SYDPATH
ST VINCENT'S PATHOLOGY

ST VINCENT'S HOSPITAL
SYDNEY
A FACILITY OF ST VINCENT'S HEALTH AUSTRALIA

Chronic Kidney Disease
Implementation of Metrological Traceability

Graham Jones
Department of Chemical Pathology
St Vincent's Hospital, Sydney

JCTLM Paris December 2019

Organisations

ifcc International Federation of Clinical Chemistry and Laboratory Medicine

World Association of Societies of Pathology and Laboratory Medicine — Paris 1947

Task Force CKD

(chair 2009 – 2015)

RCPA The Royal College of Pathologists of Australasia

aacb testing for health

RCPAQAP RCPA Quality Assurance Programs

Australasian Creatinine Consensus

(co-chair 2004 – 2012)

APFCB ASIA-PACIFIC FEDERATION FOR CLINICAL BIOCHEMISTRY AND LABORATORY MEDICINE

JCTLM

SYDPATH ST VINCENT'S PATHOLOGY

ST VINCENT'S HOSPITAL SYDNEY

A FACILITY OF ST VINCENT'S HEALTH AUSTRALIA

International Guidelines

2013

163 pages
5 parts (pt1)
(see p5 – 7)

Endorsed by IFCC/WASPaLM TF-CKD

VOLUME 3 | ISSUE 1 | JANUARY 2013

Prognosis of CKD by GFR and Albuminuria Categories: KDIGO 2012

GFR categories (ml/min/ 1.73 m²) Description and range				Persistent albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30-300 mg/g 3-30 mg/mmol	>300 mg/g >30 mg/mmol
	G1	Normal or high	≥90			
	G2	Mildly decreased	60-89			
	G3a	Mildly to moderately decreased	45-59			
	G3b	Moderately to severely decreased	30-44			
	G4	Severely decreased	15-29			
	G5	Kidney failure	<15			

markers of kidney disease, no CKD); Yellow: moderately increased risk; Orange: high risk; Red, very high risk.

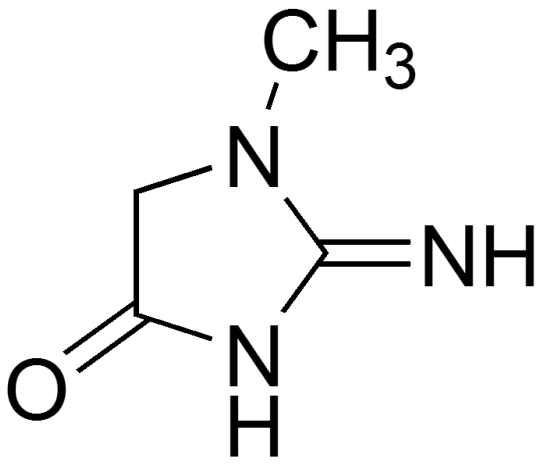
Chronic Kidney Disease

- Diagnosis and Staging of CKD based on ***Glomerular Filtration Rate (GFR)***
- GFR estimated using equations based on ***serum creatinine***

- ***Creatinine Measurements***
  - One of the most common lab tests
  - The basis of (nearly) all kidney decisions Acute, Chronic, Drug dosing

Creatinine

- Many assays (still) based on Jaffe reaction (1896)
- Limited analytical specificity
- Cross reacts with other components of serum
- Calibration with pure creatinine gives wrong answers
- Can be “adjusted” or enzymatic method



~2005

- Creatinine assays not standardised
- Needed fixing!

Creatinine Standardisation - NKDEP

- National Kidney Disease Education Program
- Laboratory Working Group
  - Clinicians
  - Laboratorians
  - Metrologists (JCTLM)
  - Manufacturers

2010: All major international suppliers have traceable assays

NKDEP National Kidney Disease Education Program

Results of the search

Your search criteria produced 6 summary results.
Select one or several higher-order reference material summary descriptions amongst the following list and click on 'View' to access more information.

Select all items from the list

Sort by : (•) Analyte ( ) Matrix/Material ( ) Organization

Select	Analyte	Analyte category	Matrix/Material	Organization
☐	creatinine	metabolites and substrates	creatinine crystalline material	NIST
☐	creatinine	metabolites and substrates	frozen human serum	CENAM
☐	creatinine	metabolites and substrates	human serum	JRC
☐	creatinine	metabolites and substrates	human serum	LGC
☐	creatinine	metabolites and substrates	creatinine crystalline material	NMIJ
☐	creatinine	metabolites and substrates	frozen human serum	LNE

Deselect all items from the list

View →

Results of the search

Your search criteria produced 4 results.
For more information on a reference measurement method/procedure for a given Analyte/Matrix (or Material)/Measurement principle (or technique) combination, select one or more of the options below.

Select all items from the list

Sort by : (•) Analyte ( ) Measurement principle/technique ( ) Matrix/Material

Select	Analyte	Measurement principle/technique	Matrix/Material
☐	creatinine	Isotope dilution mass spectrometry	blood plasma
☐	creatinine	Isotope dilution mass spectrometry	blood serum
☐	creatinine	Isotope dilution mass spectrometry	urine
☐	creatinine	Isotope dilution surface enhanced raman scattering	blood serum

Deselect all items from the list

View →

Results of the search

Your search criteria produced 14 summary results.
Select one or several reference measurement service summary descriptions amongst the following list and click on 'View' to access more information.

Select all items from the list

Sort by : (•) Analyte ( ) Matrix or Material ( ) Service provider

Select	Analyte	Matrix or Material	Country	Service provider
☐	creatinine	blood plasma	Germany	Instand e.V.
☐	creatinine	blood plasma	Germany	RfB-DGKL
☐	creatinine	blood plasma	China	Shanghai Center for Clinical Laboratory (SCCL)
☐	creatinine	blood serum	Germany	Instand e.V.
☐	creatinine	blood serum	France	LNE
☐	creatinine	blood serum	China	National Center for Clinical Laboratories (NCCL)
☐	creatinine	blood serum	Japan	ReCCS
☐	creatinine	blood serum	Germany	RfB-DGKL
☐	creatinine	blood serum	China	Shanghai Center for Clinical Laboratory (SCCL)
☐	creatinine	blood serum	United Kingdom	WEQAS
☐	creatinine	calibration solution	France	LNE
☐	creatinine	calibration solution	China	National Center for Clinical Laboratories (NCCL)
☐	creatinine	calibration solution	Germany	RfB-DGKL
☐	creatinine	urine	Germany	RfB-DGKL

Deselect all items from the list

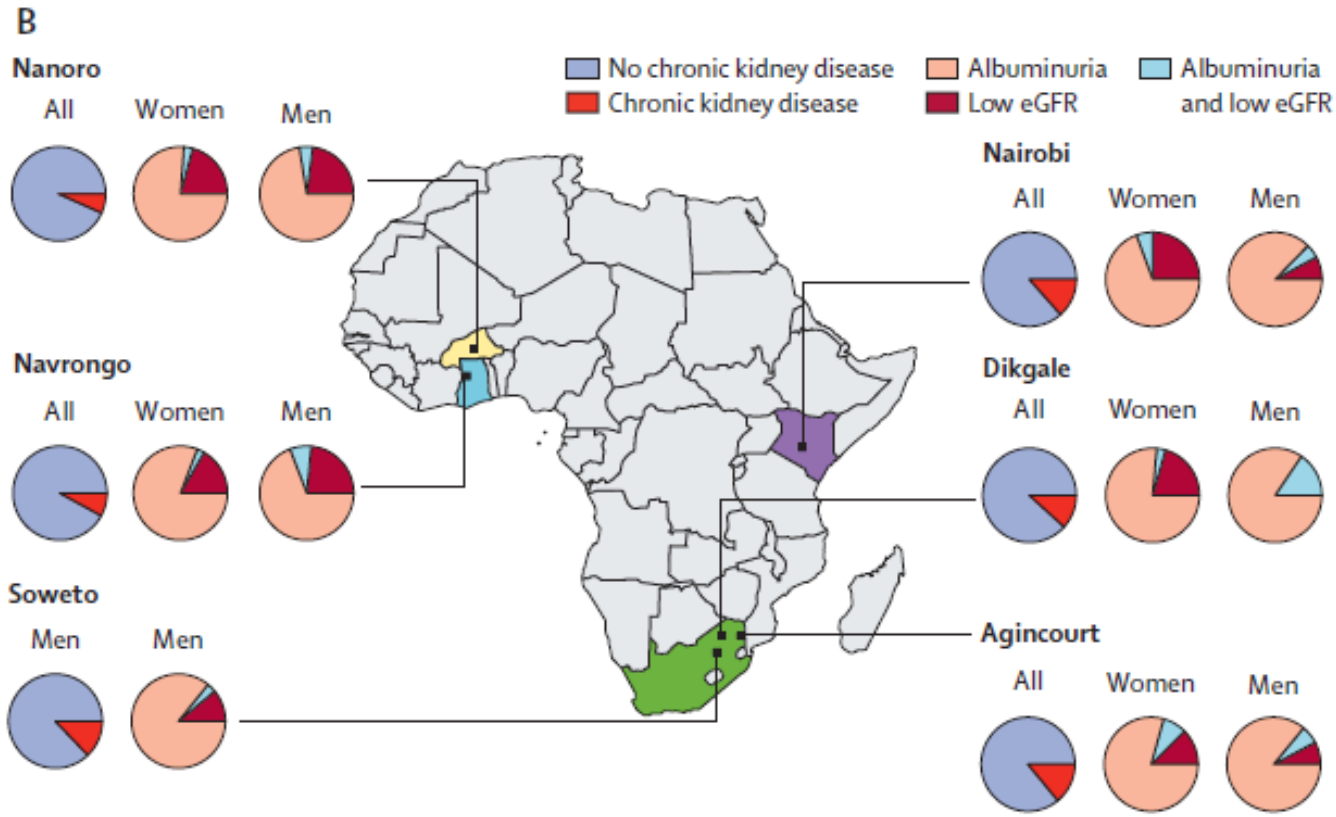
View →

Standardisation for global Epidemiology

THE LANCET
Global Health
Volume 7, Issue 12, December 2019, Pages e1632-e1643

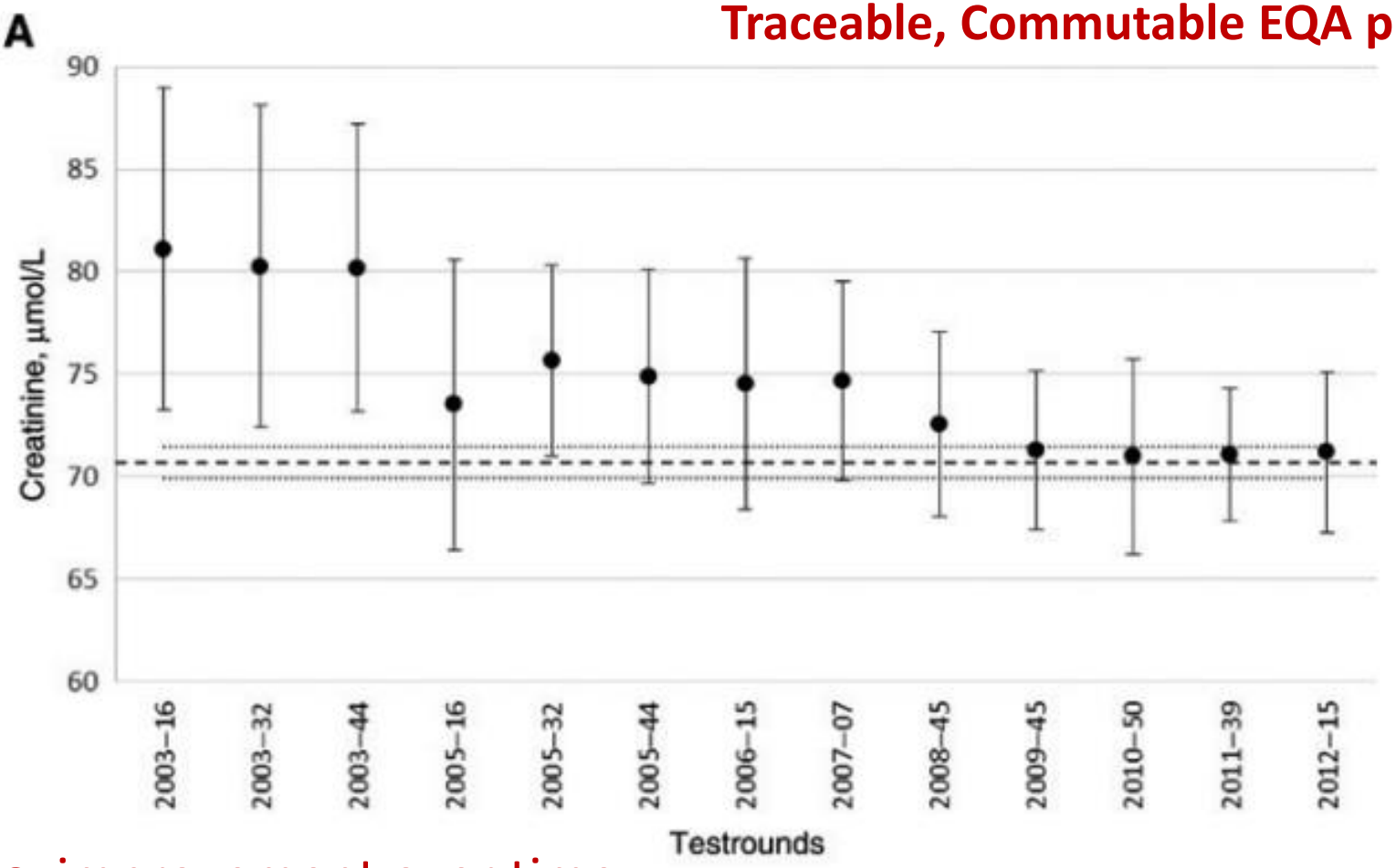
Kidney damage and associated risk fact sub-Saharan Africa (AWI-Gen): a cross-sectional population study

Jaya A George, Jean-Tristan Brandenburg*, June Fabian, Nigel J Crowther, Godfred Agongo, Marianne Alberts, Stuart Ali, Gershim Asiki, Palwende R Boua, F Xavier Gómez-Olivé, Felistas Mashinya, Lisa Micklesfield, Shukri F Mohamed, Freedom Mukomana, Shane A Norris, Abraham R Oduro, Cassandra Soo, Hermann Sorgho, Alisha Wade, Saraladevi Naicker, Michèle Ramsay as members of AWI-Gen and the H3Africa Consortium*



- Has this worked?

Traceable, Commutable EQA program



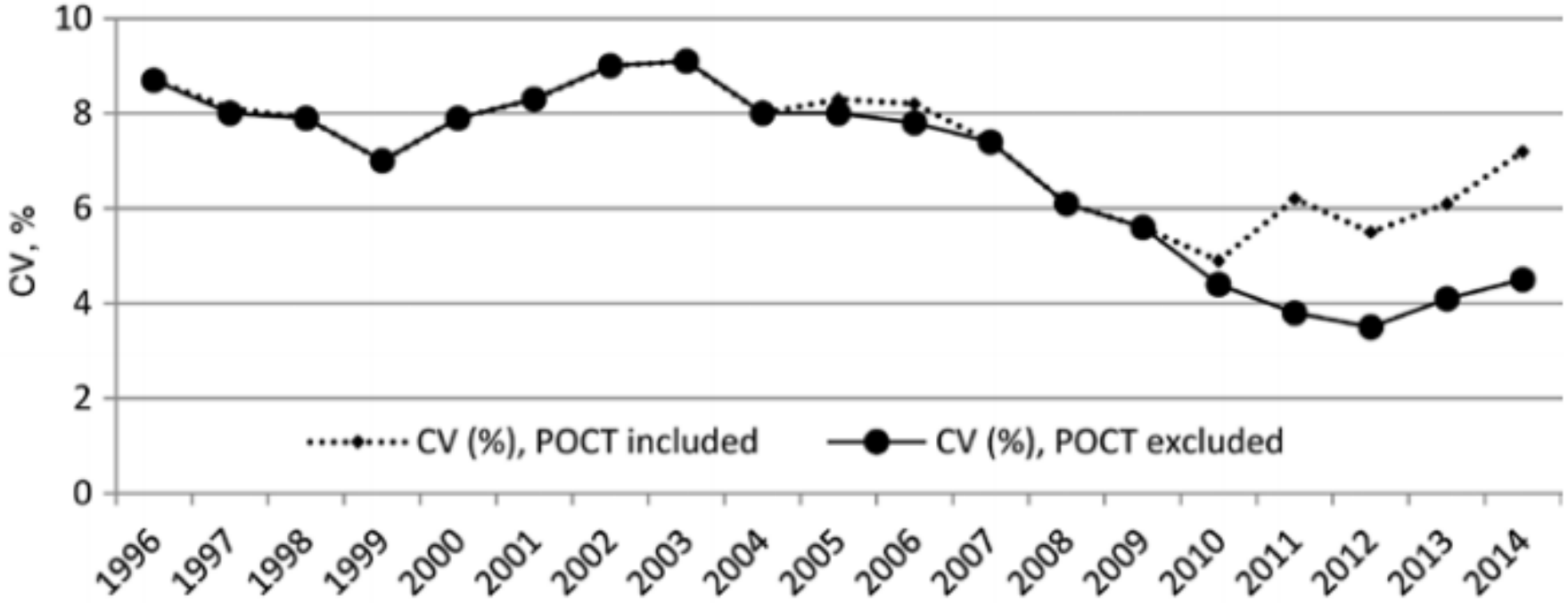
Bias: improvement over time

Clin Chem Lab Med 2019; 57(6): 838–844 DE GRUYTER

Johanna Helmersson-Karlqvist*, Peter Ridefelt, Elisabet Eriksson Boija and Gunnar Nordin

Lower creatinine concentration values and lower inter-laboratory variation among Swedish hospital laboratories in 2014 compared to 1996: results from the Equalis external quality assessment program

Traceable, Commutable EQA program



Between-lab variation: improvement over time

Clin Chem Lab Med 2019; 57(6): 838–844 DE GRUYTER

Johanna Helmersson-Karlqvist*, Peter Ridefelt, Elisabet Eriksson Boija and Gunnar Nordin

Lower creatinine concentration values and lower inter-laboratory variation among Swedish hospital laboratories in 2014 compared to 1996: results from the Equalis external quality assessment program

https://doi.org/10.15263/jlmqa.2019.41.1.13

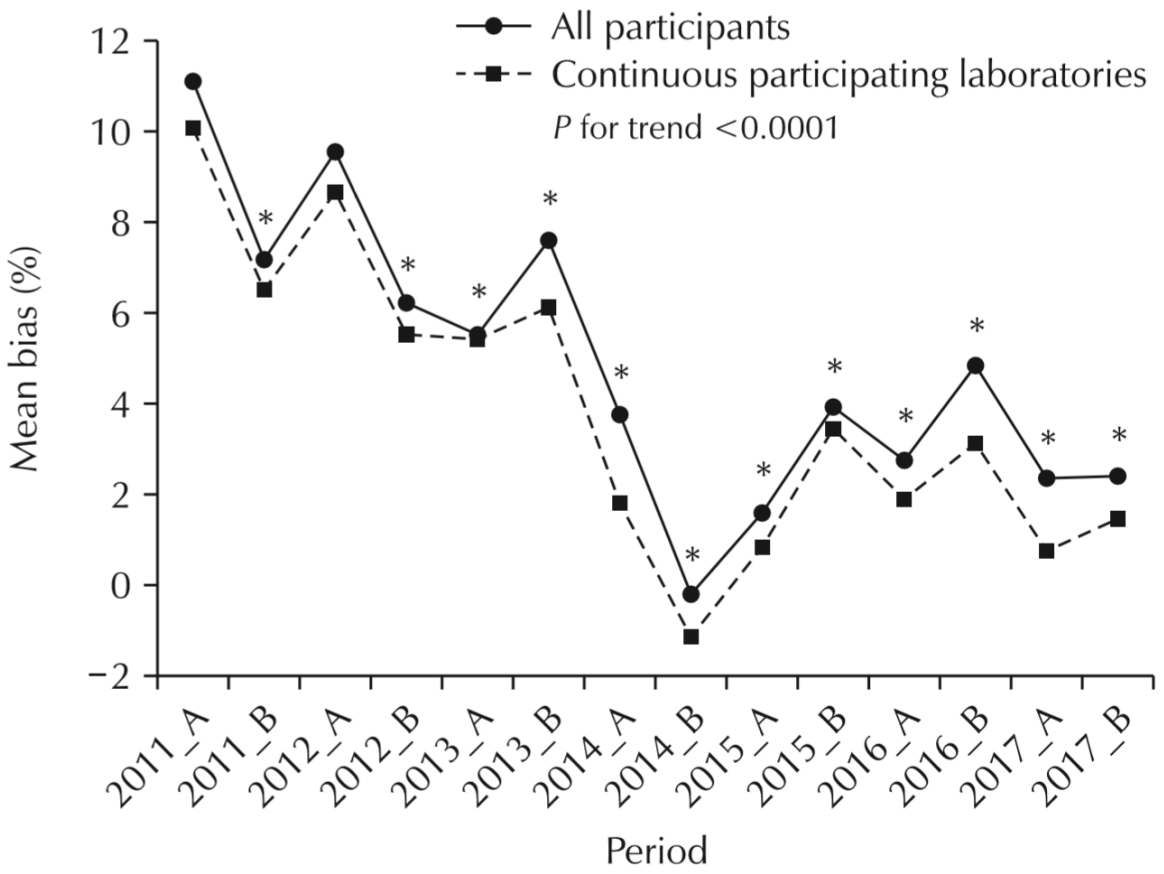
ORIGINAL ARTICLE

임상검사와 정도관리

Journal of LABORATORY MEDICINE / and QUALITY ASSURANCE

Accuracy-Based Proficiency Testing of Creatinine Measurement: 7 Years' Experience in Korea

Tae-Dong Jeong[1], Hye Ah Lee[2], Kyunghoon Lee[3], and Yeo-Min Yun[4]



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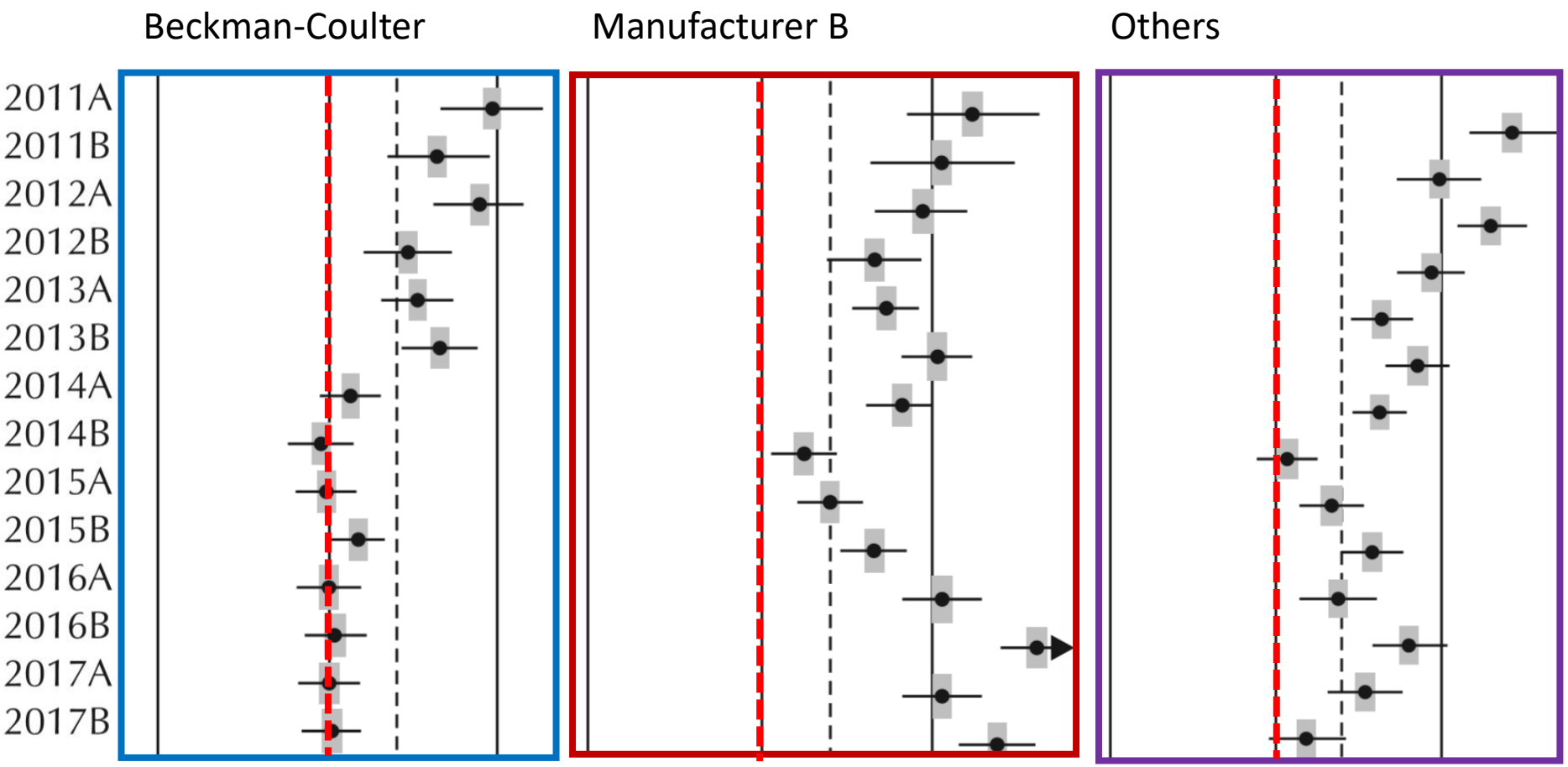
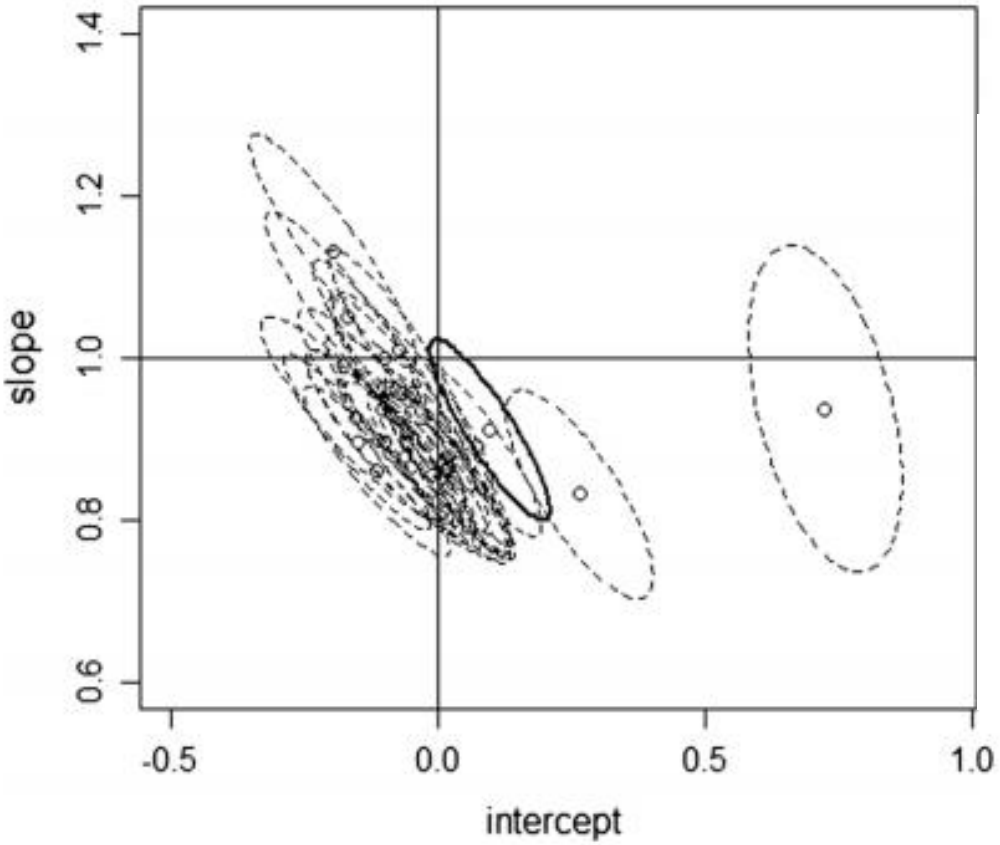


Accreditation and Quality Assurance (2019) 24:3–8

Standardization and improvement program for creatinine measurement in human serum

Gasca-Aragon et al (Mexico)



Method type	Participants
Jaffé method	16
Enzymatic method	6
Dry chemistry method	2
Photometric method	2
Reflectance method	1

Accreditation and Quality Assurance (2019) 24:3–8

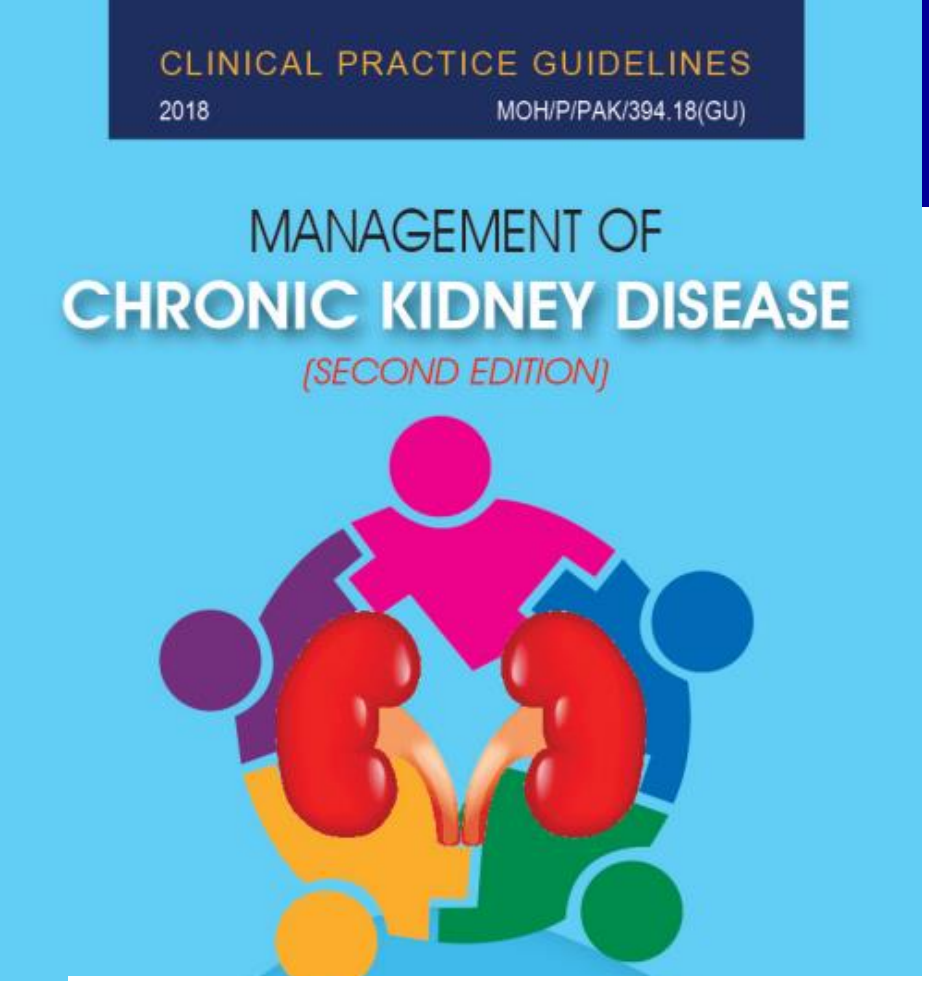
Standardization and improvement program for creatinine measurement in human serum

Gasca-Aragon et al (Mexico)

Using uncorrected data \ Using corrected data	1	2	3	4	5	
1	1171	27	54	0	0	1252
2	394	307	36	0	0	737
3	0	133	188	0	0	321
4	0	0	18	35	0	53
5	0	0	0	5	48	53
	1565	467	296	40	48	2416

Using corrected assays: 28% classified differently

Malaysia (2018) .



When creatinine-based equations are used, calibration of SCr should confer to the isotope dilution mass spectrophotometry method to minimise variations in results.[9]

In the Lab

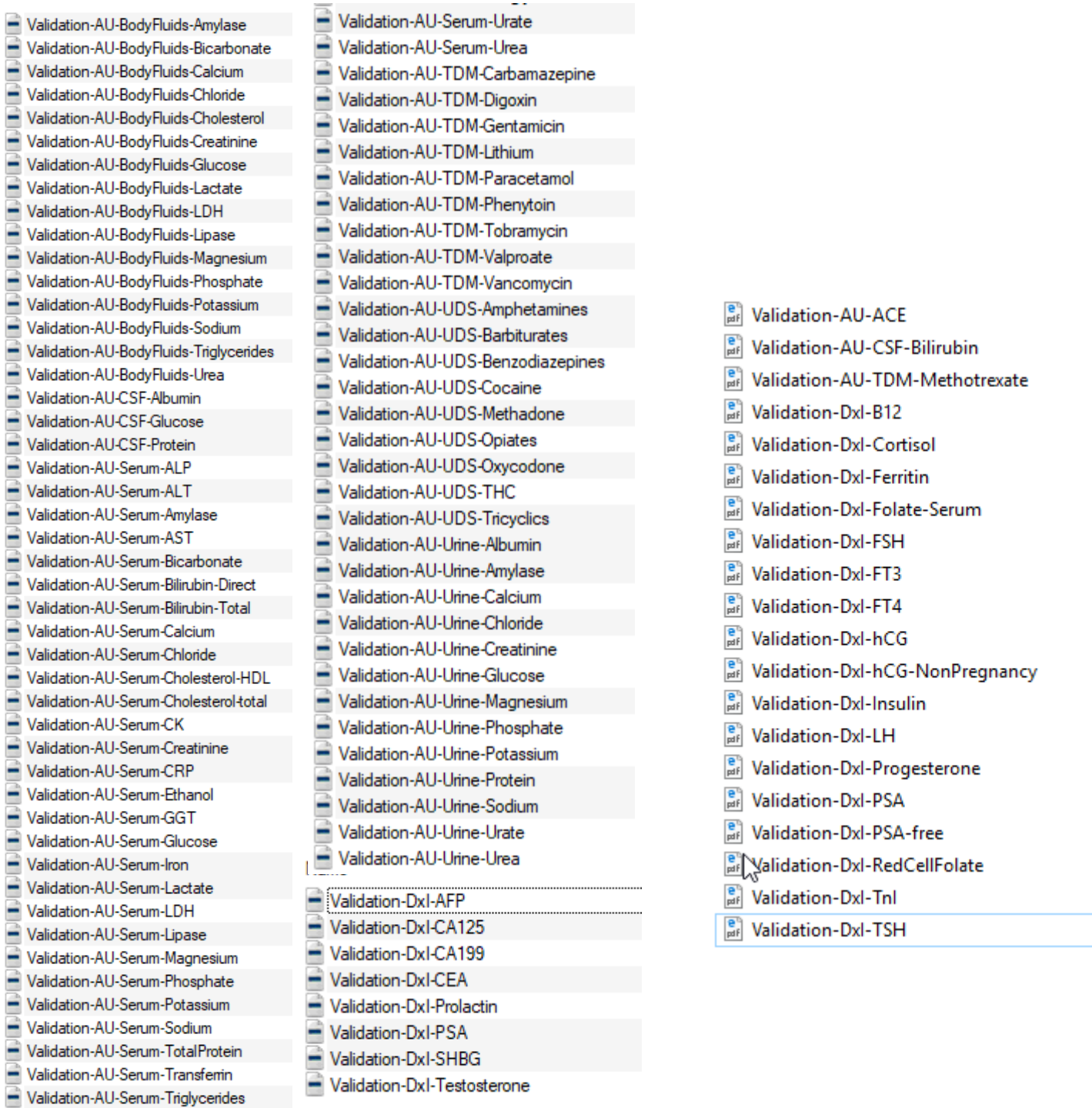
SydPath: Change of Supplier

- Change in chemistry and Immunoassay Suppliers

SYDPATH
ST VINCENT'S PATHOLOGY

- 116 measurands changed

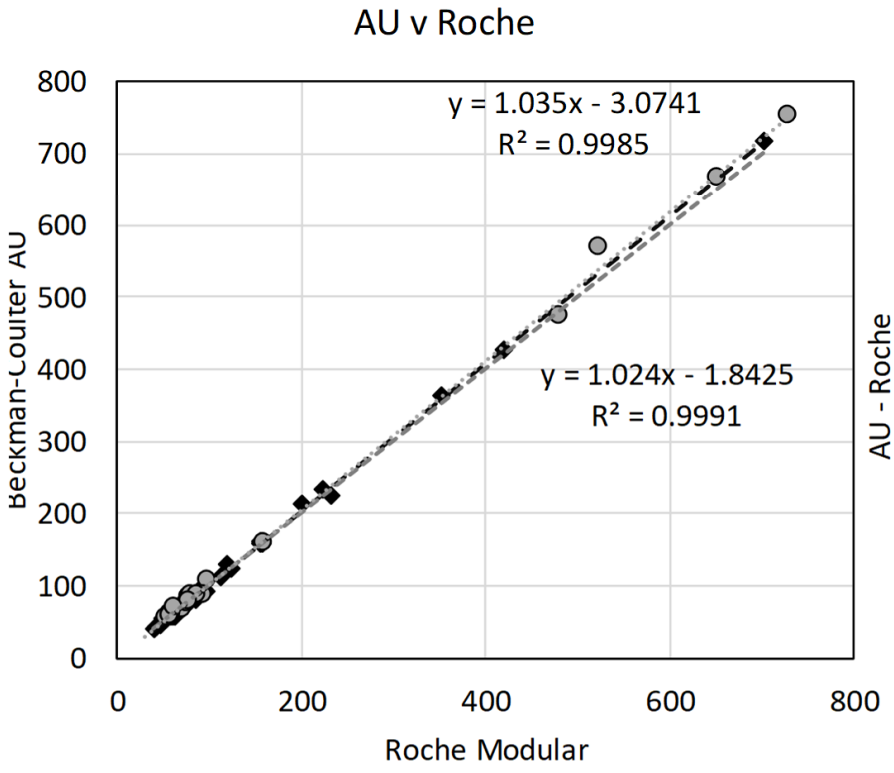
Validation Documents

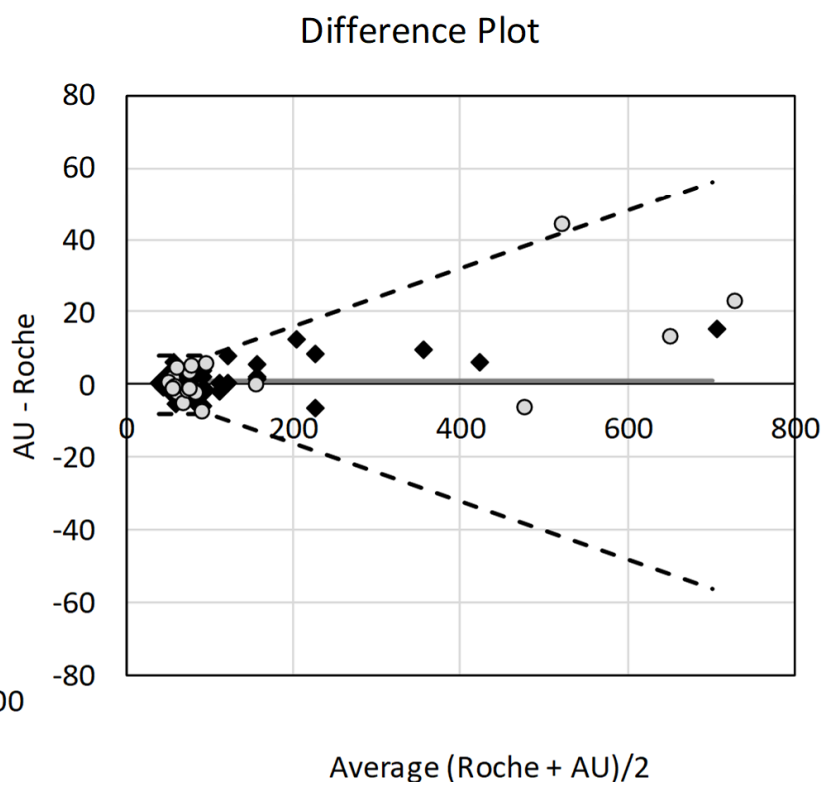


Traceability Information

Test	Beckman	Roche	Abbott
Sodium	NIST SRM 2201	calibrators (gravimetrically from purified sa	NIST SRM
Potassium	NIST SRM 2201	calibrators (gravimetrically from purified sa	NIST SRM
Chloride	NIST SRM 2201	calibrators (gravimetrically from purified sa	NIST SRM 2202
Bicarbonate	Traceable to NIST (SRM) 351	Against a primary standard	NIST 351
Creatinine (enzymatic)	IDMS via NIST SRM 967	Against ID/MS	NIST SRM 967
Urea	NIST SRM 909b level 1	Against ID/MS	NIST SRM 912
Amylase	Traceable to a manual IFCC refe	Roche reagent/manual application	IFCC Reference Procedure (2006)4/2-chl
Bilirubin-direct	Traceable to Beckman Coulter M	Against the Doumas method	Human Samples
Creatine Kinase	IFCC	Against the IFCC Method for Creatine Kinas	IFCC Reference Procedure (2002)6
CRP	IFCC standard CRM 470 by Immu	CRM470	ERM-DA472/IFCC
Ethanol	Traceable to Primary Gravimetri	Agaisnt NIST traceable material	>99% pure Ethanol Standard
Fructosamine	0	Against fructose polylysine standard	Glycated poly- L-lysine/14Cglucose
Glucose	Traceable to NIST SRM 965	Against ID/MS	NIST SRM 965
Iron	Traceable to Beckman Coulter M	Against a primary reference material (SRM	NIST SRM 3126
Lactate	Primary standard- gravimetric u	Against a primary standard	Reagent Grade Lactic Acid
LDH	Traceable to IFCC reference me	Against IFCC formulation	IFCC Reference Procedure (2002)8
Lipase	Traceable to Beckman Coulter M	Roche reagent/manual application	Purified Human Pancreatic Lipase (>900
Paracetamol	Traceable to a Gravimetrically p	Against USP reference standard	Acetaminophen Reference Standard (98
Salicylate	Traceable to IVD directives 98/7	Against USP reference standard	USP grade Salicylate
Transferrin	BCR-470	Against an in-house reference preparation	ERM-DA470/IFCC
Urate	Traceable to IDMS method	Against ID/MS	NIST SRM 913
Albumin	CRM 470	Against the ref. prep. of the IRMM BCR470/	ERM-DA470
ALP	IFCC method recommendations	Against IFCC formulation	IFCC Reference Procedure (2011)3/p-nitr
ALT	With P5P activation traceable to	Against IFCC formulation with PYP	IFCC Reference Procedure (2002)2
AST	With P5P activation traceable to	IFCC formulation with PYP	IFCC Reference Procedure (2002)5
Bilirubin-total	Traceable to NIST SRM 916a	Against the Doumas method	NIST SRM 916

Creatinine Method Comparison





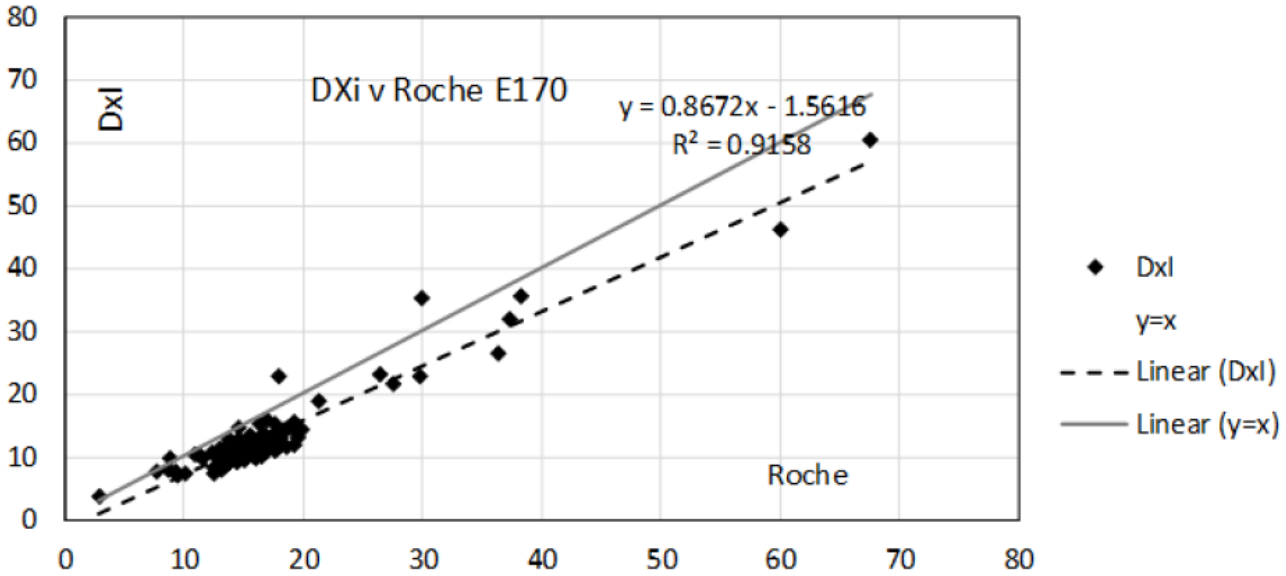
Traceability in action!

Method Comparison – Free T4

BECKMAN COULTER DxI VALIDATION - METHOD COMPARISON

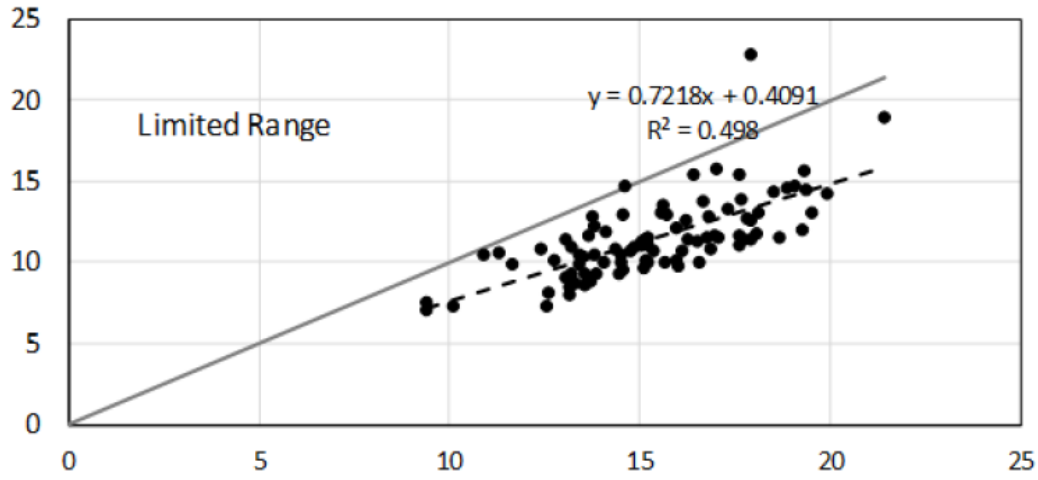
Free T4 **Units:** pmol/L **PrintDate: 11/09/2018**

Roche Ave	17.04
DxI Ave	13.18
Diff (units)	-3.86
Ratio	0.774
Slope	0.868
Intercept	-1.61
correl	0.957
Median	15.20
Min	2.90
Max	67.60
n	107
CV(est)	11.9%



Limited Range

Slope	0.722
Intercept	0.4
correl	0.71
n	93
9- 25 pmol/L	



APS: +/-12 to 1.5 then 12

Print Date: 11/9/18

Source ([Filename]sheet): [Validation-Immunoassay-DxI-2018-MASTER-BACKUP-2018-09-11.xlsx]MethCompGroup

Changes

Significant differences

- 20 (out of 90) tests
- 4 (out of 8) calculations

Actions

- Alert clinicians
- Review reference intervals
- Change reporting (+written alert)
- Period of clinical risk

Clinical Pathology

SMITH, WILLIAM

MRN: 1234567

DoB: 01/04/1960 (M) 1 MADEUP ST, ELSEWHERE, NSW, Tel: 0555-123456

Atomic Report (HTML)

Chemical Pathology - Latest Results Sets (1 - 6 of 6)

BLOOD CHEMISTRY	newest results 30 Oct 18 11:45 TC30458937	26 Apr 17 08:00 TC30269460	19 Feb 16 11:55 TC30095462	16 Feb 16 11:00 TC30024192	14 Feb 16 10:34 TC30024474	18 Mar 15 08:05 TC30025810	Range	Units
Range Comment	Com'nt	---	---	---	---	---		
Sodium	---	141	---	---	142	---	137-146	mmol/L
Sodium	139	---	---	---	---	---	135-145	mmol/L
Potassium	4.4	4.5	---	---	4.7	---	3.5-5.2	mmol/L
Chloride	106	104	---	---	106	---	95-110	mmol/L
Bicarbonate	25	23	---	---	26	---	22-32	mmol/L
Urea	---	9.8*H	---	---	6.8	---	3.0-8.5	mmol/L
Urea	7.8	---	---	---	---	---	4.5-10.0	mmol/L
Creatinine	---	62	---	---	59*L	---	60-120	umol/L
Creatinine	66	---	---	---	---	---	60-110	umol/L
eGFR	85	88	---	---	>90	---	>60	mL/mn/1.73m2
eGFR comm	Com'nt	Com'nt	---	---	---	---		
Uric acid	0.47	0.45	---	---	---	---	0.25-0.50	mmol/L
Glucose (R)	6.2	5.9	---	---	5.2	---	3.0-7.8	mmol/L
Inorg. Phos.	---	1.06	---	---	---	---	0.70-1.40	mmol/L
Inorg. Phos.	1.17	---	---	---	---	---	0.70-1.50	mmol/L
Magnesium	---	0.89	---	---	---	---	0.70-1.05	mmol/L
Magnesium	0.92	---	---	---	---	---	0.70-1.10	mmol/L
Calcium	2.36	2.34	---	---	---	---	2.10-2.60	mmol/L
Ca alb corr	2.37	2.28	---	---	---	---	2.10-2.60	mmol/L
Albumin	---	43	---	---	44	---	36-52	g/L
Albumin	39	---	---	---	---	---	33-48	g/L
Tot. protein	---	70	---	---	68	---	60-82	g/L
Tot. protein	68	---	---	---	---	---	60-80	g/L
Tot bilirubin	---	5	---	---	9	---	0-18	umol/L

Comments on reports

LFT range com - Request No: TC11315466 -- Dec 2 2018 03:53PM

LIVER FUNCTION TESTS: From 2nd September 2018 LFT assays and reference intervals have been adjusted. AST~10% higher, ALT~10% higher, GGT~15% higher, ALP~5% higher, Bilirubin~20% higher, Albumin~3g/L lower and Protein~3 g/L lower (Dr Graham Jones).

Conclusions

- Reference measurement systems for serum creatinine have been in place for some time
- There has been sigficant improvement in many locations
- Work remains to be done
- This requires actions by:
  - Manufacturers
  - Laboratories
  - EQA organisations
  - Professional organisations