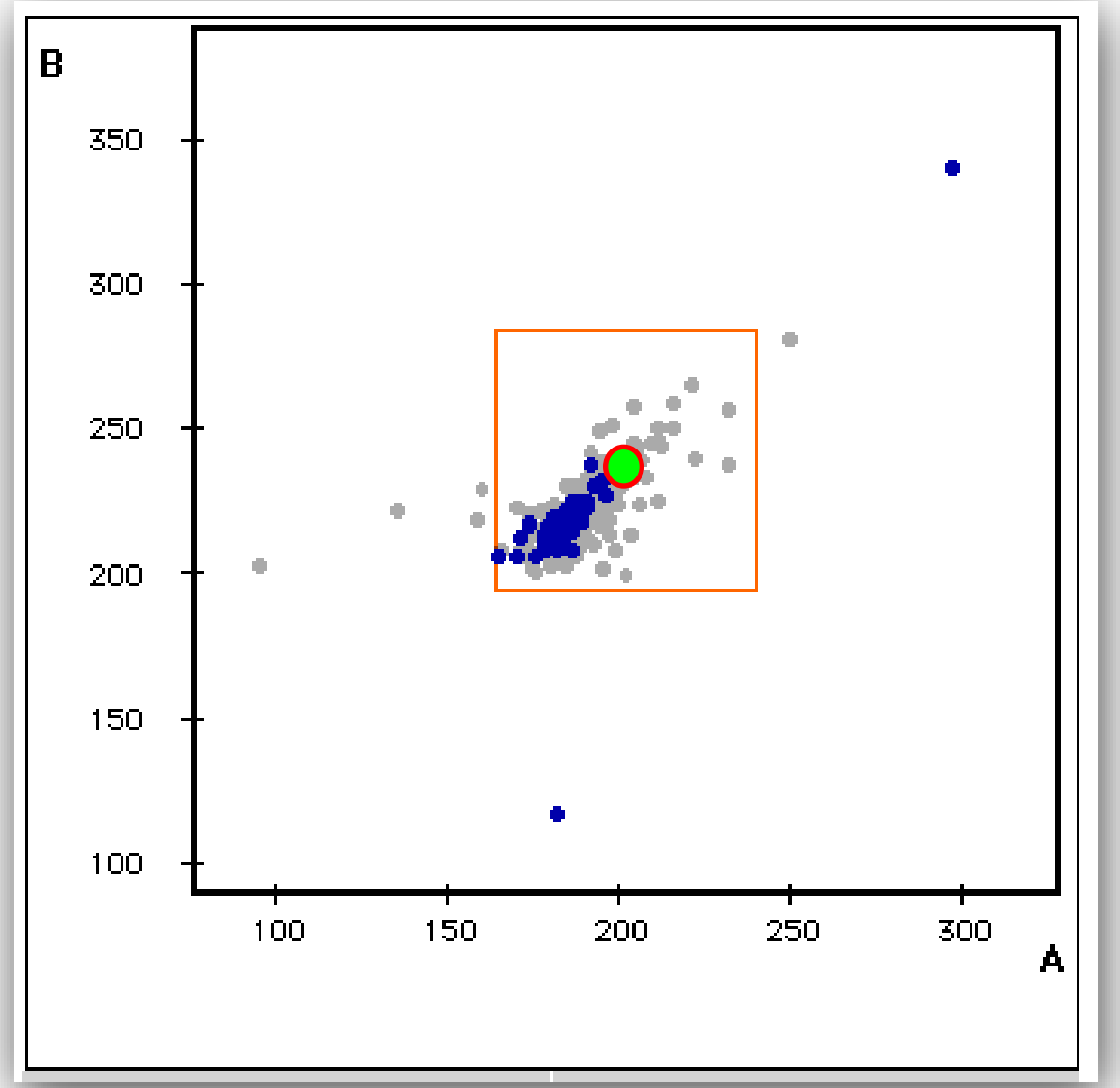
- **Total Protein**

Target Concentrations for Steroid Hormones in a Commercial Control Serum (1987)

	Aldosterone pmol/l	Cortisol nmo/l	Progesterone nmo/l	Estradiol pmol/l
ABBOTT	121.9			
AMERSHAM	113.1			
BAXTER DADE DIR		104.8	2.16	396.4
BAXTER DADE AG ER				244.1
BAXTER DADE AD EXT				196.0
BIOMERIEUX			2.54	539.6
BIOTEX PREMIX	**99.4**	70.6	3.72	759.9
CAMBRID´GE MEDICAL	120.8		**0.86**	
CIBA CORNING		110.3		
CLINICAL ASSAYS		99.3		
CYBERFLUOR FIAGEN	88.2			
DIAGNOSTIC PRODUCTS		113.1	3.12	119.3
EURODIAGNOSTICS		115.8		
FARMOS DIAGN.		99.3	4.67	394.9
IMMUNCHEM COV. COAT	110.3		348.7	
LEECO		113.1	2.99	144.2
MALLINCKRODT				96.6
NMS PHARMACEUTICALS			3.18	205.5
PANTEX IMMUNO		118.6	4.13	190.8
PANTEX IMMUNOCOAT	132.4		**7.00**	154.9
PHARMACIA DELFIA		99.9		**790.0**
RSL	**169.2**		4.77	**117.4**
SCLAVO LISO PHASE		**277.4**	3.82	
SERONO		112.0		
SIBAR ELISA		121.3	1.27	
SORIN	165.9	**68.9**	2.86	139.5
SYVA EMIT	137.9			
TECHLAND RIA			4.77	
VITEK SYSTEMS		110.0		

EQA Survey 1987





Cholesterol

in Human Serum DGKL- EQAS

2007 - 01

Method: CHOD-PAP

Manufacturer: Kit - 28

Participants: 70 (649)

http://www.dgkl-rfb.de

Cholesterol in Human Serum

DGKL- EQAS 2013 - 07

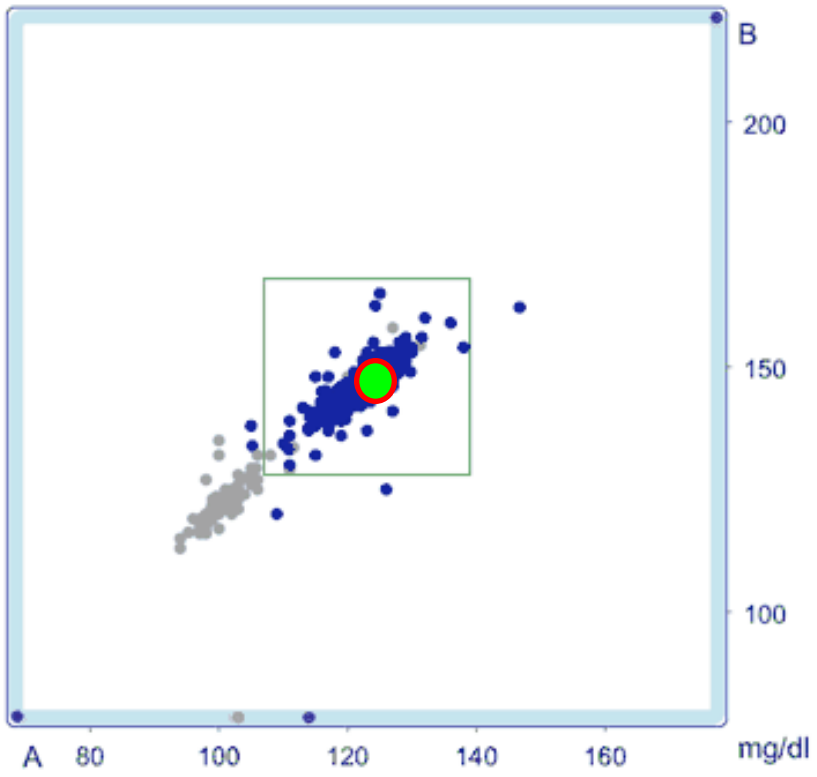
KS7/13

Cholesterin

R f B

Enzym., CHOD-PAP, anderer Farbstoff

Split 1



number of results	459	
target value	123	148
limits	107 - 139	128 - 168
mean	122,012	146,178
standarddeviation	4,138	4,715
coefficient of variation	3,391	3,226

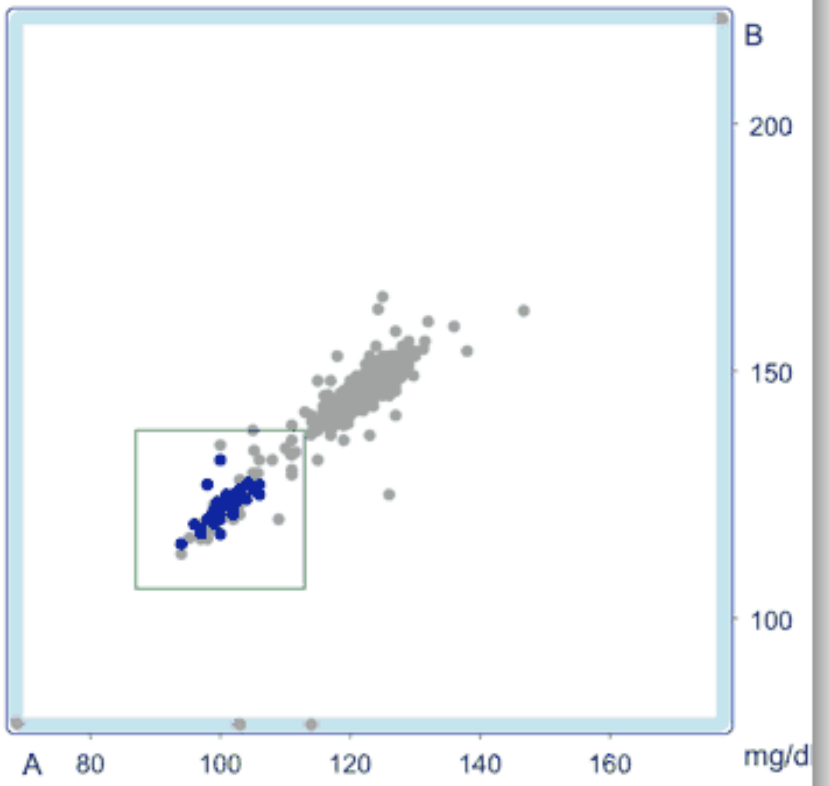
KS7/13

Cholesterin

R f B

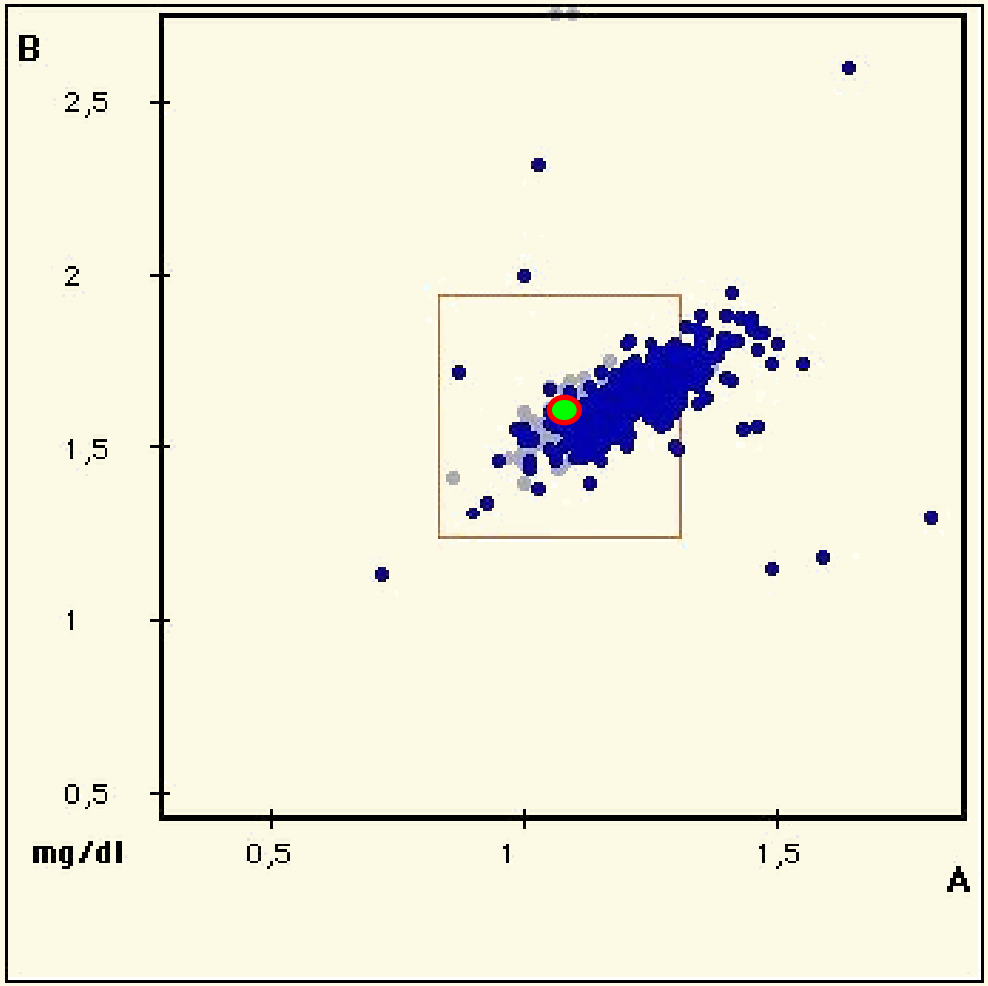
Kit 1-328 - Kit 328

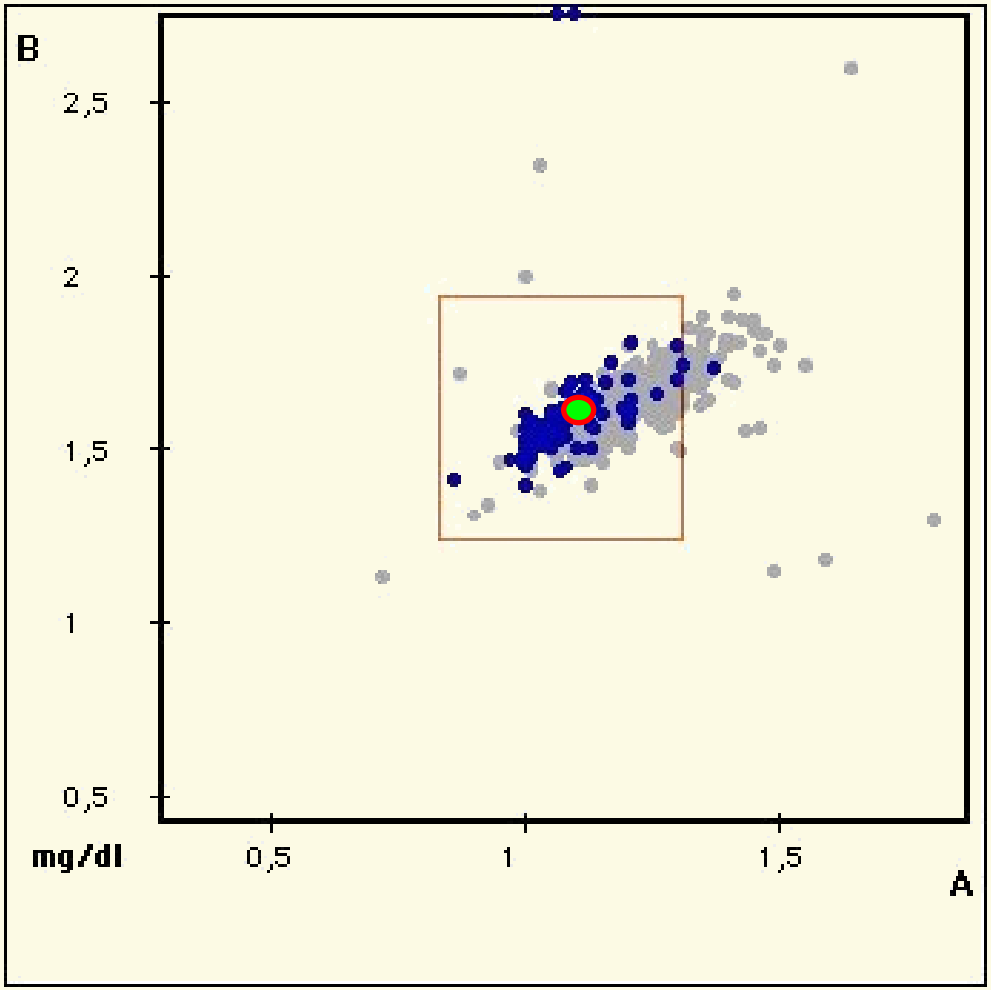
Split 1



number of results	34	
target value	100	122
limits	87 - 113	106 - 138
mean	100,068	121,947
standarddeviation	3,12	3,911
coefficient of variation	3,117	3,207

DGKL- EQAS 2007-3 - Creatinine in Human Serum

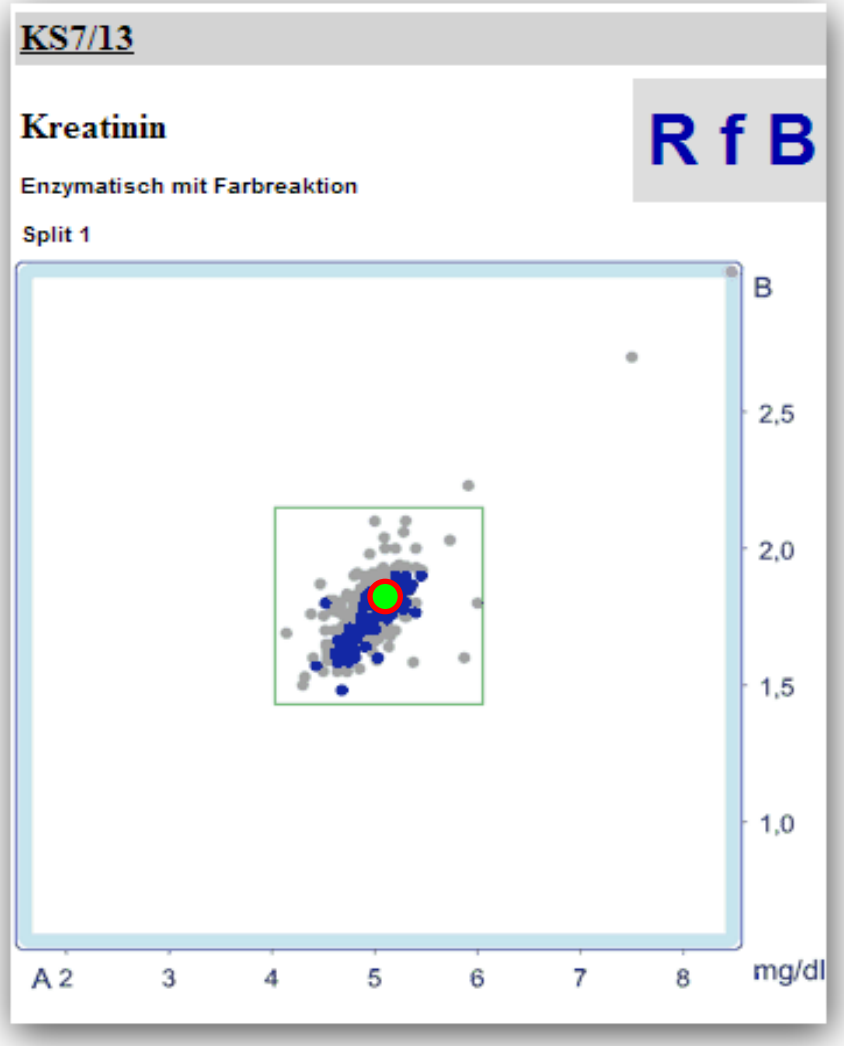




Method: Jaffe | Enzymatic

Participants: 538 (711) | 159 (711)

DGKL- EQAS 2013-7 - Creatinine in Human Serum



Method:	**Jaffe**	**Enzymatic**
Participants:	**458 (581)**	**117 (581)**

Creatinine Jaffé

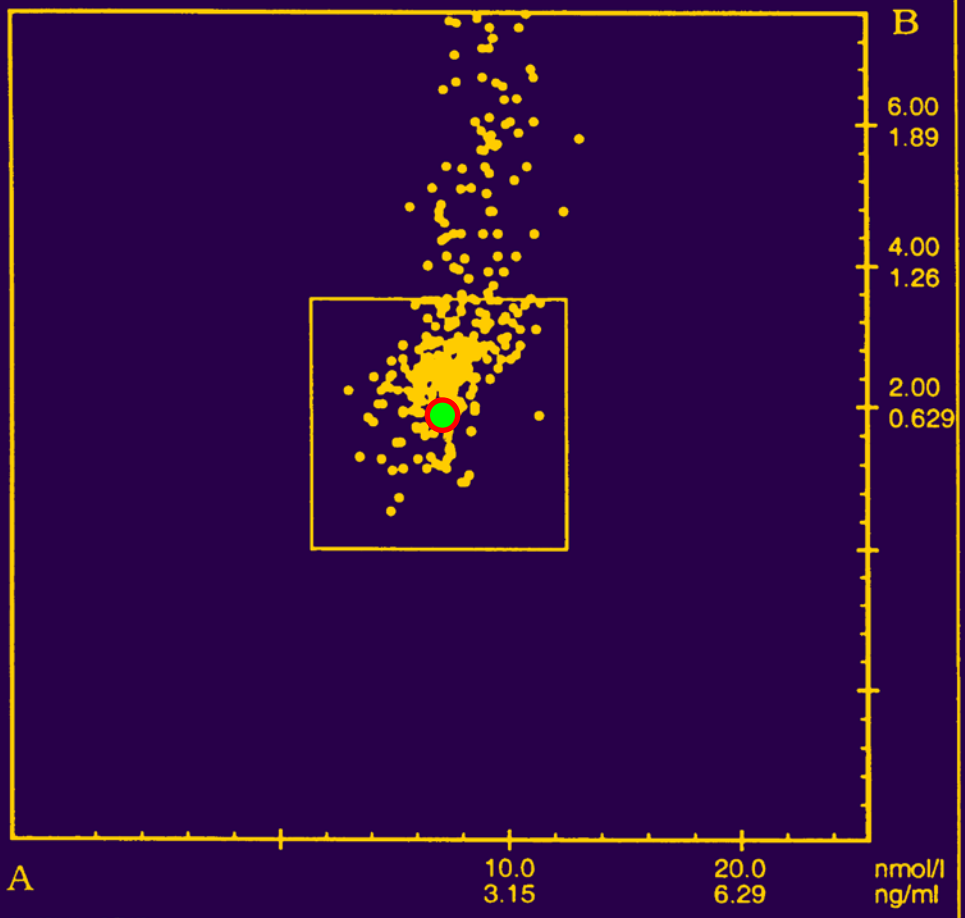
Compensated Method for Serum and Plasma

It is determined by measuring the increase in absorbance at 512 nm. Serum and plasma samples contain proteins which react non-specifically in the Jaffé method. For compensation of serum and plasma results, values are automatically corrected by -18 µmol/L (-0.2 mg/dL).

Values <0.2 mg/dL (<18 µmol/L) or negative results are reported in rare cases in children <3 years and elderly patients. In such cases use the Creatinine plus test to assay the sample.

Analyt	Methode
Progesteron	**Alle Methoden**

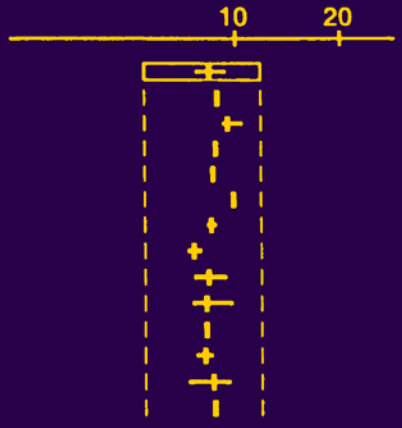
Erfolgsquote 73.0 Ausreißer 25



Teilnehmerzahl	393			
Probe/Einheit	A nmol/l	B	A ng/ml	B
Mittelwert	7.67	3.13	2.41	0.985
Standardabweichung	1.57	1.42	0.494	0.447
Variationskoeffizient	20.5	45.4	20.5	45.4

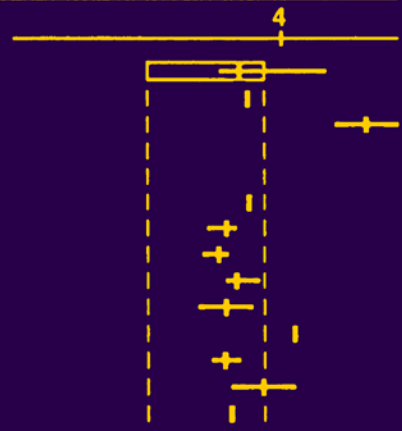
Probe A (RMW= 6.94 nmol/l)

M	Kit	N	Min	16.P	50.P	84.P	Max
Alle		393	2.58	6.27	7.66	9.28	42.9
1	8	8	7.50		8.43		9.10
1	44	38	6.70	8.83	9.40	10.8	12.1
1	76	11	6.17		8.24		10.2
1	77	7	6.94		8.00		10.3
2	4	9	8.50		9.95		10.7
2	28	39	2.58	7.28	7.82	8.33	8.55
2	68	12	5.41	5.44	6.12	6.84	7.38
2	76	77	3.88	6.04	7.54	9.22	11.4
2	98	19	3.50	5.86	7.31	9.79	11.3
3	8	9	5.95		7.31		9.86
3	40	49	4.93	6.20	7.15	7.85	9.22
3	44	41	3.02	5.45	7.95	9.54	13.1
3	72	7	6.60		8.10		9.04



Probe B (RMW= 1.76 nmol/l)

M	Kit	N	Min	16.P	50.P	84.P	Max
Alle		393	0.541	2.16	2.80	5.41	26.8
1	8	8	2.80		3.04		3.61
1	44	38	2.01	5.65	6.64	8.15	9.86
1	76	11	2.86		8.84		13.7
1	77	7	2.73		7.70		19.0
2	4	9	2.78		3.09		3.43
2	28	39	0.541	1.79	2.40	2.69	2.99
2	68	12	1.21	1.66	2.16	2.44	2.51
2	76	77	1.14	2.35	2.70	3.37	4.77
2	98	19	1.27	1.52	2.38	3.17	4.77
3	8	9	2.42		4.45		5.41
3	40	49	0.731	1.91	2.35	2.80	3.37
3	44	41	1.94	2.51	3.50	4.45	6.04
3	72	7	1.30		2.54		4.10

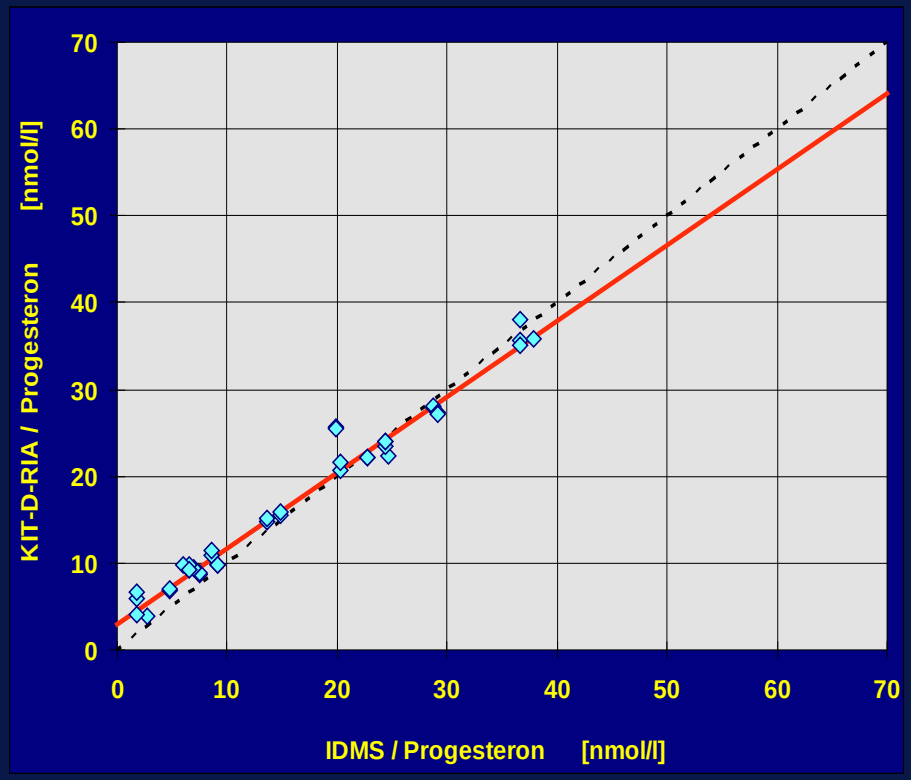


Andere Kits:
1 20(1), 1 21(6), 1 24(5), 1 32(2), 1 41(1), 1 42(1), 1 50(3), 1 53(2), 1 68(3), 1 70(4), 1 98(1), 1 99(3), 2 12(4), 2 22(4), 2 35(6), 2 40(2), 2 41(1), 2 42(2), 2 44(1), 2 53(1), 2 74(1), 2 82(1), 2 99(3), 3 04(1), 7 76(1), 7 98(3), 7 99(4),

Definition of Commutability

“Equivalence of the mathematical relationship among the results of different measurement procedures for an RM and for representative samples of the type intended to be measured“

(CLSI C-53A)

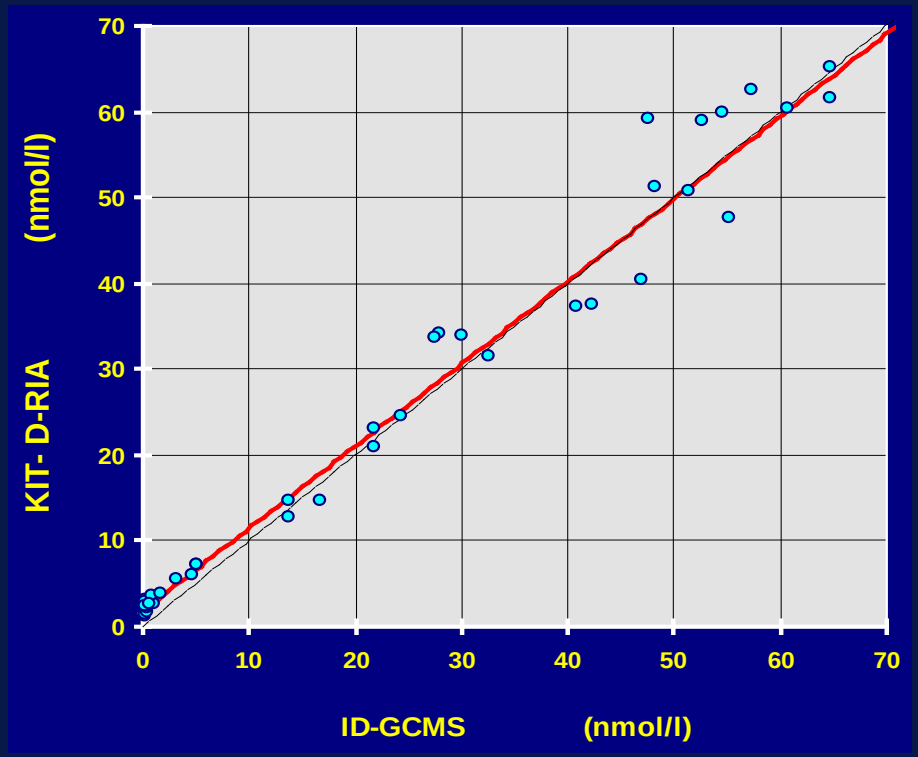


PROGESTERONE

MEDIANS IN RING TRIALS

y = 2,98 + 0,87 x
n = 40, r = 0,681

Median (x) = 14,2
Median (y) = 15,75
Median (y-x)% = 10,3

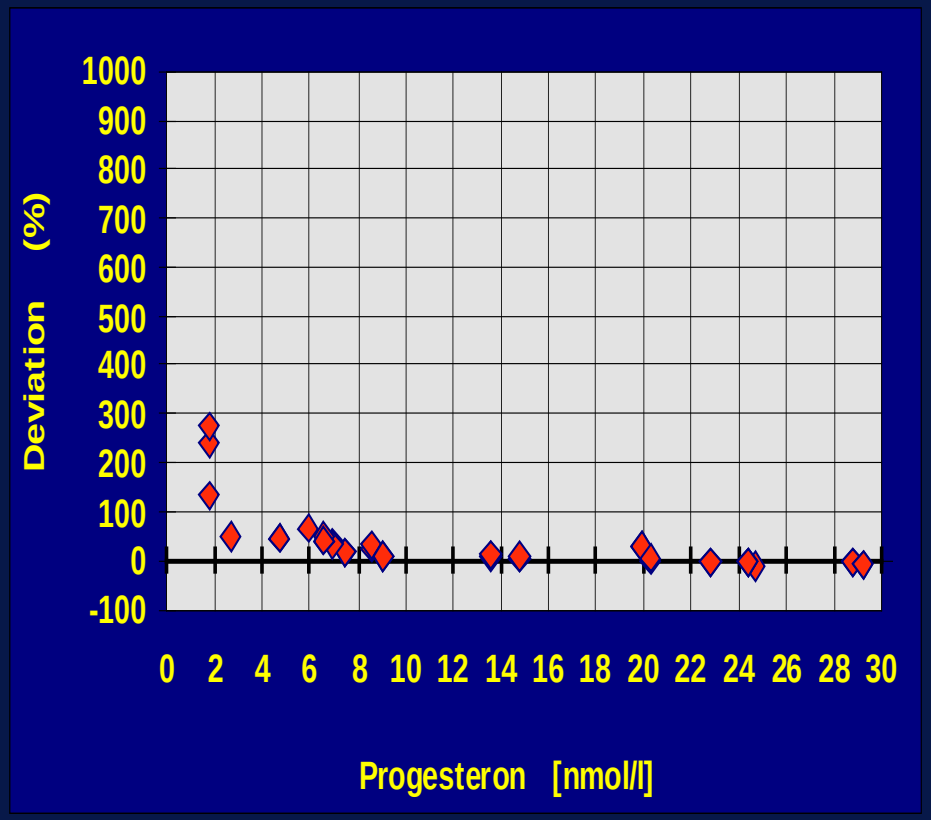


PROGESTERONE

PATIENT SAMPLES

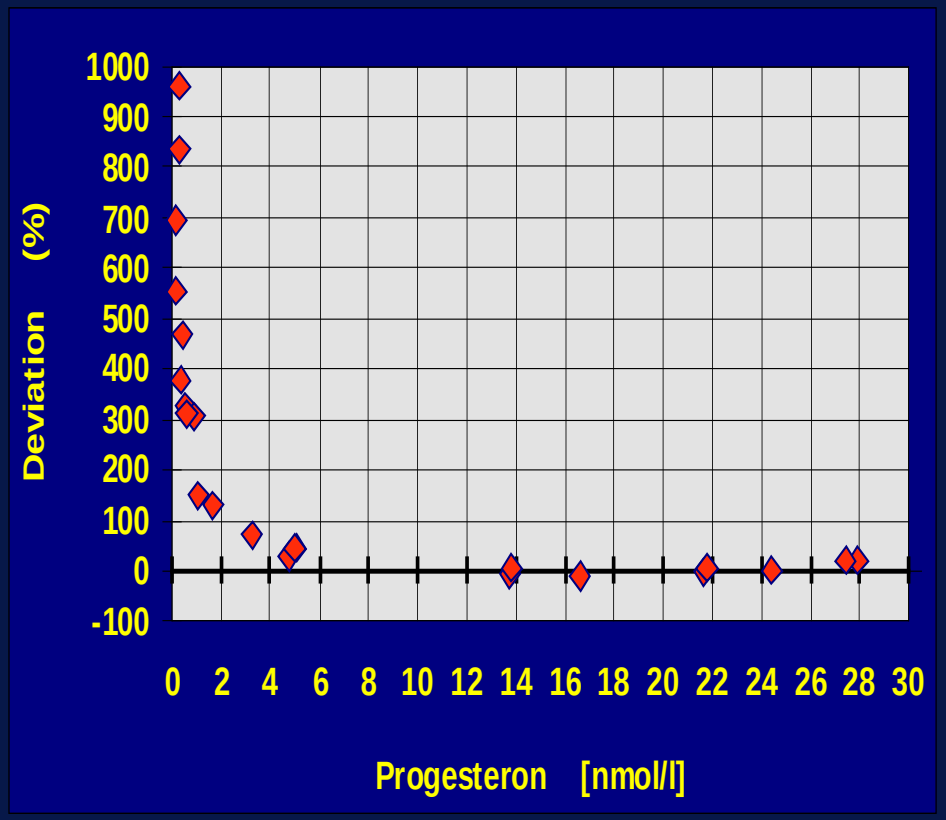
y = 1,84 + 0,96 x
n = 42, r = 0.99

Median (x) = 19,2
Median (y) = 17,9
Median (y-x)% = 17,4



PROGESTERONE

MEDIANS IN RING TRIALS



PROGESTERONE

PATIENT SAMPLES

Observations

It can be observed that usually only one of several test kits exhibits so-called “commutability“ problems.

There is an inherent relation between the commutability of a material and the properties of a routine measurement procedure.

There will be no commutability problems using measurement procedures of high specificity (e.g. mass spectrometry for steroid hormones).

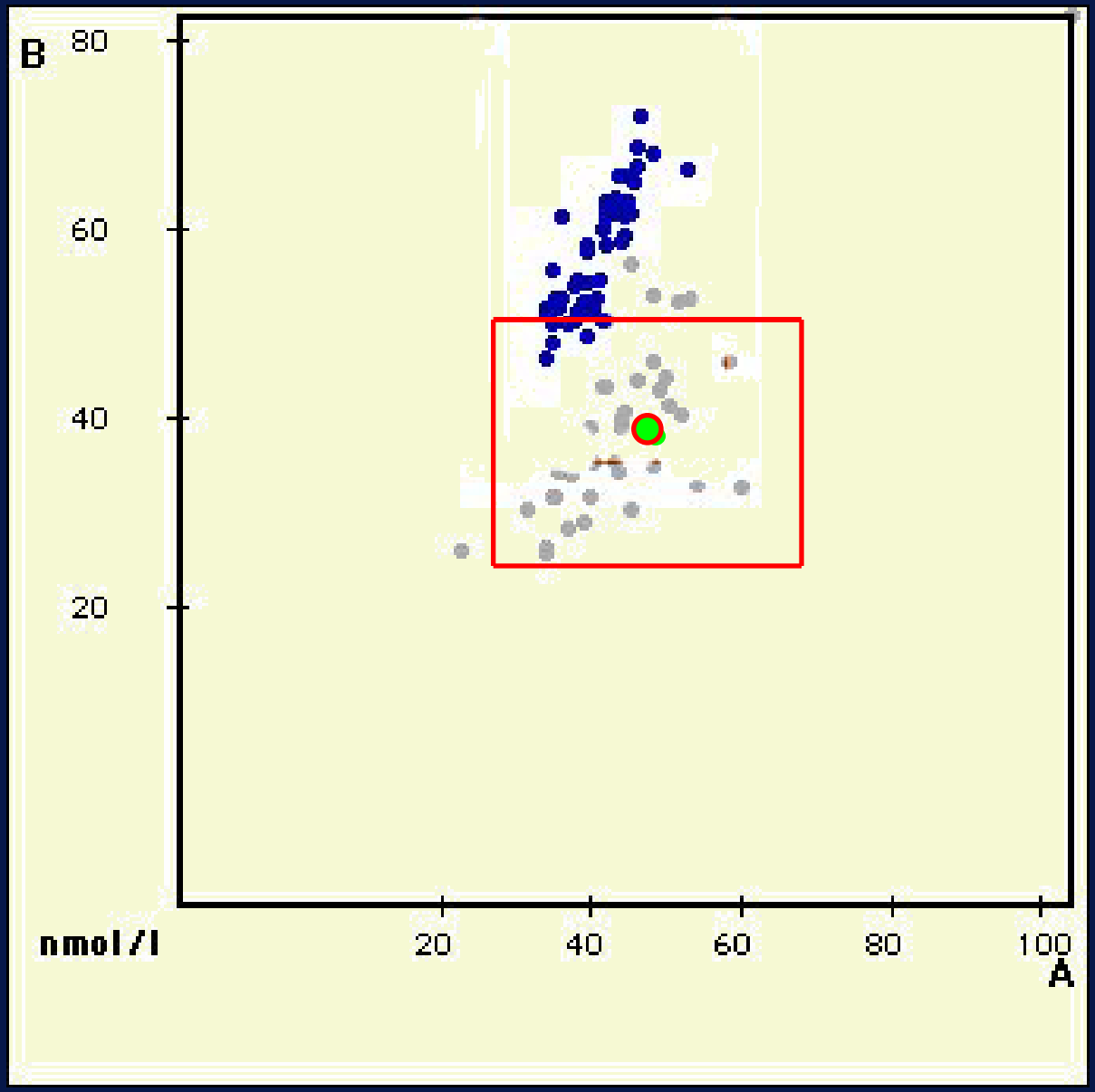
Lower specificity of a routine procedure leads to a higher risk of sensitivity to matrix effects in materials.

Estriol, unconjugated
DGKL -2005/01

Selected Participants: 54(93)
Test – KIT 44

Ref.Values
A: 44,3 nmol/l
B: 35,4 nmol/l

Limits
A: 25.6 – 62.1 nmol/l
B: 21,2 – 49,6 nmol/l



Preparation of EQA Samples for Unconjugated Estriol in Serum

It is not possible to collect enough serum for preparation of EQAS control materials from pregnant femals.

Therefore serum from healthy (non-pregnant) volunteers was spiked with estriol and partially with conjugated estriol (sulfates and glucuronides).

In this way the EQA samples are useful to mimic clinical samples from pregnant females.

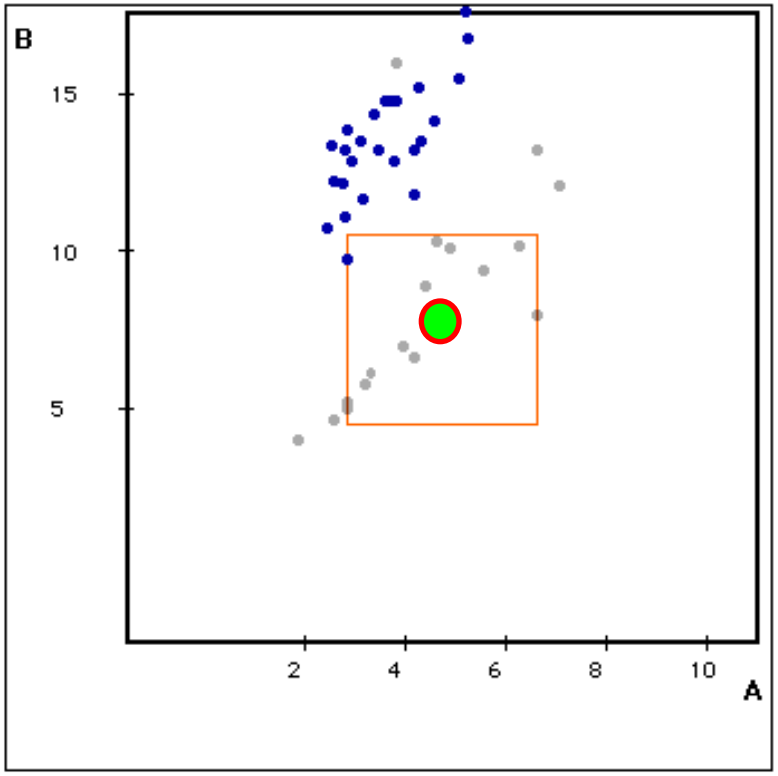
HM1/09

Unk. Estriol

Lumineszenzmessung - Kit 44

Split 1

RfB



Teilnehmer ausgewählt	30	
Zielwert	4,72	7,44
Grenzen	2,83 - 6,61	4,46 - 10,5
Mittelwert	3,599	13,435
Standardabweichung	0,787	1,851
Variationskoeffizient	21,87	13,779

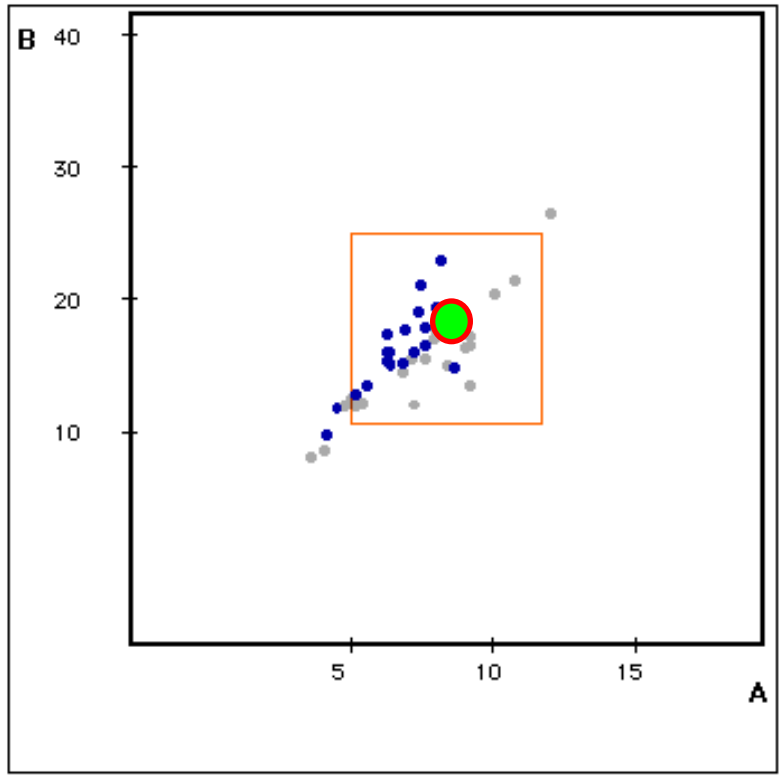
HM2/09

Unk. Estriol

Lumineszenzmessung - Kit 44

Split 1

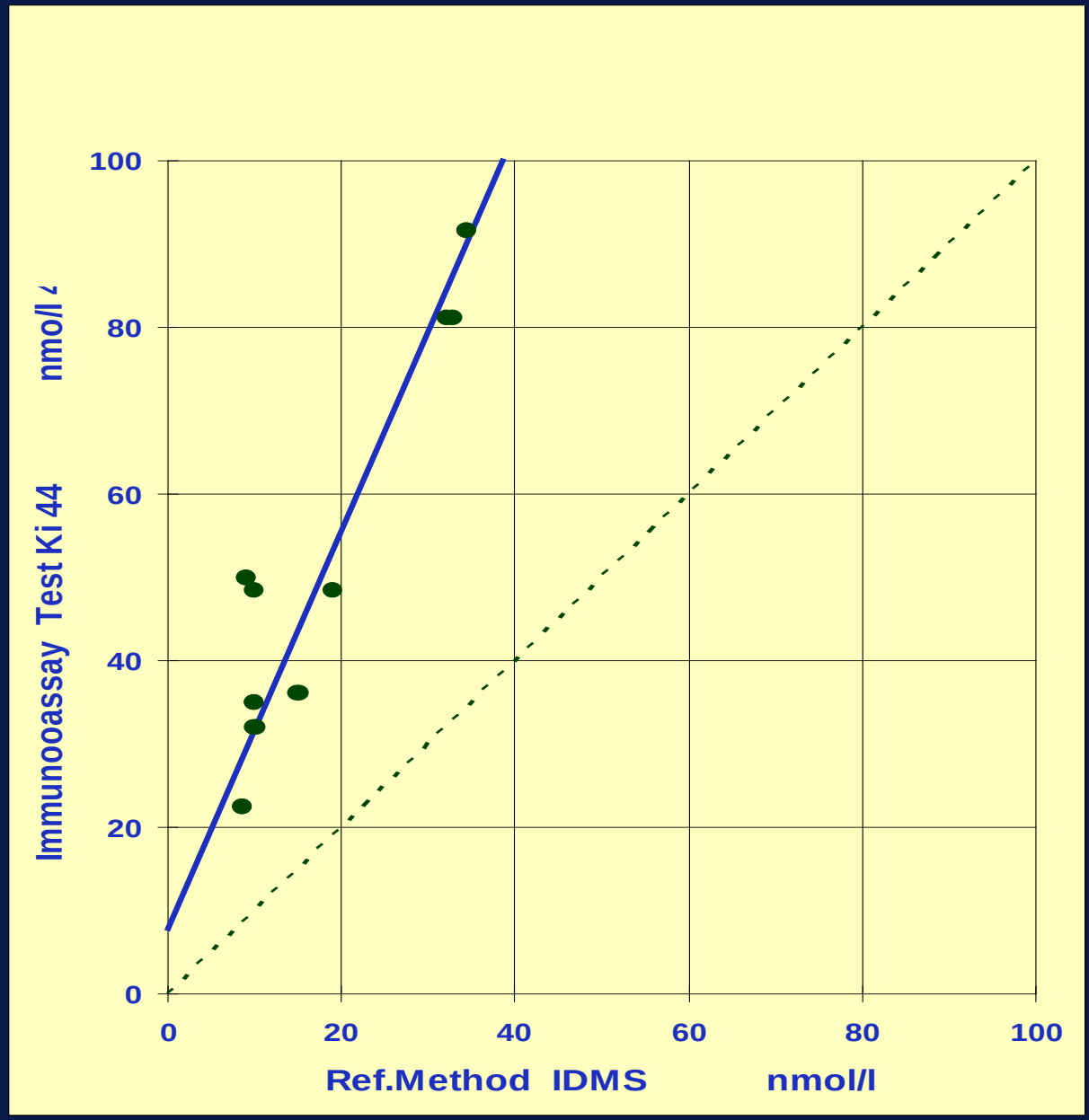
RfB



Teilnehmer ausgewählt	28	
Zielwert	8,35	17,8
Grenzen	5,01 - 11,7	10,6 - 25
Mittelwert	6,736	16,356
Standardabweichung	1,147	2,728
Variationskoeffizient	17,023	16,678

Unconjugated Estriol in Serum of Pregnant Women

Method Comparison



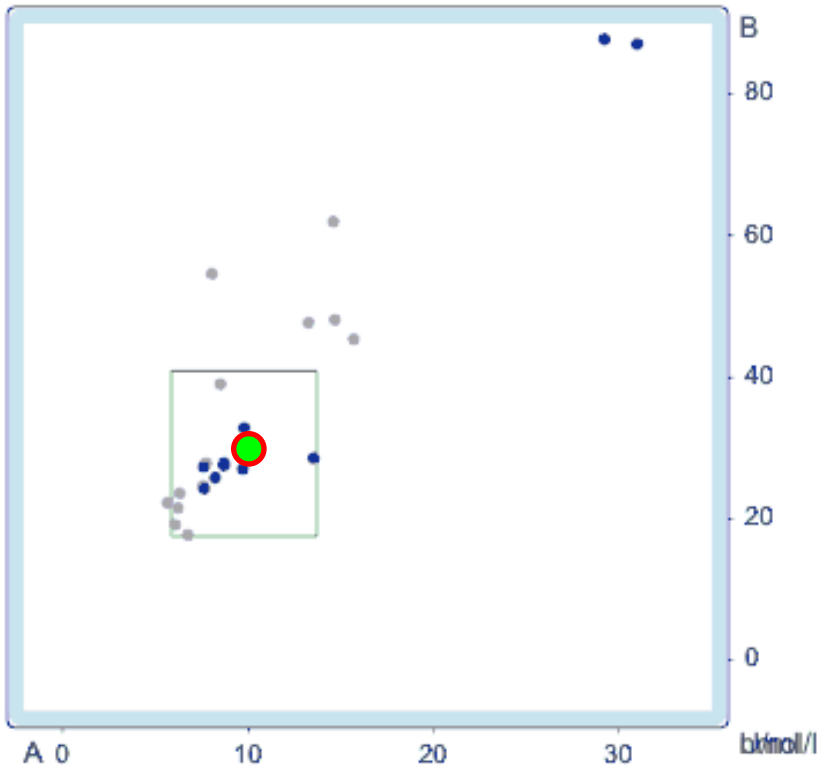
SD1/12

Freies Estriol

RfB

Lumineszenzmessung - Kit 44

Split 1



Anzahl Teilnehmer	15	
Zielwert	9,75	29,2
Grenzen	5,85 - 13,7	17,5 - 40,9
Mittelwert	12,211	36,306
Standardabweichung	7,402	20,857
Variationscoeffizient	60,613	57,448

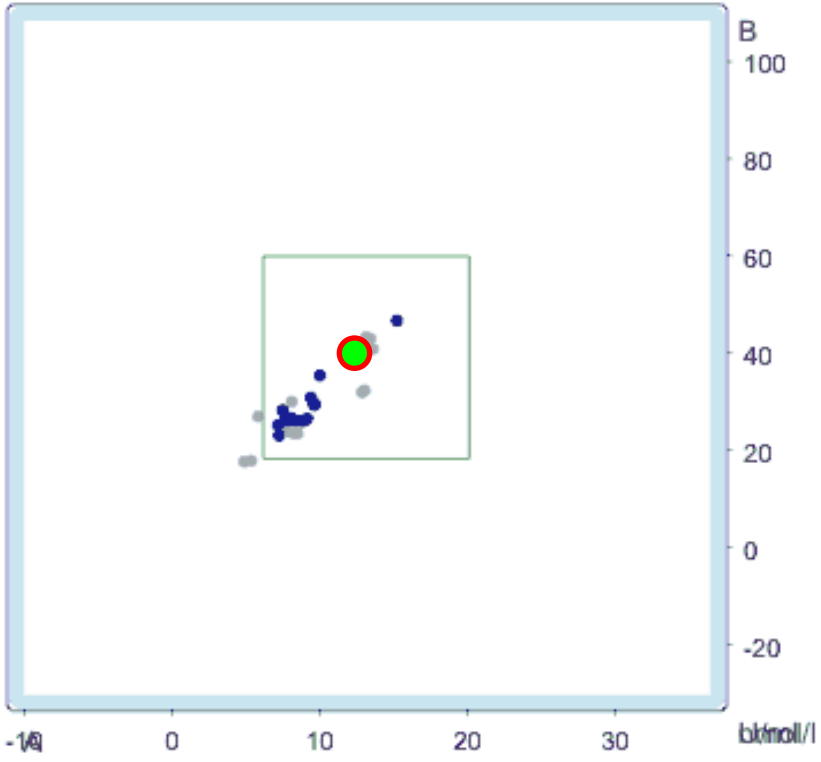
SD4/12

Freies Estriol

RfB

Lumineszenzmessung - Kit 44

Split 1



Anzahl Teilnehmer	18	
Zielwert	13,1	39,1
Grenzen	6,15 - 20,1	18,3 - 59,9
Mittelwert	8,859	28,394
Standardabweichung	1,808	5,302
Variationscoeffizient	20,41	18,674

Conclusions

The commutability of a material with certified reference method values as targets for EQA

- **cannot be demonstrated by the relation of results for only few clinical samples - e.g. from healthy volunters - and the EQA materials using reference and routine procedure.**

- **Comparison experiments to demonstrate commutability must cover the whole range of concentrations and possible matrix effects of clinical samples (interference from medication, lipaemic sera).**

- **This requires time-consuming and expensive measurement campaigns.**

JCGM 200:2012 (VIM)

5.15
commutability of a reference material

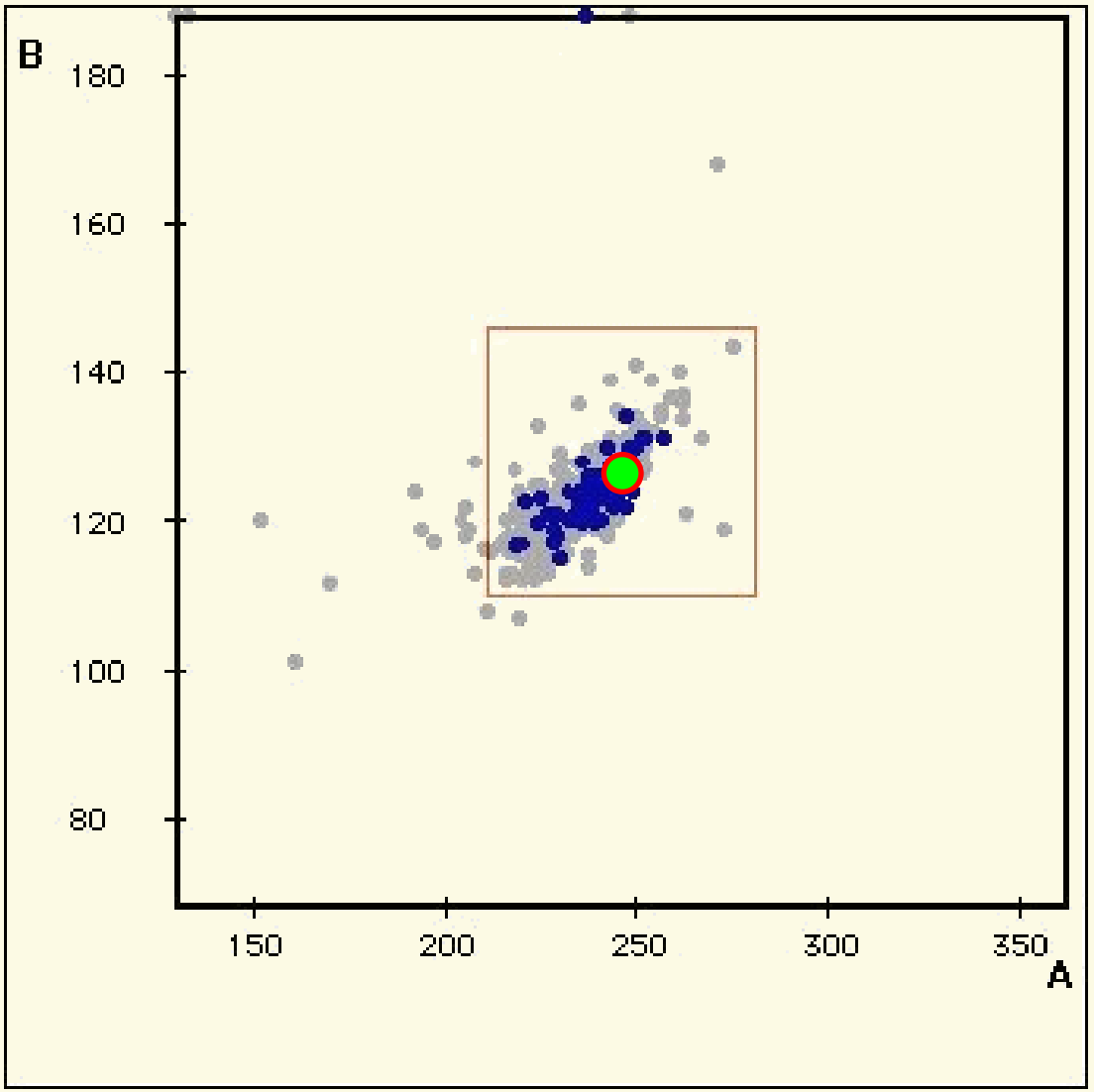
property of a **reference material**, demonstrated by the closeness of agreement between the relation among the **measurement results** for a stated **quantity** in this material, obtained according to two given **measurement procedures**, and the relation obtained among the measurement results for other specified materials

NOTE 1 The reference material in question is usually a **calibrator** and the other specified materials are usually routine samples.

NOTE 2 The measurement procedures referred to in the definition are the one preceding and the one following the reference material (calibrator) in question in a **calibration hierarchy** (see ISO 17511).

NOTE 3 The stability of commutable reference materials should be monitored regularly.

Cholesterol in Human Serum - DGKL- EQAS 2007 - 3



Method: CHOD-PAP

Manufacturer: Kit - 38

Participants: 99 (680)

http://www.dgkl-rfb.de