

Session 3:

Traceability in external quality assessment.

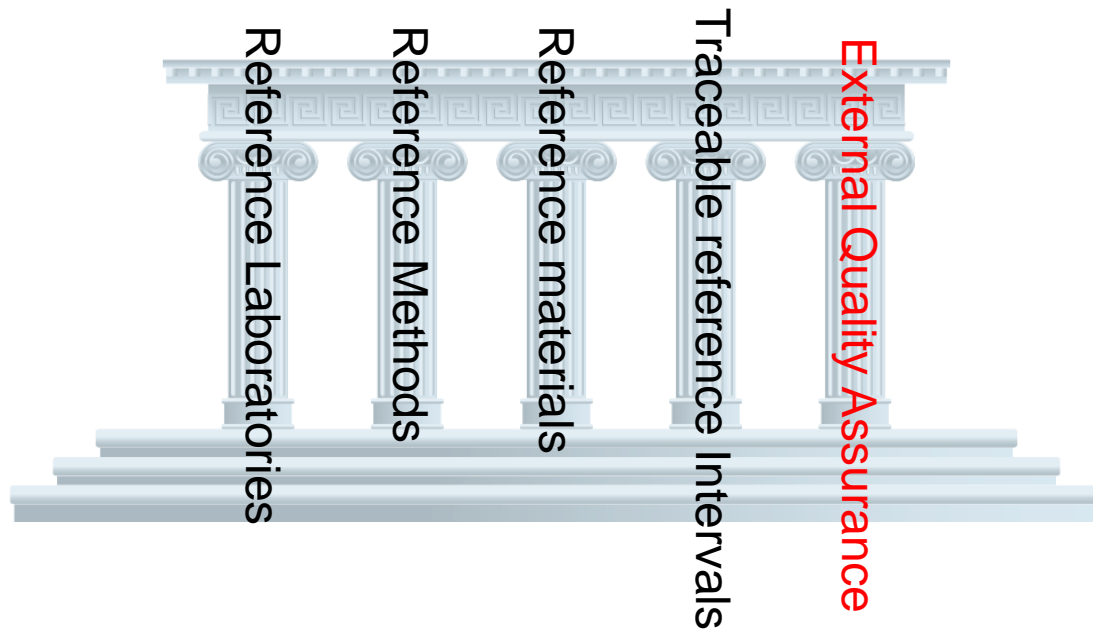
Why traceability is important to EQA providers?

Tony Badrick and Graham Jones
(RCPAQAP)

EQA – the more you look the more you see!



Laboratory Method Standardisation



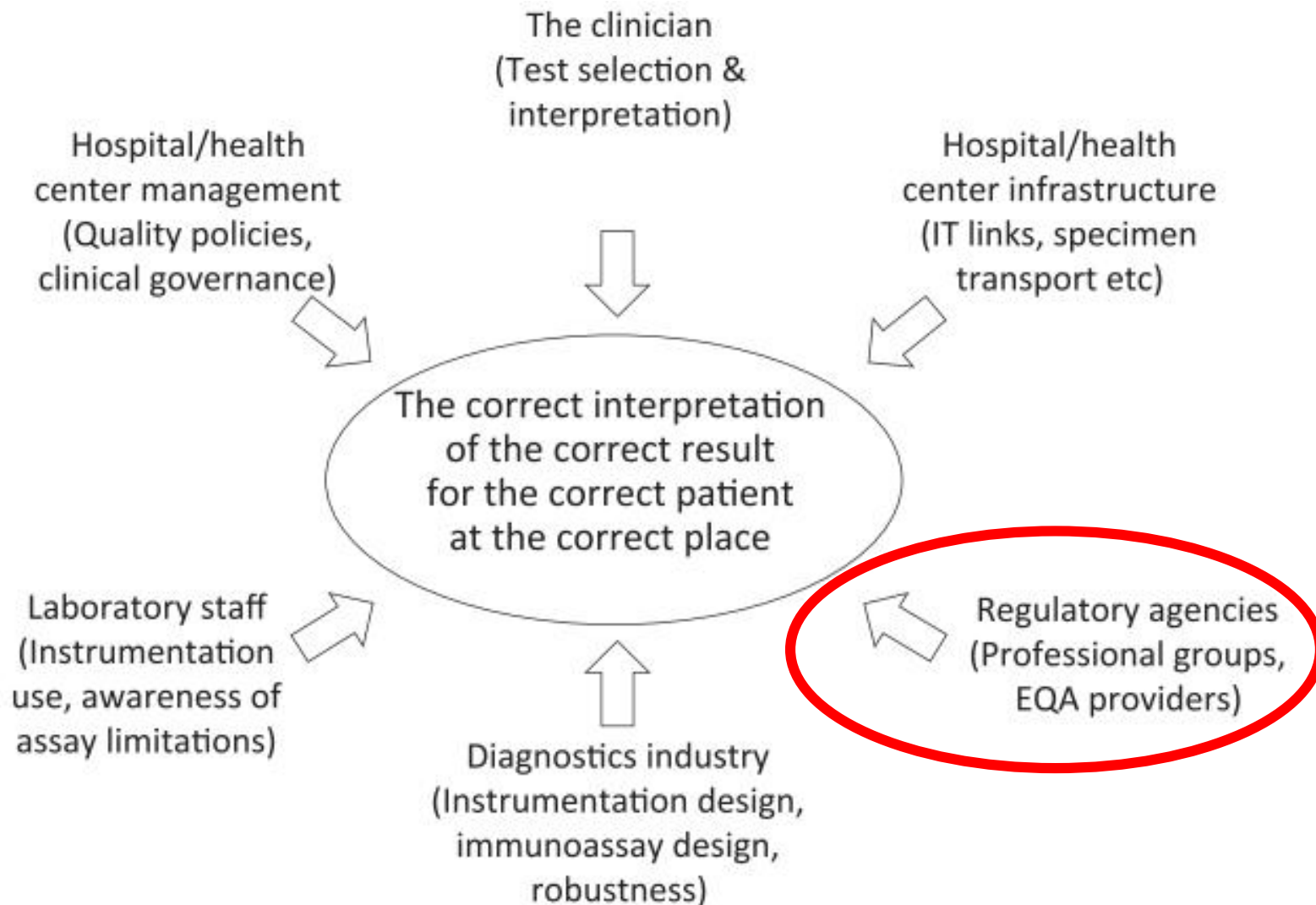


Fig. 1. Parties contributing to the effective use of endocrine tests in clinical care.

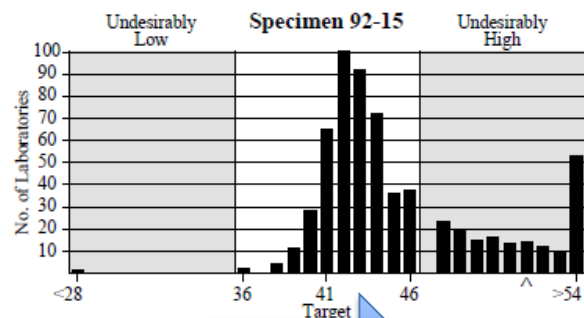
Traceability in EQA

- All QAP results are traceable, it is just a matter of what to.
- For many the way the QAP works is to answer the question (is my X analyser working like an X analyser should). This is traceability to the X analyser group.
- If your reference interval and clinical decision points come from other X analysers, this is very useful.

Due Date : 22/04/2013

Alanine Amino Transferase (U/L 37C)

Laboratory Number



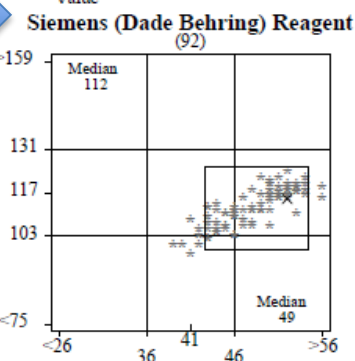
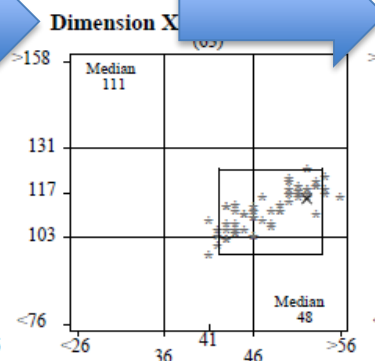
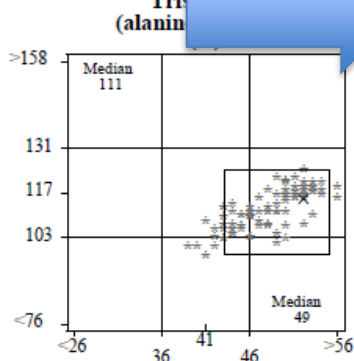
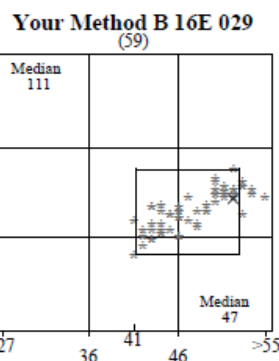
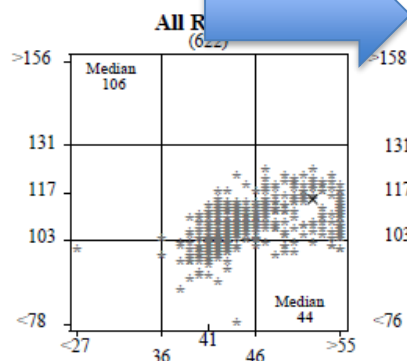
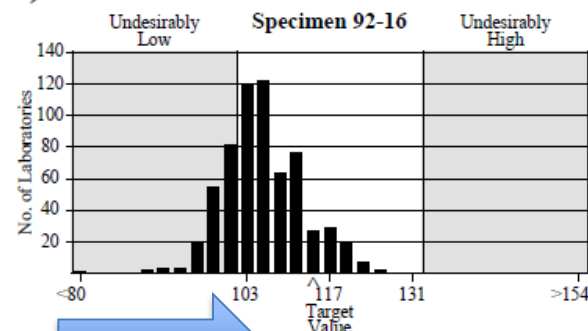
YOUR DATA

Result (^) for 92-15 = 52 U/L 37C
Result (^) for 92-16 = 115 U/L 37C

Your Method Classification : **B 16E 029 A**

B Tris Buffer (alanine >225mm)
16E Dimension XL/RXL/RXL MAX
029 Siemens (Dade Behring)
A Analyser Specific Manufac Suppl

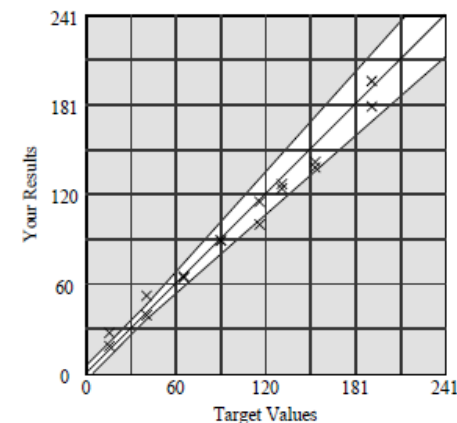
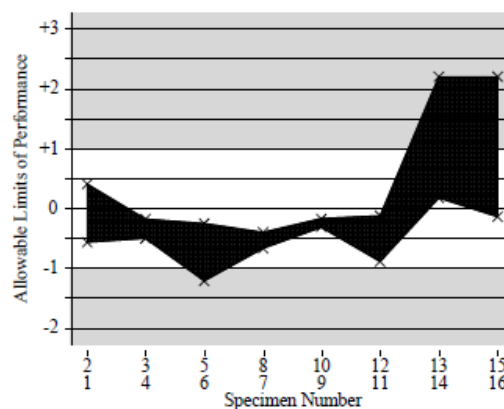
Allowable Limits of Performance
=5 up to 40; =12% >40 U/L 37C



Current Data for Cycle 92

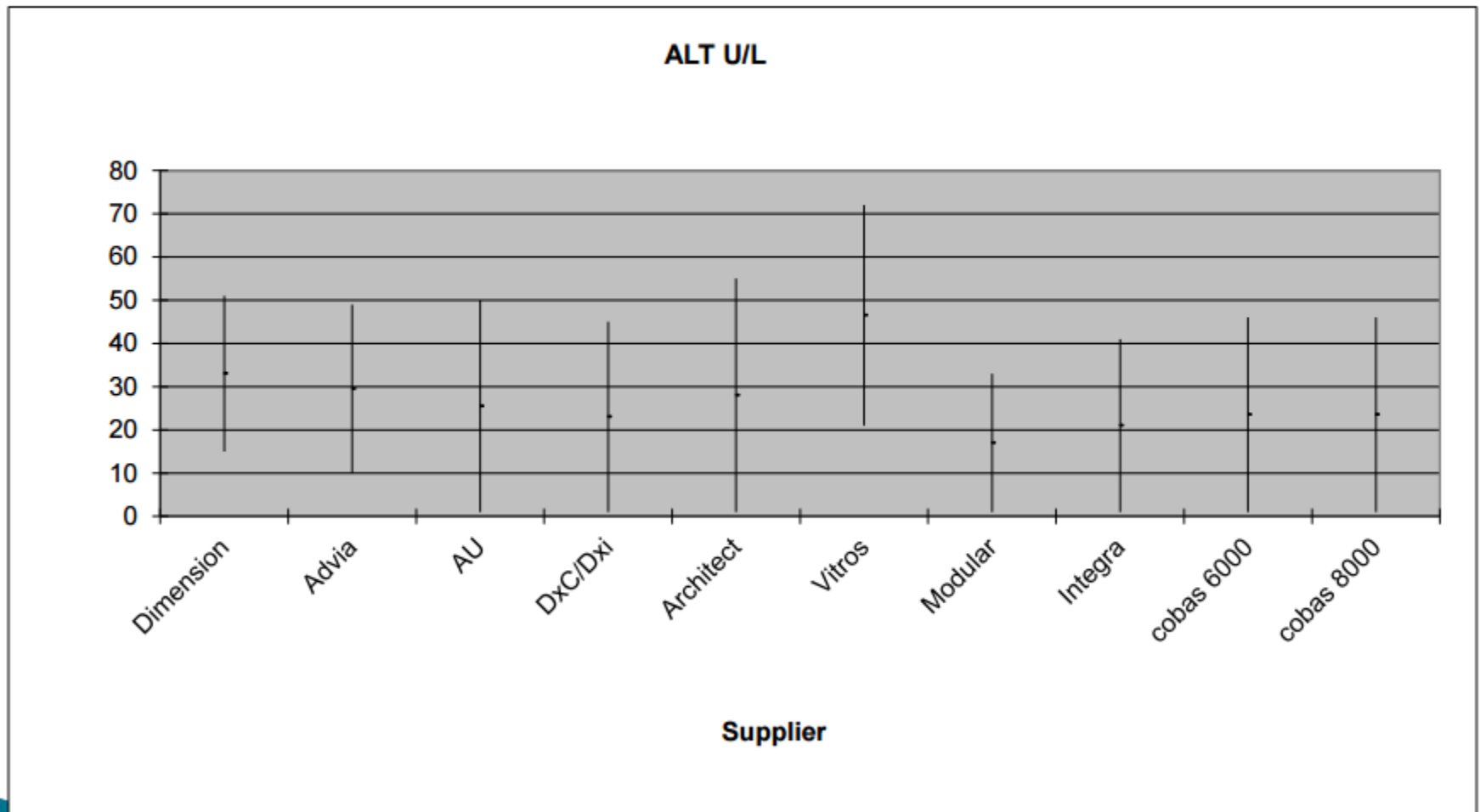
Spec.	Method	Target	Result
92-01	B 16E 029 E	192	179
92-02		16	18
92-03	B 16E 029 E	91	89
92-04		132	124
92-05	B 16E 029 E	66	64
92-06		117	100
92-07	B 16E 029 E	154	142
92-08		41	39
92-09	B 16E 029 E	132	127
92-10		91	89
92-11	B 16E 029 E	154	138
92-12		66	65
92-13	B 16E 029 A	16	27
92-14		192	196
92-15	B 16E 029 A	41	52
92-16		117	115

SUMMARY DATA



Reference limits and flagging abnormal results

ALT Reference Intervals



Proficiency Testing/External Quality Assessment: Current Challenges and Future Directions

W. Greg Miller,^{1*} Graham R.D. Jones,² Gary L. Horowitz,³ and Cas Weykamp⁴

BACKGROUND: Proficiency testing (PT), or external quality assessment (EQA), is intended to verify on a recurring basis that laboratory results conform to expectations for the quality required for patient care.

or harmonization among different measurement procedures.

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Table 3. Evaluation capabilities of PT/EQA related to scheme design.

				Evaluation capability						
				Accuracy						
				Individual laboratory			Standardization or harmonization ^b			
				Relative to participant results		Reproducibility		Measurement procedure calibration traceability		
Category	Commutable	Value assigned with RMP ^a or CRM	Replicate samples in survey	Absolute vs RMP or CRM	Overall	Peer group	Individual laboratory intralab CV	Measurement procedure interlab CV	Absolute vs RMP or CRM	Relative to participant results
1	Yes	Yes	Yes	X	X	X	X	X	X	X
2	Yes	Yes	No	X	X	X		X	X	X
3	Yes	No	Yes		X	X	X	X		X
4	Yes	No	No		X	X		X		X
5	No	No	Yes			X	X	X		
6	No	No	No			X		X		

^a RMP, reference measurement procedure; CRM, certified reference material.

^b Standardization when patient results are equivalent between measurement procedures and calibration is traceable to SI by use of a reference measurement procedure; harmonization when patient results are equivalent between measurement procedures and calibration is not traceable to a reference measurement procedure.

What is the QAP doing now in this area?

A. Target value assignment.

B. Commutability.

C. Acceptable Performance Specifications - these provide meaningful limits from targets.

Target Setting

- The QAP has reference method value assignment for some tests;
- Use of CRMs in field methods for some;
- Weighed in for some;
- "best performing labs" for some;
- Overall median for some (with method specific medians for all).

High order / reference method target setting

Where available – the RCPAQAP sends their EQA material to Reference Laboratories to determine targets e.g.:

ALT, AST, CK, GGT and LDH values were assigned by the DGKL Reference Institute of Bioanalysis, Calibration Laboratory for Clinical Chemistry, Bonn, Germany, using the 37°C IFCC reference methods.

Total Bilirubin (General Chem and Neonatal) values were assigned by the Childrens Hospital Wisconsin (USA) Reference Laboratory using the Doumas Reference Method.

High order target setting

**WEQAS Reference Laboratory, Cardiff & Vale University Health Board
Wales UK**

- Glucose by Isotope Dilution-Gas Chromatography Mass Spectrometry (ID-CGMS)
- Creatinine by ID-GCMS
- Uric Acid by ID-GCMS
- Sodium by Flame Atomic Emission Spectrometry
- Potassium by Flame Atomic Emission Spectrometry
- Calcium by Atomic Absorption Spectrometry
- Magnesium by Flame Atomic Emission Spectrometry
- Lithium by Flame Atomic Emission Spectrometry
- Cholesterol by ID- GCMS
- Triglycerides by ID-GCMS

High order target setting

National Measurement Institute, Sydney Australia

- Cortisol
- Oestradiol,
- Testosterone
- Vitamin D3

“Reference values were determined using Reference Measurement Procedures (RMPs) based on the technique of isotope dilution with ultraperformance liquid chromatography tandem mass spectrometry (UPLC-MS/MS) analysis. The reference values are metrologically traceable to the SI units for mass (kg), volume (mL) and amount of substance (mole) within their stated uncertainties”.



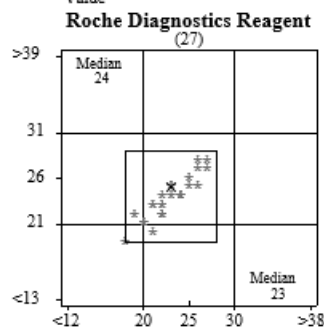
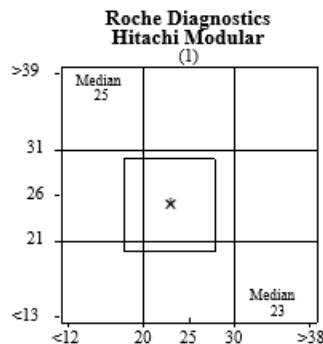
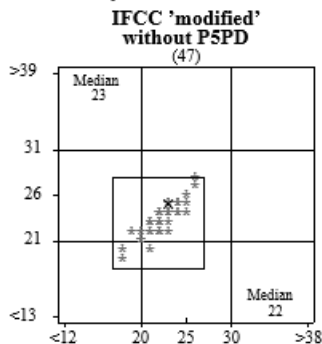
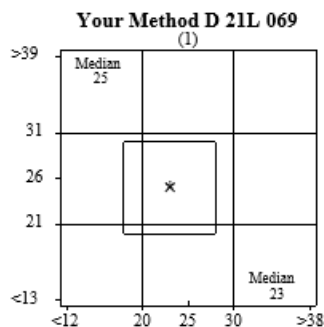
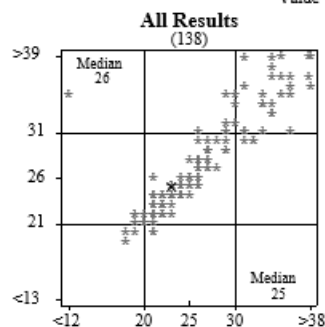
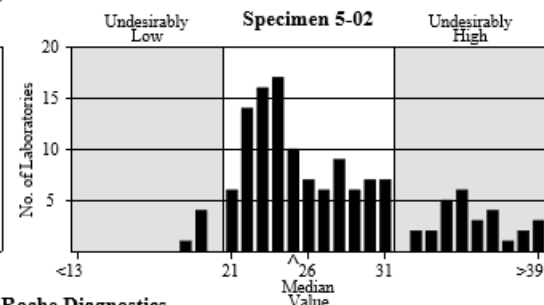
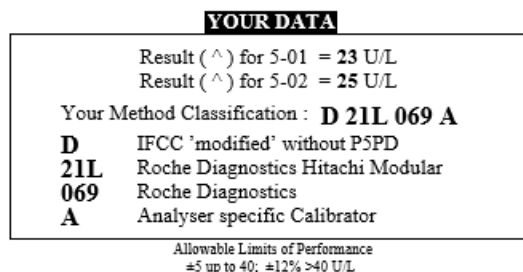
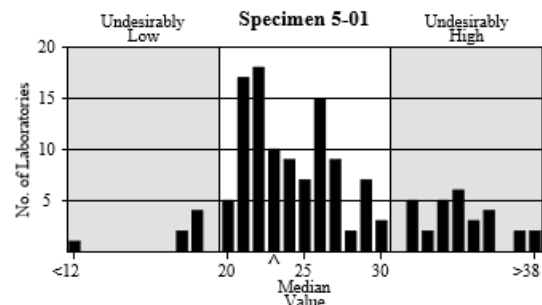
Commutability

- Liquid serum chemistry commutable (but no target assignment);
 - other materials may be single patient,
 - pooled material,
 - correct matrix base (serum, CSF or urine base).
- Other effects are stripping (some), spiking (many), lyophilised (most).
- The QAP are working on assessing the effects of these on commutability.

Due Date : 10/07/2017

Alanine Amino Transferase (U/L)

Participant No.

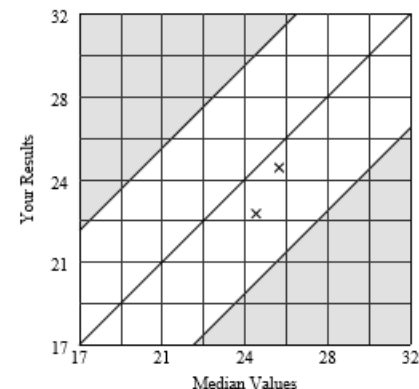
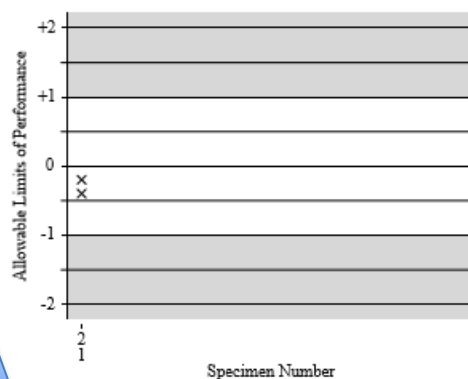


Current Data for Cycle 5

Spec.	Method	Median	Result
5-01	D 21L 069 A	25	23

5-02		26	25
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SUMMARY DATA

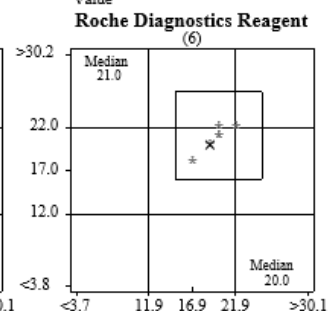
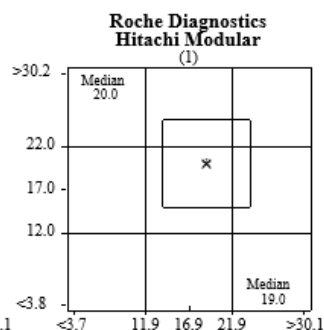
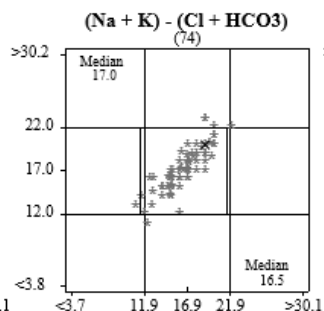
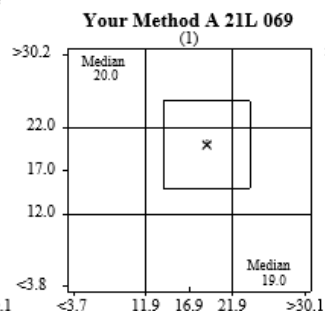
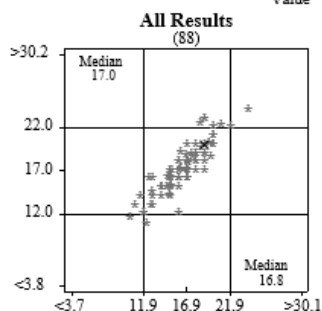
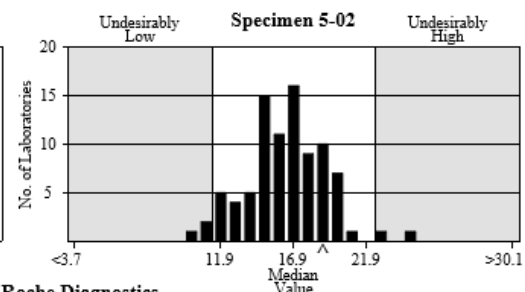
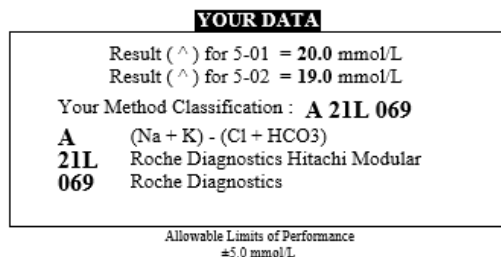
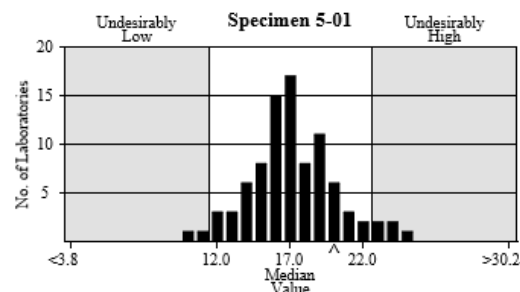


Liquid Serum Chemistry Program

Due Date : 10/07/2017

Anion Gap (mmol/L)

Participant No.

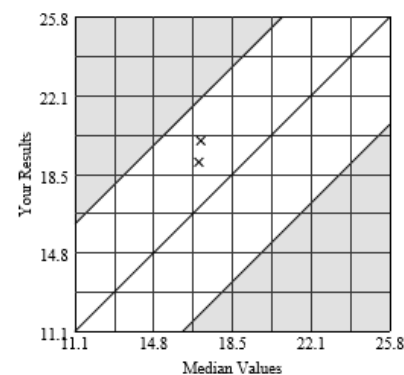
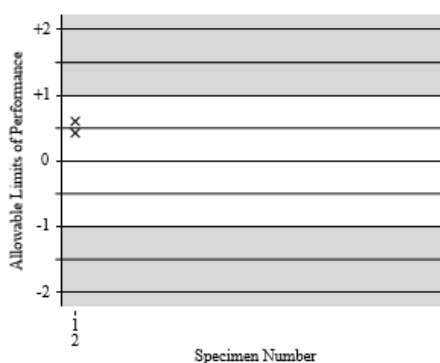


Current Data for Cycle 5

Spec.	Method	Median	Result
5-01	A 21L 069	17.0	20.0

5-02		16.9	19.0
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SUMMARY DATA

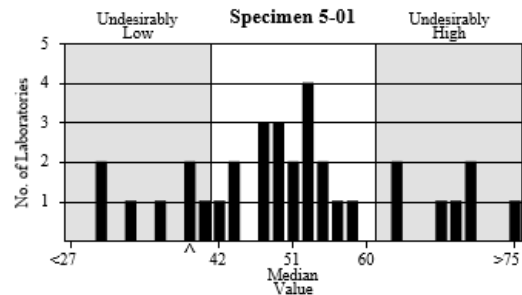


Liquid Serum Chemistry Program

Due Date : 10/07/2017

Vitamin D3 (nmol/L)

Participant No.



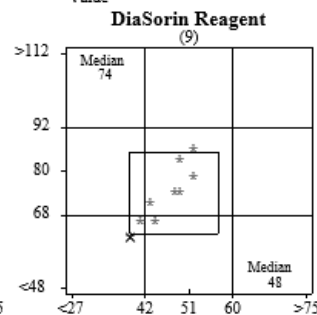
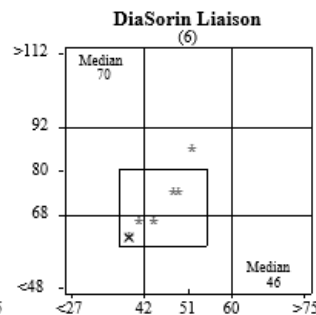
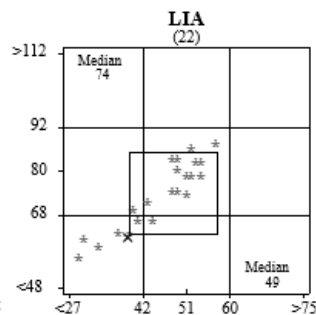
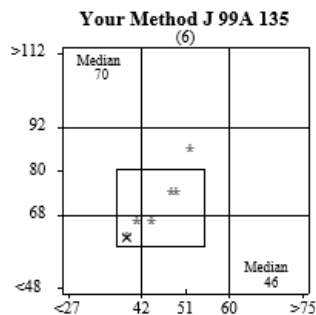
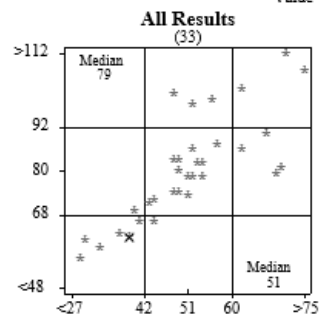
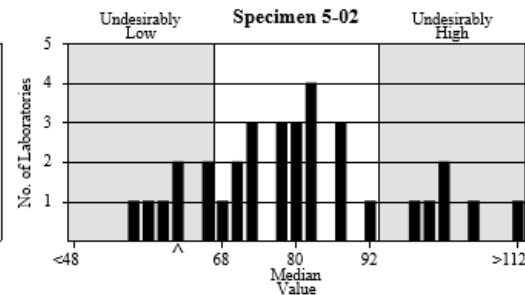
YOUR DATA

Result (^) for 5-01 = 39 nmol/L
Result (^) for 5-02 = 62 nmol/L

Your Method Classification : **J 99A 135**

J LIA
99A DiaSorin Liaison
135 DiaSorin

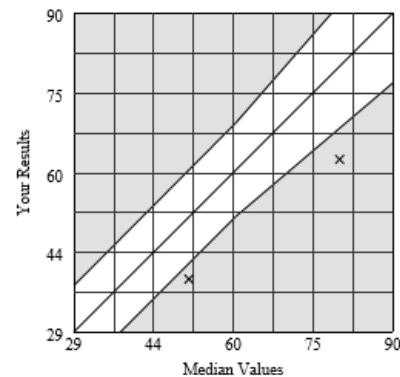
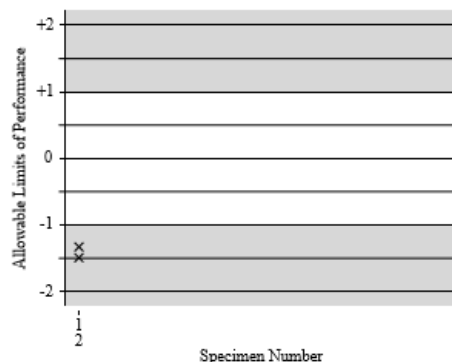
Allowable Limits of Performance
±9 up to 60; ±15% >60 nmol/L



Current Data for Cycle 5

Spec.	Method	Median	Result	
5-01	J 99A 135	51	39	Low
5-02		80	62	Low

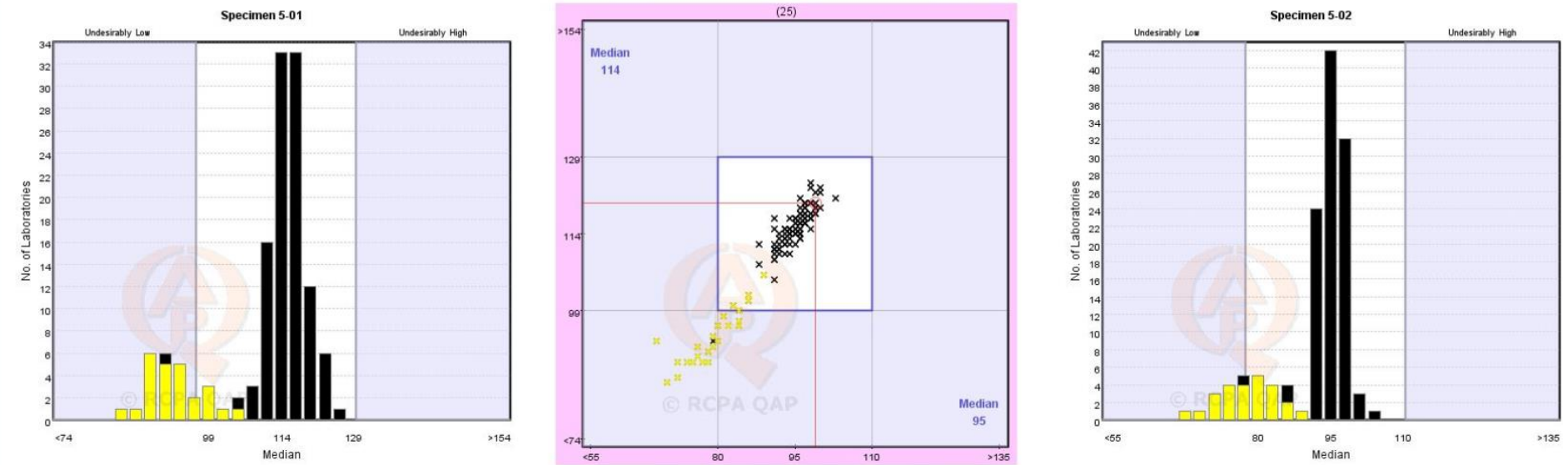
SUMMARY DATA



Data Analysis by Method Code

Filter: # ### 052 #

Your Method Classification: H 01S 001 E



Statistics	Sample 1 - All Data	Sample 1 - Filtered Data	Sample 2 - All Data	Sample 2 - Filtered Data
Median	114.0	93.0	95.0	79.0
Total	131	25	130	25
Low	21 (16%)	20 (80%)	14 (10%)	13 (52%)
High	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Analytical PrincipleInstrumentReagentCalibrator

<no selection><no selection>52 - Ortho-Clinical Diagnostics<no selection>

Acceptable Performance Specifications (APS)

- APS based on BV
- Used to allow rapid, standardised assessment of QAP results in both numerical and graphical report formats
- Results outside APS should alert a laboratory that their assay may produce results that are at risk of detrimentally affecting clinical decision making.

Programs, Analytes and Allowable Limits of Performance

ALCOHOL/AMMONIA	Reviewed January 2012	Basis	Level
Alcohol	± 2.0 up to 20.0 mmol/L; 10% > 20.0 mmol/L	Prof. Opinion	
Ammonia	± 5 up to 50 µmol/L; 10% > 50 µmol/L	Prof. Opinion	

ANTIBIOTICS	Reviewed April 2013	Basis	Level
Amikacin	± 2.0 up to 19.9 mg/L; 10% > 19.9 mg/L	Prof. Opinion	
Gentamicin	± 0.2 up to 2.0 mg/L; 10% > 2.0 mg/L	Prof. Opinion	
Tobramycin	± 0.2 up to 2.0 mg/L; 10% > 2.0 mg/L	Prof. Opinion	
Vancomycin	± 2.0 up to 20.3 mg/L; 10% > 20.3 mg/L	Prof. Opinion	

BILE ACIDS	Reviewed January 2012	Basis	Level
Total Bile Acids	± 4 up to 40 µmol/L; 10% > 40 µmol/L	Prof. Opinion	

BIOGENIC AMINES	Reviewed April 2012	Basis	Level
Adrenaline	± 30 up to 100 nmol/L; 30% > 100 nmol/L	Total Error	Optimal
Dopamine	± 0.20 up to 2.0 µmol/L; 10% > 2.0 µmol/L	Imprecision	Optimal
SHIAA	± 8 up to 40 µmol/L; 20% > 40 µmol/L	Imprecision	Desirable
HMMA	± 6 up to 40 µmol/L; 15% > 40 µmol/L	Total Error	Optimal
HVA	± 6 up to 40 µmol/L; 15% > 40 µmol/L	Imprecision	Desirable
Metanephrine	± 0.2 up to 1.0 µmol/L; 20% > 1.0 µmol/L	Total Error	Optimal
Noradrenaline	± 75 up to 500 nmol/L; 15% > 500 nmol/L	Total Error	Optimal
Normetanephrine	± 0.4 up to 2.0 µmol/L; 20% > 2.0 µmol/L	Total Error	Optimal
3 - Methoxytyramine	± 0.3 up to 2.0 µmol/L; 15% > 2.0 µmol/L	Total Error	Optimal
Serotonin	± 0.2 up to 1.0 µmol/L; 20% > 1.0 µmol/L	Prof. Opinion	

BLOOD GASES	Reviewed January 2015	Basis	Level
Chloride	± 3 up to 100 mmol/L; 3% > 100 µmol/L	Total Error	Minimal
Glucose	± 0.4 up to 5.0 mmol/L; 8% > 5.0 mmol/L	Imprecision	Desirable
Ionised Calcium	± 0.04 up to 1.00 mmol/L; 4% > 1.00 mmol/L	Total Error	Minimal
Lactate	± 0.5 up to 5.0 mmol/L; 8% > 5.0 mmol/L	Imprecision	Optimal
pH	± 0.04	Prof. Opinion	
pCO2	± 2.0 up to 34.0 mm Hg; 6% > 34.0 mm Hg	Total Error	Desirable
pO2	± 2.0 up to 34.0 mm Hg; 6% > 34.0 mm Hg	CO2 CVi & CVg	Desirable
Potassium	± 0.2 up to 4.0 mmol/L; 5% > 4.0 mmol/L	Imprecision	Desirable
Sodium	± 3 up to 150 mmol/L; 2% > 150 mmol/L	Total Error	Minimal
Urea	± 0.5 up to 4.0 mmol/L; 12% > 4.0 mmol/L	Imprecision	Desirable
Creatinine	± 8.0 up to 100.0 µmol/L; 8% > 100.0 µmol/L	Imprecision	Minimal

CO-OXIMETRY	Reviewed January 2015	Basis	Level
Haemoglobin Concentration	± 5 up to 100 g/L; 5% > 100 g/L	Total Error	Desirable
Fractional Oxyhaemoglobin	± 3 up to 75.0%; 4% > 75.0%	Prof. Opinion	
Fractional Carboxyhaemoglobin	± 1.0 up to 5.0%; 20% > 5.0%	Prof. Opinion	

BNP	Reviewed January 2012	Basis	Level
NT-Pro BNP	± 25 up to 125 ng/L; 20% > 125 ng/L	Total Error	Optimal
BNP	± 20 up to 100 ng/L; 20% > 100 ng/L	Prof. Opinion	

CSF	Reviewed April 2013	Basis	Level
Albumin	± 0.02 up to 0.1 g/L; 20% > 0.1 g/L	Prof. Opinion	
Glucose	± 0.2 up to 2.0 mmol/L; 10% > 2.0 mmol/L	Prof. Opinion	
Immunoglobulin G	± 0.02 up to 0.10 g/L; 20% > 0.10 g/L	Prof. Opinion	
Lactate	± 0.3 up to 3.0 mmol/L; 10% > 3.0 mmol/L	Prof. Opinion	
Total Protein	± 0.05 up to 0.50 g/L; 10% > 0.50 g/L	Prof. Opinion	
Bilirubin Concentration	± 0.12 up to 0.60 µmol/L; 20% > 0.60 µmol/L	Prof. Opinion	
Xanthochromia-Bilirubin screen	± 0.002 up to 0.007 AU; 20% > 0.007 AU	Prof. Opinion	
Xanthochromia – Haemoglobin screen	± 0.02 up to 0.100 AU; 20% > 0.100 AU	Prof. Opinion	

ENDOCRINE	Reviewed January 2012	Basis	Level
AFP	± 2 up to 17 kIU/L; 12% > 17 kIU/L	Imprecision	Desirable
Aldosterone	± 24 up to 160 pmol/L; 15% > 160 pmol/L	Imprecision	Optimal
Androstenedione	± 1.5 up to 10 nmol/L; 15% > 10 nmol/L	Total Error	Optimal
CA125	± 6 up to 50 kU/L; 12% > 50 kU/L	Imprecision	Optimal
CEA	± 0.6 up to 5.0 µg/L; 12% > 5.0 µg/L	Imprecision	Desirable
Cortisol	± 15 up to 100 nmol/L; 15% > 100 nmol/L	Imprecision	Optimal
DHEA Sulphate	± 1.2 up to 10.0 µmol/L; 12% > 10.0 µmol/L	Total Error	Desirable
Ferritin	± 4.0 up to 27.0 µg/L; 15% > 27.0 µg/L	Imprecision	Desirable
Folate	± 1.5 up to 6.0 nmol/L; 25% > 6.0 nmol/L	Imprecision	Desirable
FSH	± 1.0 up to 10.0 IU/L; 10% > 10.0 IU/L	Imprecision	Desirable
Growth Hormone	± 1 up to 7 mU/L; 15% > 7 mU/L	Imprecision	Optimal
hCG	± 1 up to 10 IU/L; 10% > 10 IU/L	Prof. Opinion	
Homocysteine	± 1.5 up to 15.0 µmol/L; 10% > 15.0 µmol/L	Total Error	Optimal
17-Hydroxyprogesterone	± 2.0 up to 10.0 nmol/L; 20% > 10.0 nmol/L	Total Error	Optimal
Insulin	± 0.6 up to 5.0 mU/L; 12% > 5.0 mU/L	Imprecision	Optimal
LH	± 1.5 up to 10.0 IU/L; 15% > 10.0 IU/L	Imprecision	Desirable
Oestradiol	± 25 up to 100 pmol/L; 25% > 100 pmol/L	Total Error	Desirable
Oestriol(Unconjugated)	± 0.9 up to 6.0 nmol/L; 15% > 6.0 nmol/L	Prof. Opinion	
PTH	± 1.0 up to 8.0 pmol/L; 12% > 8.0 pmol/L	Imprecision	Optimal
Progesterone	± 2 up to 10 nmol/L; 15% > 10 nmol/L	Imprecision	Optimal
Prolactin	± 40 up to 400 mIU/L; 10% > 400 mIU/L	Imprecision	Minimal
SHBG	± 6 up to 50 nmol/L; 12% > 50 nmol/L	Imprecision	Desirable
Testosterone	± 0.4 up to 2.7 nmol/L; 15% > 2.7 nmol/L	Imprecision	Minimal
TSH	± 0.10 up to 0.50 mU/L; 20% > 0.50 mU/L	Imprecision	Desirable
Free T3	± 0.7 up to 3.5 pmol/L; 20% > 3.5 pmol/L	Total Error	Desirable
Free T4	± 1.5 up to 12 pmol/L; 12% > 12 pmol/L	Total Error	Desirable

Basis

- **Total Error** – Diagnosis
 - Can share reference interval
- **Imprecision - Monitoring**
 - Can monitor patient across laboratories

	Monitoring (ALP = 2 x CV _a)	Diagnosis (ALP = TE)
Optimal	CV _a = ¼ CV _i	TE = 0.125 (CV _i ² + CV _g ²) ^½ + 2.33 x ¼ CV _i
Desirable	CV _a = ½ CV _i	TE = 0.250 (CV _i ² + CV _g ²) ^½ + 2.33 x ½ CV _i
Minimal	CV _a = ¾ CV _i	TE = 0.375 (CV _i ² + CV _g ²) ^½ + 2.33 x ¾ CV _i

Table 3 Main differences between EQAS and IPs.

	EQA Program	Interlab
Control samples	Different from IQC and in accordance with quality specifications	IQC sample
Sample	Desirable treatment as patient sample	Identifiable immediately
Manufacturer of sample	Not traceable and, if possible, independent	Traceable and conflict of interest
Concentration samples	Unknown and different in the time	Known and the same all the time
Data treatment	Same among participants	Different among participants; selection of results to communicate on the basis of different laboratory criteria
Statistical processing	Entrusted to laboratory professionals	Entrusted to manufacturers (conflict of interest)
Report information	Statistical data and assessment of analytical performance	Only statistical data
Improvement stimulus	High: communication of unsatisfactory performance; advice to resolve problems; promotion of work groups to carry out improvement projects	None
Education and training	Available and continuous	Unavailable
Advisory service to laboratories	Available and continuous	Unavailable
Advisory service to manufacturers	Available and continuous	Unavailable
Attention to pre-analytical phase	Possibility of specific surveys	None
Attention to post-analytical phase	Possibility of specific surveys	None
Assessment of clinical cases	Possibility of specific surveys	None

Review

Risk management in laboratory medicine: quality assurance programs and professional competence

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implement procedures to minimize further risks c errors. Quality Assurance Programs (QAPs) represent an important tool that allows us to identify errors an

Opinion Paper

Graham R.D. Jones*, Stephanie Albarede, Dagmar Kessler, Finlay MacKenzie, Joy Mammen, Morten Pedersen, Anne Stavellin, Marc Thelen, Annette Thomas, Patrick J. Twomey, Emma Ventura and Mauro Panteghini, for the EFLM Task Finish Group – Analytical Performance Specifications for EQAS (TFG-APSEQA)

Analytical performance specifications for external quality assessment – definitions and descriptions

Table 2: Example of summary description of analytical performance specifications (APS) based on the RCPAQAP General Serum Chemistry External Quality Assurance (EQA) Scheme.

1. The EQA material is not validated as commutable
2. The overall target-setting method for each measurand is shown below. In addition, method, instrument, reagent manufacturer-based consensus targets are provided based on returned results
3. The APS are to be applied to each individual measurement result
4. The APS are applied for assessment of total error (i.e. the effects of imprecision and bias combined)
5. The rationale for the APS is 'Aspirational' (to improve performance) where this is required. The response of the laboratory to 'out of range' results should be to review performance and seek improvement
6. The APS are established based on biological variation and state of the art (levels 2 and 3 from Milan conference). The components of biological variation and the level (optimal, desirable, or minimal) are shown below

Further details on the RCPAQAP process used to establish these APS are available [9, 15]

Measurand	Assignment of target	Analytical performance specifications	Employed component(s) of biological variation	Quality level
S/P-ALT	IFCC reference procedure in a JCTLM-listed reference laboratory	± 5 U/L up to 40 U/L; $\pm 12\%$ >40 U/L	Within-individual (imprecision)	Optimal
S/P-Bicarbonate	Selected well-controlled commercial measuring system by an ISO 15189 accredited clinical laboratories	± 2.0 mmol/L up to 20.0 mmol/L; $\pm 10\%$ >20.0 mmol/L	Within- and between-individual (total error)	Minimal
S-Transferrin	Median of laboratories participating in EQA	± 0.20 g/L up to 2.50 g/L; $\pm 8\%$ >2.50 g/L	Within- and between-individual (total error)	Minimal

FRUCTOSAMINE

2. Consensus survey median for each QAP specimen.

GGT

1. IFCC primary reference method.
2. Linear regression of values determined by DGKL Reference Institute for levels 2 to 8 and the DGKL assigned value for level 1.

GLUCOSE

1. Hexokinase or Glucose Oxidase.
2. Linear regression of values determined by WEQAS Reference Laboratory for levels 2 to 8 and the WEQAS assigned value for level 1.

HDL CHOLESTEROL

2. Target set from consensus survey median for levels 1 to 8.

IRON

1. Colorimetric-Ferrozine/Ferene or other colour reagent.
2. Linear regression of data from selected target setting laboratories.

LACTATE

1. Enzymatic, Enzyme Electrode Sensor.
2. Linear regression of data from selected target setting laboratories.

LACTATE DEHYDROGENASE

Three values are provided:

LD (L → P)

1. IFCC reference method.
2. Linear regression of values determined by DGKL Reference Institute for levels 2 to 8 and the DGKL assigned value for level 1.

LD (P → L) - pyruvate > 0.7 mmol/L

1. Pyruvate Substrate > 0.7 mmolar
2. Consensus survey median for each QAP specimen.

LD (P → L) - pyruvate < 0.7 mmol/L and Non-rate reactions

1. Pyruvate Substrate < 0.7 mmolar and pyruvate substrates using a non-rate reaction.
2. Consensus survey median for each QAP specimen.

Two values are provided:

Lipase (Reference Range > 300 U/L).

1. Siemens (Dade Behring) users & Ortho Clinical Diagnostics users.
2. Consensus survey median for each QAP specimen

Lipase (Reference Range < 300 U/L).

1. All other methods (excluding above).
2. Consensus survey median for each QAP specimen

LITHIUM

1. Flame Atomic Absorption Spectrometry reference method.
2. Linear regression of values determined by WEQAS Reference Laboratory.

MAGNESIUM

1. Flame Atomic Absorption Spectrometry reference method.
2. Linear regression of values determined by WEQAS Reference Laboratory.

OSMOLALITY

2. Consensus survey median for each QAP specimen.

PHOSPHATE

1. Phosphomolybdate formation and phosphomolybdate reduction.
2. Linear regression of data from selected target setting laboratories.

POTASSIUM

1. Flame Atomic Emission Spectrometry reference method (WEQAS) and Indirect (Diluted) Ion Selective Electrode (selected target setting laboratories).
2. Linear regression of data from selected target setting laboratories.

PROTEIN

1. Biuret - end point with blank or end point no blank.
2. Linear regression of data from selected target setting laboratories.

SODIUM

1. Flame Atomic Emission Spectrometry reference method.
2. Linear regression of values determined by WEQAS Reference Laboratory.

TIBC

2. Consensus survey median for each QAP specimen.

