EUROPEAN FEDERATION OF CLINICAL CHEMISTRY AND LABORATORY MEDICINE

1222 · 2022 800 ANNI

UNIVERSITÀ DEGLI STUDI DI PADOVA

THE FUTURE OF EXTERNAL QUALITY ASSESSMENT SCHEMES

MARIO PLEBANI

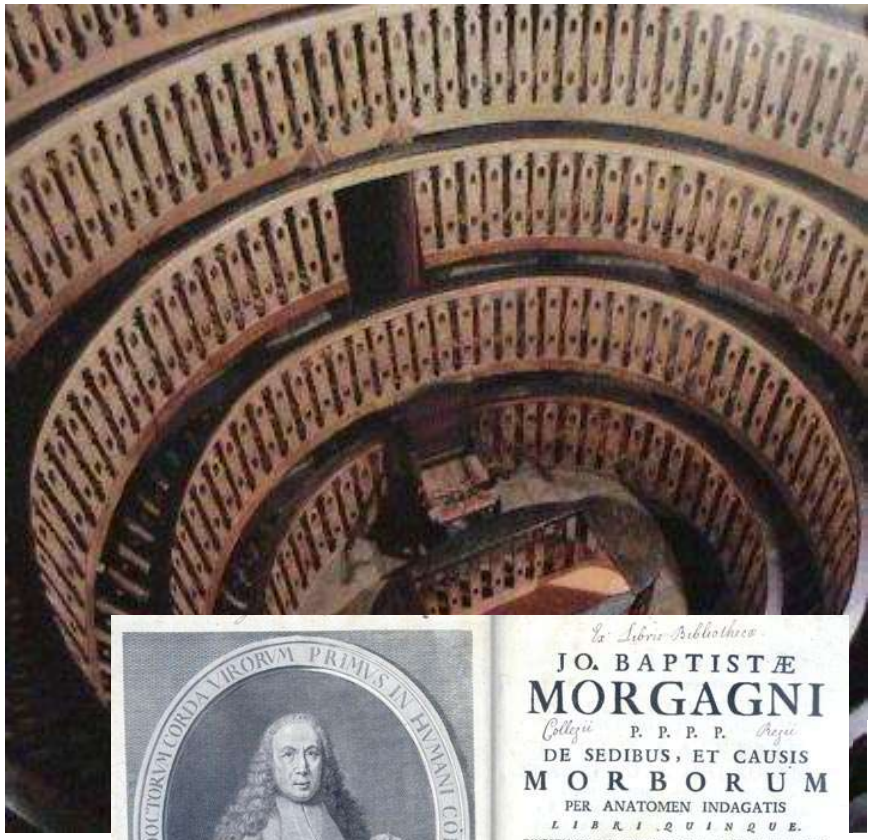
HONORARY PROFESSOR OF CLINICAL BIOCHEMISTRY AND CLINICAL MOLECULAR BIOLOGY

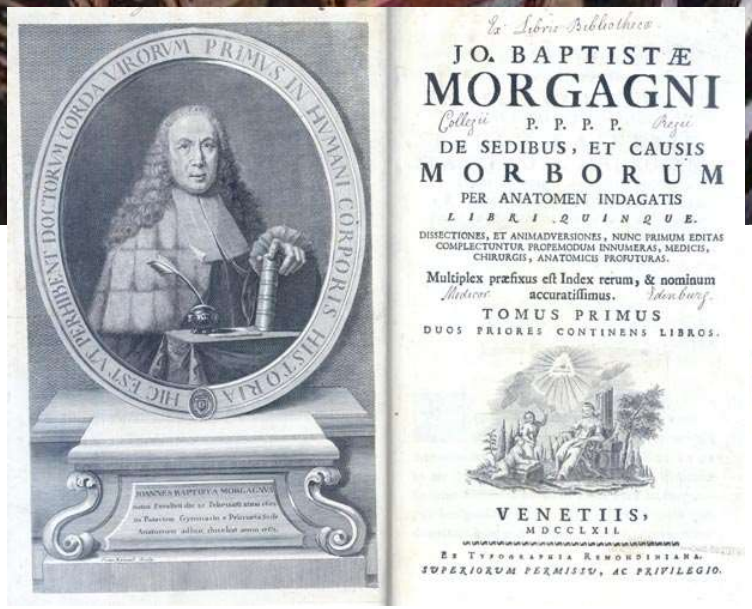
UNIVERSITY OF PADOVA

ADJUNCT PROFESSOR, DEPARTMENT OF PATHOLOGY, UNIVERSITY OF TEXAS-MEDICAL BRANCH

PRESIDENT OF THE EUROPEAN FEDERATION OF LABORATORY MEDICINE (EFLM)

EDITOR IN CHIEF, CLINICAL CHEMISTRY AND LABORATORY MEDICINE





Ex Libris Bibliothecæ

JO. BAPTISTÆ
MORGAGNI
Collegii P. P. P. P. Patavini
DE SEDIBUS, ET CAUSIS
MORBORUM
PER ANATOMEN INDAGATIS
LIBRI QUINQUE.

DISSECTIONES, ET ANIMADVERSIONES, NUNC PRIMUM EDITAS COMPLECTUNTUR PROPEMODUM INNUMERAS, MEDICIS, CHIRURGIS, ANATOMICIS PROFUTURAS.

Multiplex præfixus est Index rerum, & nominum Medicor. accuratissimus. Edenburg.

TOMUS PRIMUS
DUOS PRIORES CONTINENS LIBROS.

VENETIIS,
MDCCLXII.

Ex Typographia Remondiniana.
SUPERIORUM PERMISSU, AC PRIVILEGIO.

OUTLINE OF TALK

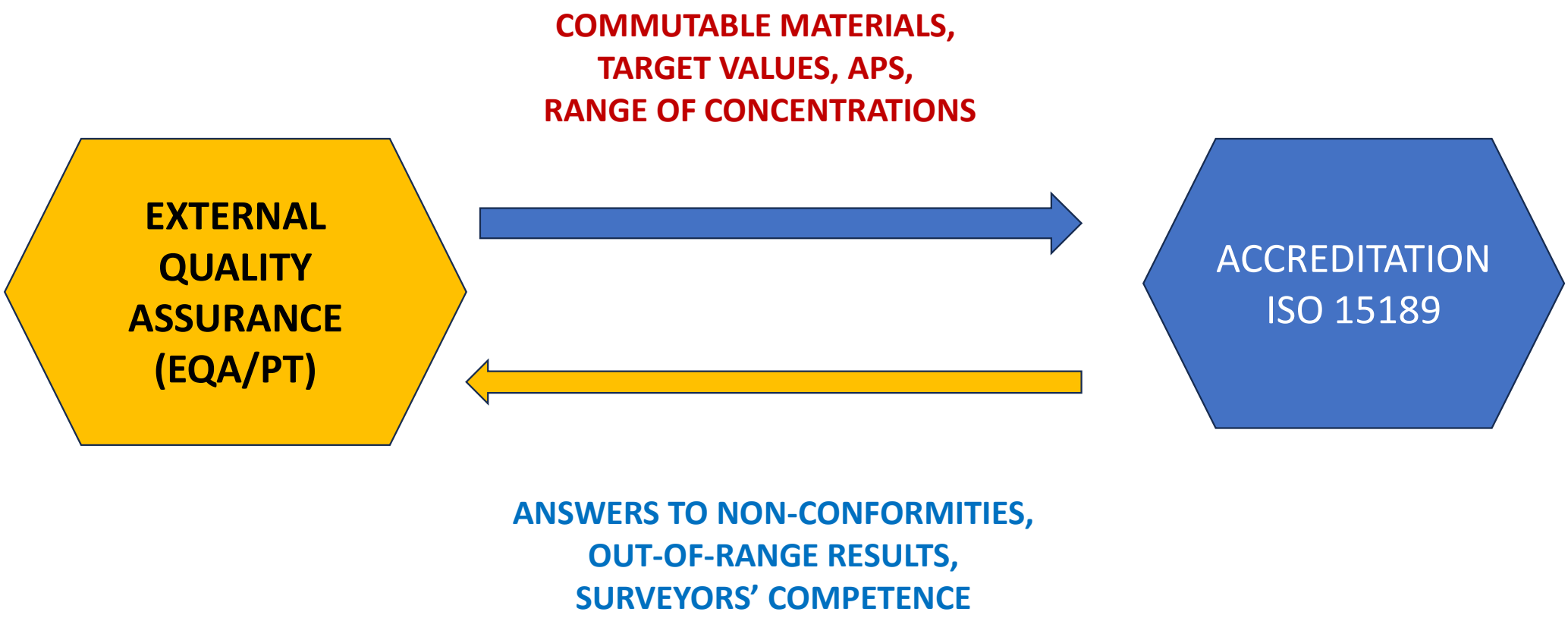
- Quality in laboratory medicine: ***EQA/PT and accreditation***
- Type of EQA programs: ***regulatory versus educational***
- Elements and ***categories of EQAs***
- ***Harmonization*** of EQAs and how EQAs may improve harmonization
- EQA/PT. Not only clinical chemistry and not only for analytical phase
- ***Take home messages***

DEMONSTRABLE QUALITY OF LABORATORY SERVICES ENTAILS TWO PARTS

1) First, one needs a ***quality policy statement***, identification of ***user needs***, choice of measurement procedures, reference measurement system to provide traceability, control materials, and ***proficiency testing with materials having reference-measurement-assigned values***.

2) Second, it may be useful to ***obtain recognition of competence*** in addition to the director's certificate, such as Good Laboratory Practice (when studying toxicity of chemicals), ISO 9000 certification of a self-defined quality system, ***nongovernmental professional accreditation***, or, most demanding, governmental accreditation according to European Standard EN 45 001 with some modifications.

Dybkaer R. Clin Chem 1994


COMMUTABLE MATERIALS,
TARGET VALUES, APS,
RANGE OF CONCENTRATIONS
EXTERNAL QUALITY ASSURANCE (EQA/PT)
ACCREDITATION ISO 15189
ANSWERS TO NON-CONFORMITIES,
OUT-OF-RANGE RESULTS,
SURVEYORS' COMPETENCE

EQA/PT: A MANDATORY REQUIREMENT

Inter-laboratory comparisons are ***mandatory requirements*** for accreditation to the international standard applicable to medical laboratories (ISO 15189)

PT/EQA is a ***component of laboratory accreditation requirements*** in many countries.

EQA programmes offer an ***organized approach for these appraisals***, allowing large-scale statistical comparisons to be made.

PT/EQA programs have ***evolved in scope and sophistication*** and are now an essential component of a laboratory's quality management system.

Clin Chem Lab Med 2018; 56(10): 1644–1654 DE GRUYTER

Opinion Paper

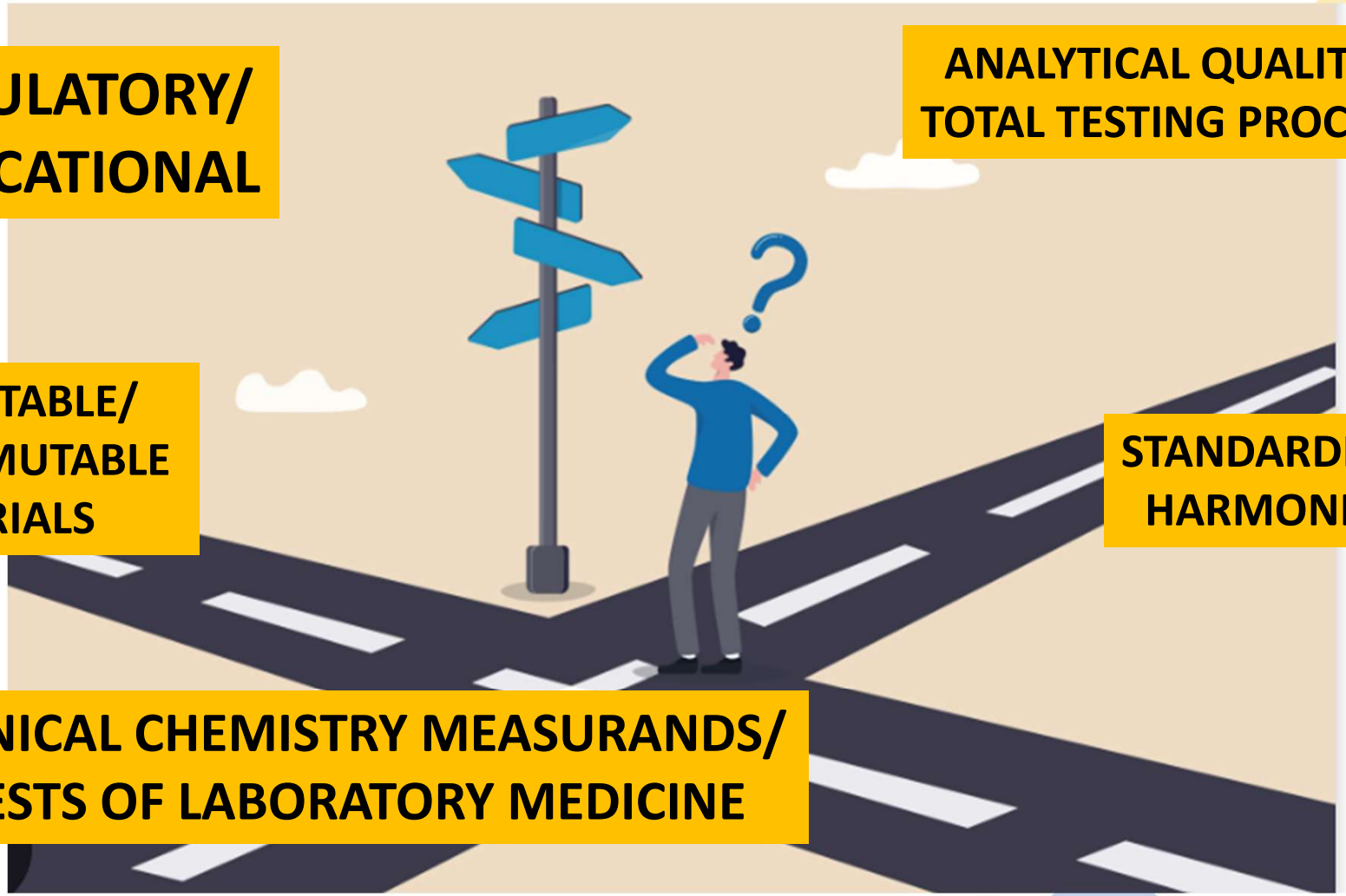
Laura Sciacovelli*, Sandra Secchiero, Andrea Padoan and Mario Plebani

External quality assessment programs in the context of ISO 15189 accreditation

The International Standard ISO 15189:2012 requires ***participation in interlaboratory comparison*** [e.g. external quality assessment (EQA)] for ***all tests provided*** by an individual laboratory.

If EQAS is not commercially available, alternative approaches should be identified, although clinical laboratories may find it challenging to choose the EQAS that comply with the international standards and approved guidelines.

EQA AT THE CROSSROADS



REGULATORY/
EDUCATIONAL

ANALYTICAL QUALITY/
TOTAL TESTING PROCESS

COMMUTABLE/
NONCOMMUTABLE
MATERIALS

STANDARDIZATION/
HARMONIZATION

CLINICAL CHEMISTRY MEASURANDS/
TESTS OF LABORATORY MEDICINE

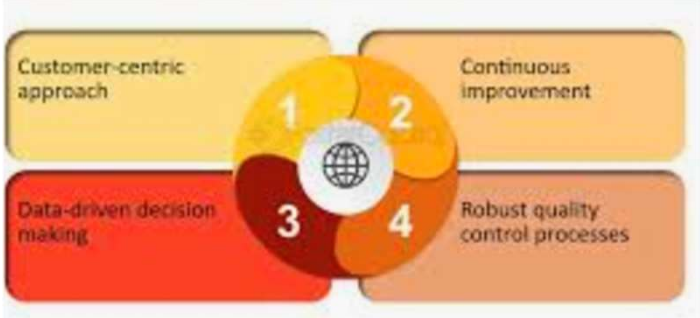
OUTLINE OF TALK

- Quality in laboratory medicine: ***EQA/PT and accreditation***
- Type of EQA programs: ***regulatory versus educational***
- Elements and ***categories of EQAs***
- ***Harmonization*** of EQAs and how EQAs may improve harmonization
- EQA/PT. Not only clinical chemistry and not only for analytical phase
- ***Take home messages***

EXTERNAL QUALITY ASSESSMENT

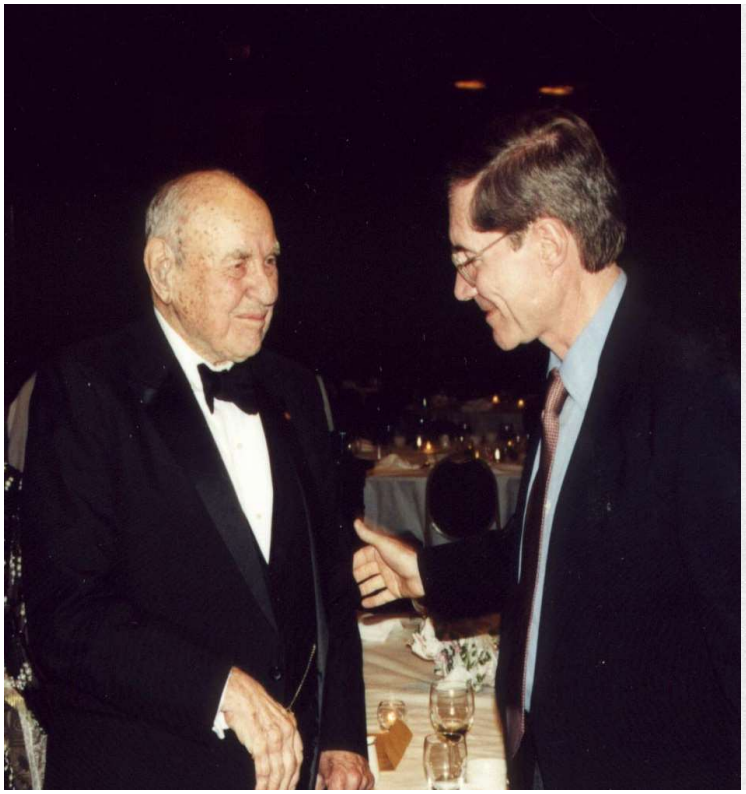
EQA is an ***integrated professional quality assurance activity*** of medical laboratories

Adam Urdall 1999



EXTERNAL QUALITY ASSESSMENT and F. WILLIAM SUNDERMAN

(23 October 1898 – 9 March 2003)



A SURVEY OF THE ACCURACY OF CHEMICAL ANALYSES IN CLINICAL LABORATORIES*

WILLIAM P. BELK, M.D.,† AND F. WILLIAM SUNDERMAN, M.D.†

In 1946 the Committee on Laboratories of the Medical Society of the State of Pennsylvania proposed a survey‡ to check the accuracy of some of the more common chemical measurements made in hospital laboratories throughout the state. It undertook to do this by distributing solutions which had been carefully

TABLE 1

NUMBER OF DETERMINATIONS CLASSED AS SATISFACTORY, UNSATISFACTORY AND GROSS ERROR

September Analyses

SUBSTANCE TESTED	SATISFACTORY LIMITS OF RESULTS PER 100 ML.	NUMBER SATISFACTORY	NUMBER UNSATISFACTORY**	GROSS ERROR**
Hemoglobin	9.8 ± 0.3 gm.	17	34	11
Hemoglobin	15.1 ± 0.5 gm.	21	31	3
Glucose	60 ± 10 mg.	33	19	5
Glucose	375 ± 30 mg.	27	24	4
Sodium chloride	456 ± 50 mg.	30	14	2
Total protein	6.6 ± 0.4 gm.	18	29	7
Albumin	4.6 ± 0.3 gm.	9	35	7

October Analyses

DIFFERENT TYPES OF PT/EQA SCHEMES

REGULATORY

Many jurisdictions require the performance of pathology laboratories to ***achieve a basic minimum standard*** and ***failure to achieve*** these standards may result in significant consequences for the laboratory's right to practice

EDUCATIONAL

The aim of these programs is to ***improve the quality*** of laboratory testing, may also ***offer support to participants*** in the form of additional troubleshooting advice, webinars on interpretation of QC and EQA, and workshops

DIFFERENT TYPES of EQA SCHEMES

The first type is regulatory.

Because of the importance of pathology results in healthcare, many jurisdictions require the performance of pathology laboratories to achieve a basic minimum standard and failure to achieve these standards may result in significant consequences for the laboratory's right to practice.

The need to "pass" this type of EQA can lead to ***unintended consequences.***

For example, laboratories ***may treat these EQA specimens differently to patient samples*** to ensure acceptable performance.

In addition, the ***performance criteria are usually able to be achieved by nearly all laboratories.***

Tony Badrick. Clin Chem 2022

DIFFERENT TYPES of EQA SCHEMES:REGULATORY

A clear ***pro for regulatory*** programs is that ***poorly performing laboratories may be removed*** from providing patient care. This outcome can be seen as ***protecting patients*** by ensuring analytical quality. Clearly, if the standards are set too tightly, too many laboratories may be suspended with consequent loss of service.

A ***particular con*** may be the ***behavioral response*** to this type of program. With the threat of regulatory action, laboratories may be ***tempted to optimize the measurement process***, for example, testing just after calibration, in duplicate, by a senior analyst.

Thus, the results do ***not reflect the actual quality delivered*** for patient care.

Jones GRD et al. Clin Chem 2022

DIFFERENT TYPES of EQA SCHEMES

The other type of EQA programs are described as ***"aspirational or educational."***

The aim of these programs is to improve the quality of laboratory testing, and therefore ***not all laboratories will achieve the performance goals*** at the time of implementation.

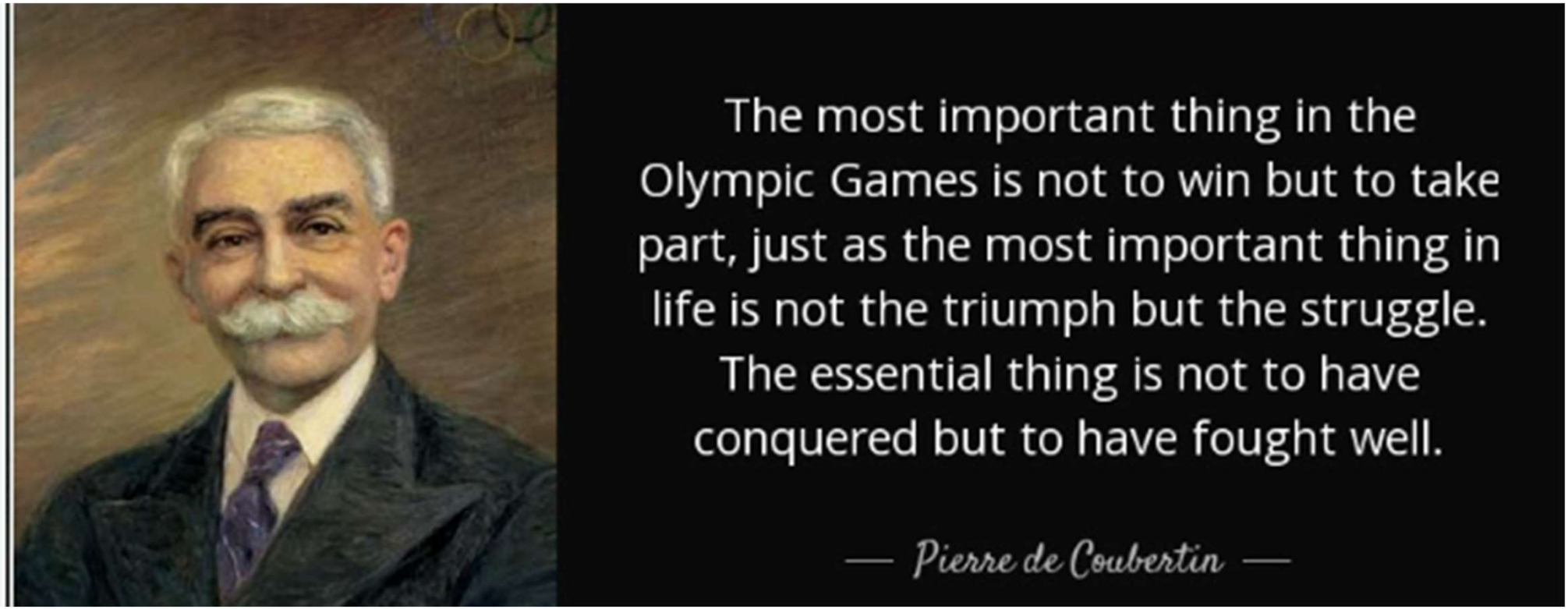
Educational programs may also offer ***support to participants*** in the form of additional troubleshooting advice, webinars on interpretation of QC and EQA, and workshops on addressing measurement problems identified in the EQA program.

Tony Badrick. Clin Chem 2022

DIFFERENT TYPES of EQA SCHEMES:EDUCATIONAL

- A ***pro for an educational*** scheme is EQA samples intended to ***challenge the limitations***, e.g., ***interfering substances***, of measurement procedures can be included without fear that a non-passing result will jeopardize a laboratory's accreditation status. Instead, the result can be used to ***educate*** a laboratory that a measurement procedure has a limitation they might not have been aware of.
- A ***potential con*** of an educational EQA scheme is a laboratory may ***fail repeatedly*** without jeopardy of being shut down, although most accreditation agencies will review EQA for acceptable performance even without strict regulatory requirements for the EQA scheme itself.

EQA: PARTICIPATION IS NOT ENOUGH



IS THERE A THIRD WAY?

An ***improvement program***, by using **achievable targets** and ***without threat of regulatory responses***, may be more likely to be performed with the goal of representing actual performance.

The hoped-for ***outcome is that responses to out-of-range results lead to improvements on routine testing*** and thus patient care.

Thus, the response in the laboratory to a failure should be ***"how can we improve this assay."***

EQA: OUTCOME MEASURES

Out-of-range results should be clearly notified and clinical laboratories should be requested to document ***corrective (and preventive) actions***

This information should be acknowledged as an ***OUTCOME measure.***

Corrective/preventive actions related to EQA results should be evaluated as fundamental quality requirements in accreditation programs

Advice and support by EQA providers are fundamental tools which have to be taken into consideration by participant laboratories

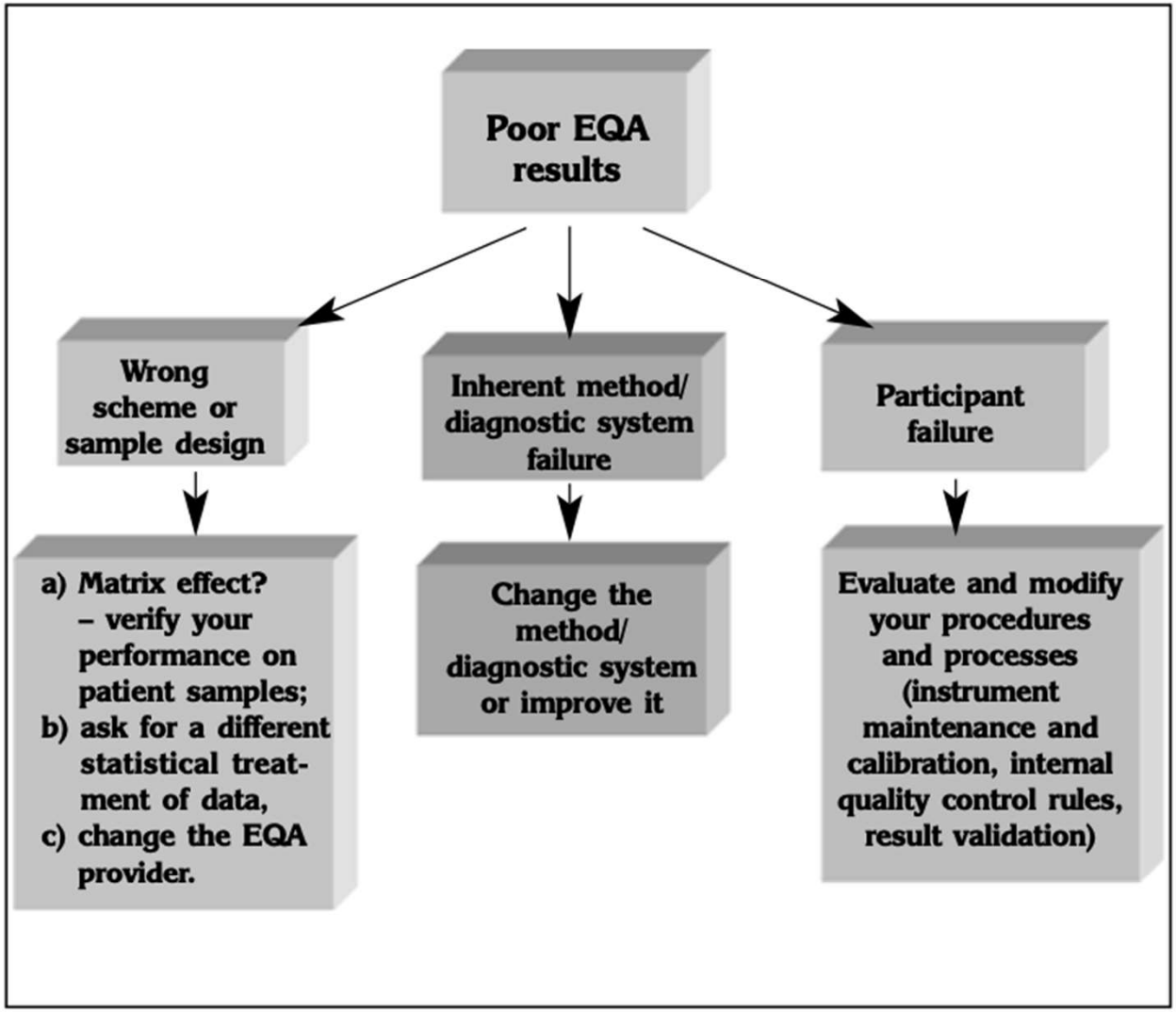


Figure 3 Possible reasons for unsatisfactory EQA/PT results

Plebani M 2005

OUTLINE OF TALK

- Quality in laboratory medicine: ***EQA/PT and accreditation***
- Type of EQA programs: ***regulatory versus educational***
- Elements and ***categories of EQAs***
- ***Harmonization*** of EQAs and how EQAs may improve harmonization
- EQA/PT. Not only clinical chemistry and not only for analytical phase
- ***Take home messages***

SIX ELEMENTS FOR IMPROVING EXTERNAL QUALITY ASSESSMENT

1) Nature of EQA materials, including ***commutability***
2) Procedures used to assign the ***target value***
3) Data set to which ***APS*** are applied
4) ***Analytical property*** assessed (total error, bias, imprecision)
5) Rationale for ***APS selection***
6) Type(s) of model used to set them

Jones GRD et al CCLM 2017

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

	Sample characteristics			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.

Miller WG et al Clin Chem 2011

EQA/PT: MAIN CHARACTERISTICS

Evaluation capability depends on 3 characteristics: sample ***commutability,*** process for ***target value assignment***, and inclusion or noninclusion of ***replicate samples***.

Category 1 is the ***most desirable*** because programs in this category use ***commutable samples*** with ***target values*** established by a ***reference system*** and can evaluate both individual laboratories and measurement procedures for reproducibility, calibration traceability, and uniformity between laboratories and between measurement procedures.

Programs in ***category 2*** have the same attributes as category 1 ***except that within-laboratory reproducibility cannot be evaluated*** because replicate samples are not used within a survey cycle.

Miller WG et al Clin Chem 2011

EQA/PT: MAIN CHARACTERISTICS

Programs in ***categories 3 and 4 also use commutable samples*** but, because the target values are not established by a reference system, the ***evaluation is limited to the uniformity among results (harmonization),*** a feature of considerable value for laboratory medicine.

Programs in ***categories 5 and 6 use samples likely to be noncommutable,*** thereby l***imiting evaluation to peer-group comparisons*** and failing to provide information on bias between different measurement procedures.

EQA and STANDARDIZATION

- ***Metrological traceability*** resulting in equivalence of measurement results is currently best established for small homogenous molecules whose measurement results have been standardized
- ***Standardized results represent less than 20% of the measurands*** analyzed in current medical laboratories.

Theodorsson E et al Clin Chim Acta 2024

EQA IN THE METROLOGICAL ERA: QUESTIONS and CURRENT CONSTRAINTS

Table 2
Constraints limiting the introduction of External Quality Assessment (EQA) schemes that meet metrological criteria. Adapted from ref. 20.

- Technical aspects: lack of certified control materials or difficulties to prepare commutable samples
- Practical considerations: complicated logistics of distribution of frozen samples
- Educational limitations: lack of awareness of which quality factors make an EQA important
- Economic concerns: higher costs

Braga F et al Clin Biochem 2018

THE TRUE CHALLENGE

A ***challenge*** shared by regulatory and aspirational/educational EQA schemes is that EQA samples that are ***commutable with clinical samples*** are ***only available or a relatively small number of measurands, possibly 20 to 30*** of the thousands in a test order catalog.

Consequently, most measurement procedures for a measurand are grouped into ***"peer groups"*** that are expected to have the same noncommutability bias, and thus results are likely to agree.

However, there is ***no information to determine if results from different "peer groups"*** of measurement procedures agree with each other or if measurement procedures are correctly calibrated to a higher order reference system.

Miller WG. Clin Chem 2022

UTILITY OF PEER-GROUP COMPARISON

The first question that an individual laboratory wants to answer from EQA is whether the measurement system used in the laboratory provides results that are equivalent to those from other laboratories using the same system.

In such a closed system, where all data is based on results from one manufacturer, this becomes the predominant issue for a laboratory. In this setting the method of assigning the EQA target is the ***middle of the measurement*** system group.

This approach is a ***surrogate*** for confirming the assay is performing as expected by the manufacturer.

Jones GRD et al. Clin Chem Lab Med 2022

Costituente	Metodo	Sistema
Magnesio	Blu di xilidile	Thermo/Sclavo, Indiko/Konelab

	Risultato del Laboratorio		Valutazione della prestazione			
Camp.	Unità Lab.	Unità S.I.	N°	VA	IS	Prestazione
BS24-01	2,45 mg/dL	1,01 mmol/L	**Valore di consenso per metodo**			
			252	0,93 mmol/L	132	Accettabile
			Valore di consenso per Sistema			
			10	0,97 mmol/L	67	Buona
BS24-02	3,92 mg/dL	1,61 mmol/L	**Valore di consenso per metodo**			
			267	1,79 mmol/L		Outlier
			Valore di consenso per Sistema			
			10	1,66 mmol/L	-44	Ottima

Costituente	Metodo	Sistema
Creatinina	Enzimatico	Roche, Cobas (COBAS-2 C702 21B4-09 C702 21B8-10)

	Risultato del Laboratorio		Valutazione della prestazione			
Camp.	Unità Lab.	Unità S.I.	N°	VA	IS	Prestazione
BS24-03	396,0 µmol/L	396,0 µmol/L		**Valore Target** 396,0 µmol/L	0	Ottima
				Valore di consenso per Sistema 396,0 µmol/L	0	Ottima
BS24-04	134,0 µmol/L	134,0 µmol/L		**Valore Target** 130,0 µmol/L	42	Ottima
				Valore di consenso per Sistema 130,8 µmol/L	33	Ottima

Note

Il VA della Creatinina è il Valore Target assegnato con metodo di riferimento gas-chromatography-isotope diluition mass spectrometry (GC-IDMS).
BS24-03 = 396 umol/L con un'incertezza di misura espansa di ± 4 (limite di confidenza 95% = 392 - 400 umol/L);
BS24-04 = 130 umol/L con un'incertezza di misura espansa di ± 1 (limite di confidenza 95% = 129 - 131 umol/L).

EQA: REALLY VALUABLE TOOLS ?

In the last 20 years, many efforts have been dedicated on clarifying and discussing the specific requirements for the ***applicability of information given by External Quality Assessment (EQA) programs*** in the evaluation of the IVD-MD performance in terms of metrological traceability of the performed measurements.

A unique benefit of this type of programs is their ability of identifying measurands that ***need improved harmonization and stimulating standardization initiatives*** that are required to support the use of clinical practice guidelines.

Unfortunately, the ***majority of current EQA programs are not adequate*** to assess harmonization of laboratory results as, once again, they ***disregard the commutability of employed materials.***

Panteghini M. Clin Chem Lab Med 2024

DE GRUYTER Clin Chem Lab Med 2017; 55(7): 949–955

Opinion Paper

Graham R.D. Jones*, Stephanie Albarede, Dagmar Kesseler, Finlay MacKenzie, Joy Mammen, Morten Pedersen, Anne Stavelin, 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

1) a statement on the ***EQA material matrix and its commutability***;

2) the method used to assign the ***target value***;

3) the ***data set*** to which APS are applied;

4) the ***applicable analytical property*** being assessed (i.e. total error, bias, imprecision, uncertainty);

5) the rationale for the selection of the APS; and

6) the ***type of the Milan model(s)*** used to set the APS.

MODELS TO ASSIGN APS to EQA SCHEMES

Table 1: Examples of current variation in models used to assign analytical performance specifications (APS) to External Quality Assurance (EQA) schemes.

EQA Program	Models
CSCQ Switzerland	Governmental regulations (combination of BV and state of the art) and Combination of limits given by scientific societies and Z-score
CTCB France	Z-score/state of the art/limits given by scientific societies or other/limits based on clinical impact
DEKS Denmark	Combination of BV, state of the art and expert opinion
NOKLUS Norway	Fixed percentage limits and based on a combination of BV, state of the art and expert opinion
RCPAQAP Australia	Combination of BV and state of the art
SEHH Spain	Statistical/state of the art/BV
SEQC Spain	Combination of BV and statistical results
SKML The Netherlands	Combination of BV and state of the art
WEQAS UK	Combination of BV and state of the art
CMCEQAS	Combination of state of the art and statistical considerations

APS: CRITERIA TO BE USED IN EQAS

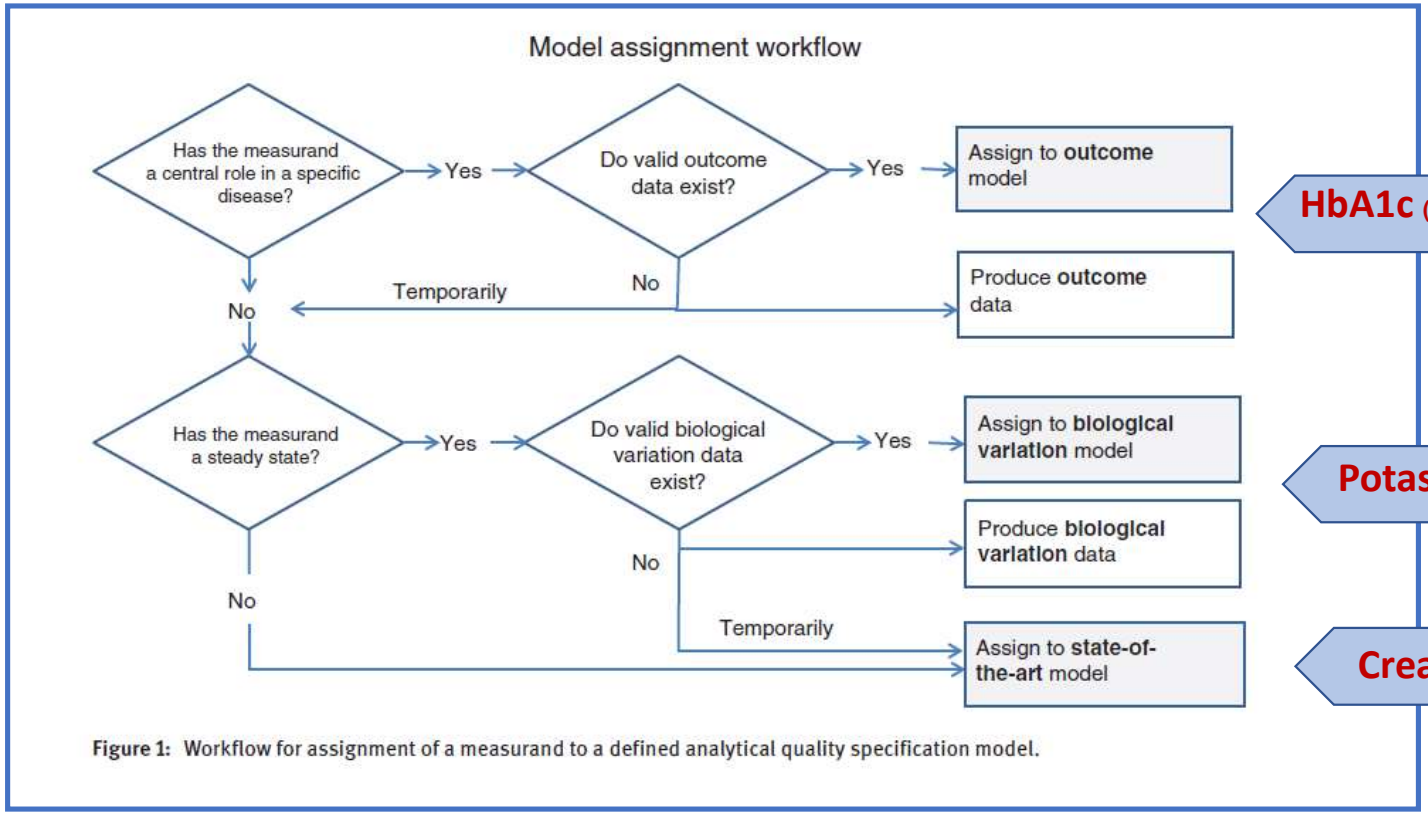


Figure 1: Workflow for assignment of a measurand to a defined analytical quality specification model.

HbA1c (whole blood)

Potassium (plasma)

Creatinine (urine)

Ferruccio Ceriotti*, Pilar Fernandez-Calle, George G. Klee, Gunnar Nordin, Sverre Sandberg, Thomas Streichert, Joan-Lluis Vives-Corrons and Mauro Panteghini, on behalf of the EFLM Task and Finish Group on Allocation of laboratory tests to different models for performance specifications (TFG-DM)

Criteria for assigning laboratory measurands to models for analytical performance specifications defined in the 1st EFLM Strategic Conference

Clin Chem Lab Med 2017; 55(2): 189–194

APS: ANALYTICAL PERFORMANCE SPECIFICATION

The most commonly issued EQA program in Australia is the RCPAQAP where APS have been determined based on a ***combination of biological variation and state of the art***

The approximate definition of state of the art used is that ***about 80 % of laboratories*** can achieve the standard.

The effect of using APS set in this way should be to improve the less well-performing laboratories.

APS: A VALUABLE TOOL

Using imprecision criteria relative to biological variation, there are ***two measurands (triglycerides and iron) for which the total country CV (CVC, the CV of results from all participating laboratories) meet the optimal level*** (CVC<0.25 × CVI),

8 measurands which meet the desirable level (CVC<0.5 × CVI), and

another ***13 which meet the minimal level*** (CVC<0.75 × CVI).

With this knowledge, laboratories can advise that patients can be **monitored across the country with these tests using results from any laboratories.**

DE GRUYTER Clin Chem Lab Med 2024; aop

Christopher J.L. Farrell*, Graham R.D. Jones, Kenneth A. Sikaris, Tony Badrick, Peter Graham and Jonathan Bush

Sharing reference intervals and monitoring patients across laboratories – findings from a likely commutable external quality assurance program

Conclusions: Analysis of data from ***commutable EQA programs*** can provide a mechanism for monitoring whether analytical performance justifies the ***interpretations*** made in contemporary laboratory practice.

EQA providers should establish systems for routinely providing this information to the laboratory community.

COMPARABILITY OF LABORATORY INFORMATION, NOT ONLY OF ANALYTICAL RESULTS IS NEEDED

Patients are commonly tested at more than one laboratory, and results from more than one laboratory are increasingly compared with one another.

When single results are reported, the same ***interpretation*** should be reached regardless of the testing laboratory. If results from different laboratories are similar, the same interpretation will be made if the ***reference intervals or decision points*** are the same.

If instruments give dissimilar results, different reference intervals and decision points are required.

Farrell CJL et al CCLM 2024

COMPARABILITY OF LABORATORY INFORMATION

For analytes with AACB CRIs, between-instrument agreement was considered acceptable if all instrument groups ***agreed with one another within ±0.1 × CRI width for both samples.***

Among the 18 analytes with AACB CRIs, ***11 met specification*** for all instruments on both samples.

These were alkaline phosphatase, creatine kinase, creatinine, gamma glutamyltransferase, lactate dehydrogenase, phosphate, potassium, protein, sodium, total bilirubin, and urea.

Farrell CJL et al CCLM 2024

Six analytes that use clinical decision limits had between-instrument agreement assessed against bias criteria from the CDC and ADA. ***Triglycerides was the only analyte that met specification*** for all instrument groups, while total cholesterol and HDL cholesterol failed for only one instrument group.

Measurand	Method	Bias specification, % & source	Instrument groups (n)	Specification met?[a]	Instruments outside specification
Triglycerides		5 CDC [17]	7	Yes	
Cholesterol		3.3 CDC [18]	7	6 passed	Beckman AU
HDL-C		5 CDC [19]	7	6 passed	Siemens Atellica CH
Glucose		2.2 ADA [8]	7	4 passed	Siemens Dimension EXL, Siemens Atellica CH (borderline), Ortho VITROS (borderline)
LDL-C	All	5 CDC [20]	10	8 passed	Siemens Atellica CH Friedewald, Abbott Alinity c other equation (borderline)
	Friedewald		6	4 passed	Siemens Atellica CH (borderline), Beckman AU (borderline)
	Other eqn		4	3 passed	Beckman AU (borderline)
Vitamin D		5 CDC [21]	4	2 passed	Roche Cobas e (borderline), Siemens Atellica (borderline)

MONITORING PATIENTS WITH TESTING AT DIFFERENT LABORATORIES

The CVAust for both Liquid Serum Chemistry samples was calculated for all analytes.

Analytes without decision limits were evaluated against CV_I. For these 46 analyte-method groups, the results spanned the full range of classifications: ***3 (6.5 %) were optimal***, ***6 (13.0 %) were desirable***, 6 (13.0 %) were minimal, 11 (23.9 %) were borderline, ***11 (23.9 %) were poor***, and 9 (16.5 %) were out of range.

For analytes with decision limits, evaluation was performed against imprecision specifications from the CDC and ADA. The CVAust met specification for ***triglycerides*** and ***vitamin D***, and was borderline for total cholesterol and glucose. Both LDL cholesterol methods, as well as HDL cholesterol failed to meet specification.

Farrell CJL et al CCLM 2024

Risk Management and Healthcare Policy

Dovepress

open access to scientific and medical research

Open Access Full Text Article

REVIEW

Navigating Quality Assessment Hurdles in Clinical Laboratory Services: A Comprehensive Review in Resource-Limited Settings

Negesse Cherie[1], Teshiwal Deress[1], Dereje Mengesha Berta[2], Elias Chane[3], Bisrat Birke Teketelew[2], Kasaw Adane[1], Mesele Nigus[1]

- The laboratory services in resource-limited countries suffer from insufficiencies in consumables, basic equipment, skilled employees, training programs, logistical assistance, and national standard quality evaluation.
- Participation in the EQA program in resource-limited countries faced different challenges, including sample commutability and assigned target values; transportation and shipment; expenses from the EQA program; equipment and reagent supplies; awareness and motivation of laboratory professionals; and utilization of feedback, which has a direct impact on the implementation of the EQA.

EQA IN RESOURCE-LIMITED SETTINGS

We conclude from this analysis that there are several obstacles to overcome when applying or implementing an EQA program in clinical laboratory services. The ***majority of the difficulties found fall under the category of external difficulties*** and involve managing and preparing samples, allocating funds and supplies, shipping, and transporting goods.

Other issues that were shown to be related to ***internal issues*** included employee engagement, equipment validation and maintenance, and integrated national management systems.

Overcoming these obstacles through ***establishing national EQA program*** and providing training about quality management system for laboratory professionals is vital for better quality of laboratory results and continuous improvement.

DE GRUYT 1EQA cclm-2024.pdf Clin Chem Lab Med 2024; aop

Renze Bais, Anne Vassault, Ivan M. Blasutig, Pradeep Kumar Dabla, Ji Lin, Armand Perret-Liaudet, Annette Thomas, Kandace A. Cendejas, Sarah E. Wheeler, Jean-Marc Giannoli, Qing H. Meng* and Egon P. Amann*

External quality assessment performance in ten countries: an IFCC global laboratory quality project

This study shows that not all countries perform to globally accepted EQA performance standards (note: all participating countries of this study are IFCC member countries) and that additional future efforts should be devoted to improve this unsatisfactory situation to the good of improved medical diagnostics and disease treatment of patients.

EQA IN RESOURCE-LIMITED SETTINGS

The simple EQA design applied fulfilled our aim of identifying poor performing laboratories in low to middle income countries that required further help and support.

We ***didn't need commutable, metrological traceable material*** with APS based on clinical or biological goals to achieve our aim.

We needed ***cheap, stable material*** from a provider that had global EQA presence where we could use simple peer review using pragmatic APS criteria.

Answer to referees' criticisms by the authors of the paper «External quality assessment performance in ten countries: an IFCC global laboratory quality project « (accepted for publication in CCLM)

DE GRUYTER

Clin Chem Lab Med 2024; aop

Editorial

Mario Plebani*

External quality assurance (EQA): navigating between quality and sustainability

OUTLINE OF TALK

- Quality in laboratory medicine: ***EQA/PT and accreditation***
- Type of EQA programs: ***regulatory versus educational***
- Elements and ***categories of EQAs***
- ***Harmonization*** of EQAs and how EQAs may improve harmonization
- EQA/PT. Not only clinical chemistry and not only for analytical phase
- ***Take home messages***

EQAS: AN INTERNAL TOOL for CLINICAL LABORATORIES or FOR HARMONIZATION ?

Individual clinical laboratories are often seen as the primary target for most EQA programs.

Laboratories try to answer the question, ***"is my assay working as expected" ?***

However, individual ***laboratories are often not well-placed to act upon between-laboratory differences*** such as may be identified by commutable EQA samples, especially if they are using measurement systems from manufacturers.

Still other organisations (often not paying customers for EQA programs) are explicitly concerned with those same between-laboratory differences as they are responsible for either reducing any such inter-laboratory differences or acting on the knowledge of those between laboratory differences.

EQA and HARMONIZATION

HARMONIZATION OF EQA PROGRAMS

Criteria for harmonization (samples, target values, phase(s) of the TTP)

Purpose(s) of the programs

EQA AS A TOOL FOR HARMONIZATION IN LABORATORY MEDICINE

Analytical results,

Comparators (measurement units, reference intervals, interpretative comments etc)

HARMONIZATION

The European Organization for External Quality Assurance Providers in Laboratory Medicine (EQALM) and the “International Consortium for Harmonization of Clinical Laboratory Results” (ICHCLR) collaborate in an initiative called ***HALMA (HArmonization of measurands in Laboratory Medicine through data Aggregation***).

The initiative intends to ***combine the results*** from EQA providers that use ***commutable samples*** to assess the harmonization of measurement procedure results from different IVD MDs used in medical laboratories

Theodorsson E et al Clin Chim Acta 2024

HARMONIZATION

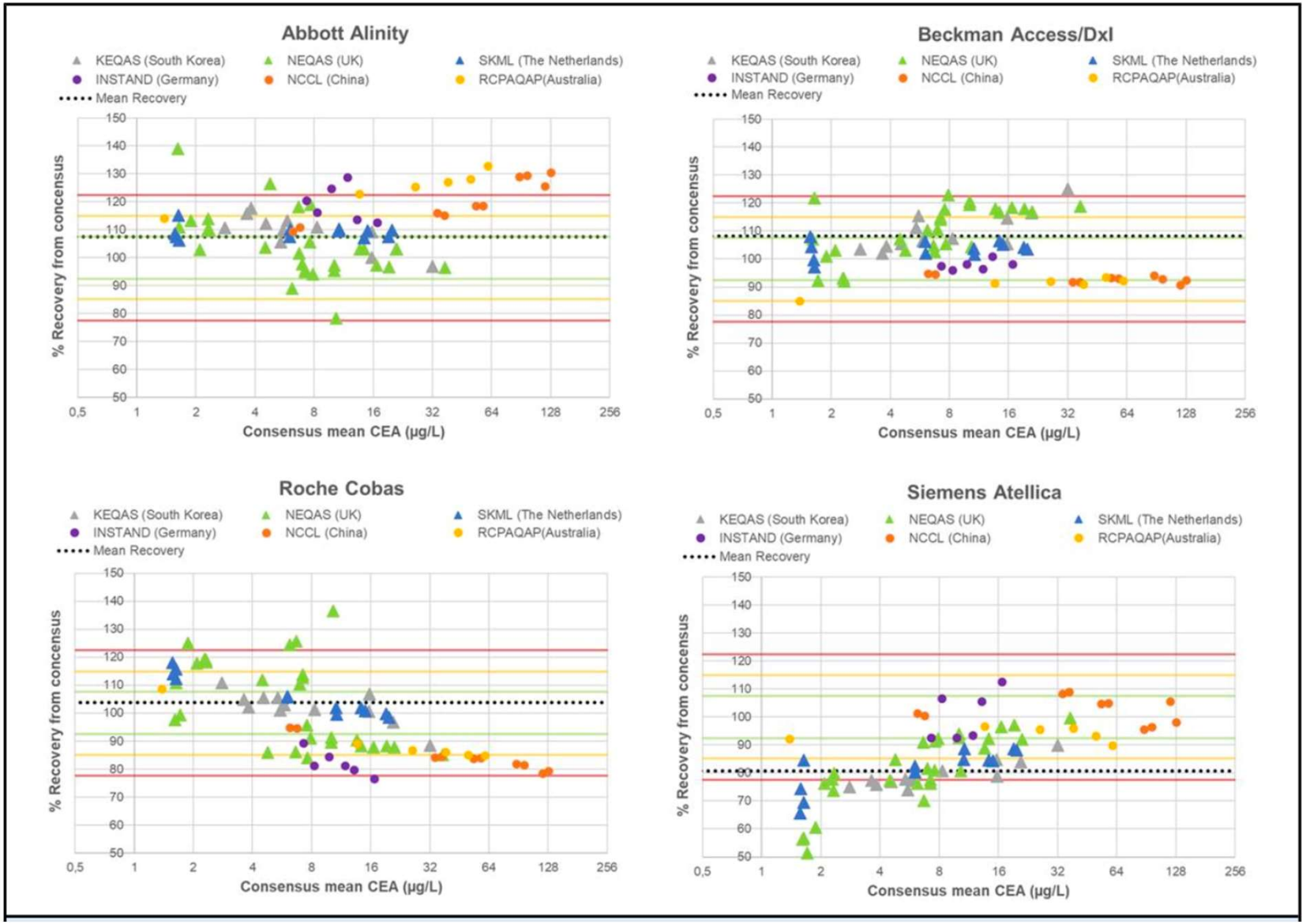
- Investigating the harmonization of in vitro diagnostics using data from EQA programs has recently gained interest as a tool to provide ***insights*** into ***between measurement procedure relationships*** and ***correlations***
- A major advantage of using EQA data is that, in general, a ***large number of measurements*** are performed per measurement procedure and the median (or mean) of each EQA sample thereby reflects true operational performance.
- A key and essential requirement is that the EQA materials are commutable

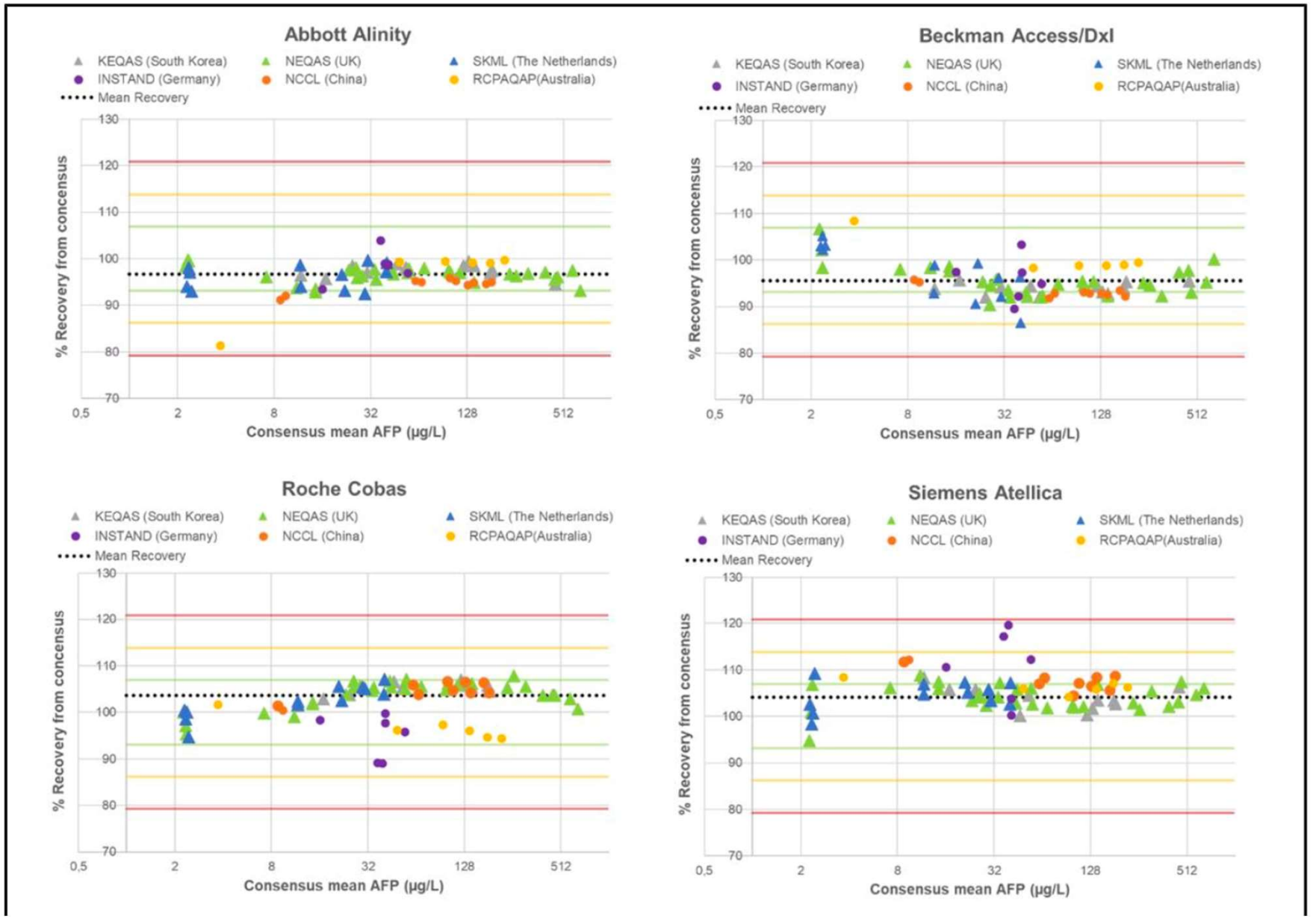
Clinical Chemistry 70:4
669–679 (2024)

Investigating the Current Harmonization Status of Tumor Markers Using Global External Quality Assessment Programs: A Feasibility Study

Huub H. van Rossum [a,*] Stefan Holdenrieder,[b,c] Bart E.P.B. Ballieux,[d] Tony C. Badrick,[e] Yeo-Min Yun,[f] Chuanbao Zhang,[g] Dina Patel,[h] Marc Thelen,[i,j] Junghan Song,[k] Nathalie Wojtalewicz,[c] Nick Unsworth,[l] Hubert W. Vesper,[m] Wei Cui,[n] Lakshmi V. Ramanathan,[o] Catharine Sturgeon,[l] and Qing H. Meng [p]

The mean differences with the consensus mean of patient-pool–based EQA samples for all measurement procedures were within the optimum bias criterion for AFP, the desirable bias for PSA, and the minimum bias criterion for CEA. However, CEA results <8 µg/L exceeded the minimum bias criterion. For CA125, CA15-3, and CA19-9, the harmonization status was outside the minimum bias criterion, with systematic differences identified.


Abbott Alinity
KEQAS (South Korea)
NEQAS (UK)
SKML (The Netherlands)
INSTAND (Germany)
NCCL (China)
RCPAQAP(Australia)
Mean Recovery
% Recovery from concensus
Consensus mean CEA (µg/L)
Beckman Access/Dxl
KEQAS (South Korea)
NEQAS (UK)
SKML (The Netherlands)
INSTAND (Germany)
NCCL (China)
RCPAQAP(Australia)
Mean Recovery
% Recovery from concensus
Consensus mean CEA (µg/L)
Roche Cobas
KEQAS (South Korea)
NEQAS (UK)
SKML (The Netherlands)
INSTAND (Germany)
NCCL (China)
RCPAQAP(Australia)
Mean Recovery
% Recovery from concensus
Consensus mean CEA (µg/L)
Siemens Atellica
KEQAS (South Korea)
NEQAS (UK)
SKML (The Netherlands)
INSTAND (Germany)
NCCL (China)
RCPAQAP(Australia)
Mean Recovery
% Recovery from concensus
Consensus mean CEA (µg/L)


Abbott Alinity
KEQAS (South Korea)
NEQAS (UK)
SKML (The Netherlands)
INSTAND (Germany)
NCCL (China)
RCPAQAP(Australia)
Mean Recovery
% Recovery from concensus
Consensus mean AFP (µg/L)
Beckman Access/DxI
KEQAS (South Korea)
NEQAS (UK)
SKML (The Netherlands)
INSTAND (Germany)
NCCL (China)
RCPAQAP(Australia)
Mean Recovery
% Recovery from concensus
Consensus mean AFP (µg/L)
Roche Cobas
KEQAS (South Korea)
NEQAS (UK)
SKML (The Netherlands)
INSTAND (Germany)
NCCL (China)
RCPAQAP(Australia)
Mean Recovery
% Recovery from concensus
Consensus mean AFP (µg/L)
Siemens Atellica
KEQAS (South Korea)
NEQAS (UK)
SKML (The Netherlands)
INSTAND (Germany)
NCCL (China)
RCPAQAP(Australia)
Mean Recovery
% Recovery from concensus
Consensus mean AFP (µg/L)

HARMONIZATION and COMMUTABILITY

- Based on the patient-pool–based EQA samples, ***AFP*** seems to be harmonized within the ***optimal bias*** criterion (±6.9%), ***PSA*** within the ***desirable bias criterion*** (±10.6%), and ***CEA within the minimum bias criterion*** (22.4%).
- The current harmonization status of ***CA125, CA15-3, and CA19-9 is outside the minimum bias*** criteria of ±10.1%, ± 13.9%, and ±21.6%, respectively.
- Results suggest that ***spiked or modified materials*** and patient pools might ***not provide an adequate EQA material*** in this case and, preferably, ***individual patient samples should be used.***

EQA/PT: FUTURE EFFORTS

- ***Harmonization*** of EQA/PT programs is need
- Programs ***not only for clinical chemistry***, but covering all subdisciplines of laboratory medicine (quantitative and qualitative data)
- Programs covering ***not only the analytical*** but also extra-analytical phases
- Cooperation at an international level should be promoted

Taylor & Francis
Taylor & Francis Group

Critical Reviews in Clinical Laboratory Sciences

ISSN: (Print) (Online) Journal homepage: www.tandfonline.com/journals/ilab20

The European Organisation of External Quality Assurance Providers in Laboratory Medicine (EQALM) Statement: guidelines for publishing about interlaboratory comparison studies (PubILC)

Christoph Buchta, Gro Gidske, Gitte M. Henriksen, Tony Badrick & on behalf of the European Organisation of External Quality Assurance Providers in Laboratory Medicine (EQALM)

INTERNATIONAL STANDARD

ISO/IEC 17043

First edition
2010-02-01

Conformity assessment — General requirements for proficiency testing

Évaluation de la conformité — Exigences générales concernant les essais d'aptitude

Reference number
ISO/IEC 17043:2010(E)

Contents

Page

OUTLINE OF TALK

- Quality in laboratory medicine: ***EQA/PT and accreditation***
- Type of EQA programs: ***regulatory versus educational***
- Elements and ***categories of EQAs***
- ***Harmonization*** of EQAs and how EQAs may improve harmonization
- EQA/PT. Not only clinical chemistry and not only for analytical phase
- ***Take home messages***

DE GRUYTER Clin Chem Lab Med 2019; 57(1): 115–126

Opinion Paper

Emmanuel J. Favaloro*, Ian Jennings, John Olson, Elizabeth M. Van Cott, Roslyn Bonar, Robert Gosselin and Piet Meijer

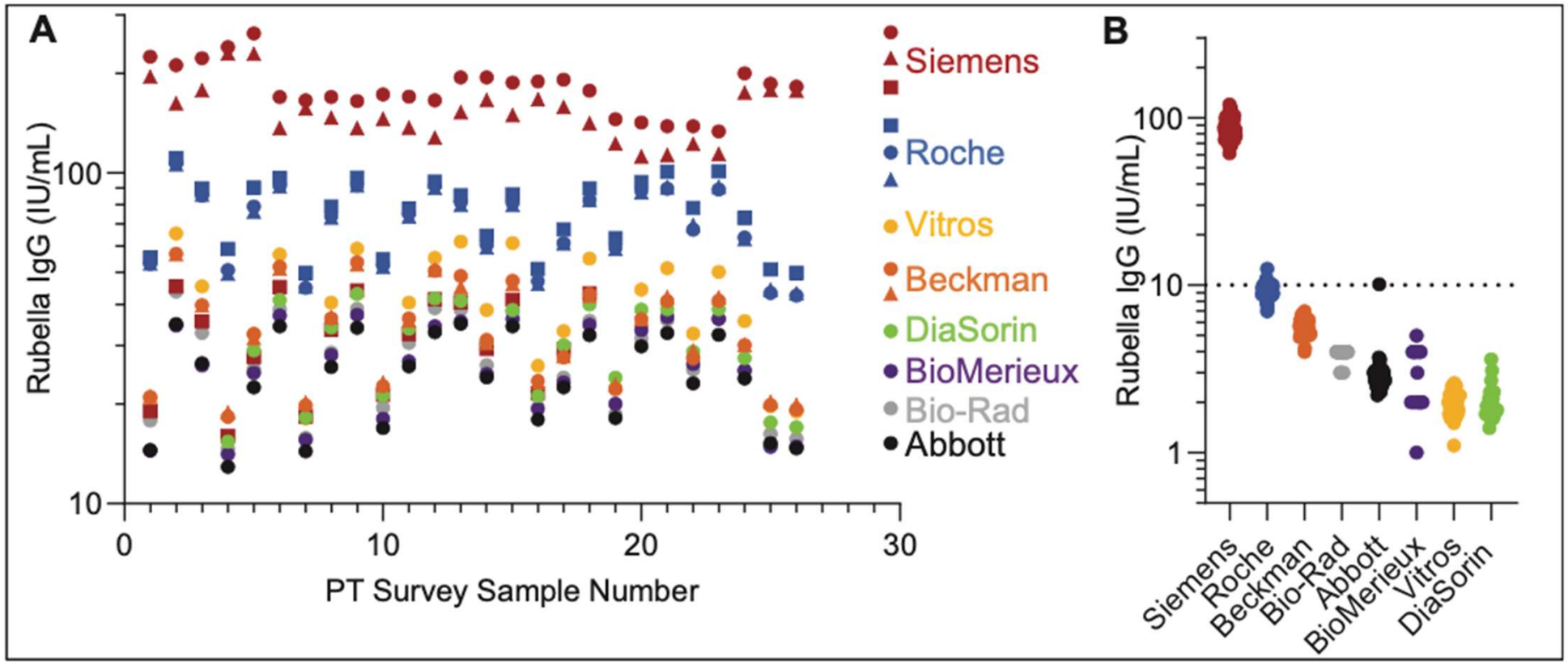
Towards harmonization of external quality assessment/proficiency testing in hemostasis

The goals of External quality assurance in thrombosis and hemostasis (EQATH) include exchanging of information regarding program operations, exchanging split specimens among programs to determine if there are differences in practice, participating in value setting of standards, providing outreach to locations in the world without EQA support of hemostasis testing in laboratories and targeting improvement in EQA practice by harmonizing towards best practice.

PERFORMANCE ASSESSMENT: NOT AN EASY TASK

A key element in performance assessment of participants in EQA programs is the use of proper performance criteria and specifications. Currently, the majority of EQA programs in the field of hemostasis use the ***state-of-the-art approach*** for setting their acceptance limits (e.g. a particular % deviation from the consensus value, Z-scores, etc.). However, there is no consensus yet about which acceptance criteria are most appropriate for performance assessment.

EQA/PT as a TOOL FOR HARMONIZATION



Treger RS et al. Arch Pathol Lab Med 2024

Smit et al. BMC Infectious Diseases 2013, 13:102
http://www.biomedcentral.com/1471-2334/13/102

BMC
Infectious Diseases

TECHNICAL ADVANCE Open Access

The development and validation of dried blood spots for external quality assurance of syphilis serology

Table 2 Correlation between detection of *Treponema pallidum* antibodies by plasma TPPA and DBS TPPA

(n=1147)		TPPA plasma		
		Positive	Negative	Total
DBS TPPA	Positive	169	10	179
	Negative	8	960	968
	Total	177	970	1147*

sensitivity of DBS against plasma 95.5% (95% CI: 91.3–98,0%).
specificity of DBS against plasma 99.0% (95% CI: 98.1–99.5%).
* excluding 34 indeterminate results.

Clinical Chemistry 62:8
1084–1095 (2016)

Thirteen Years of an International External Quality Assessment Scheme for Genotyping: Results and Recommendations

Verena Haselmann,[1] Wolf J. Geilenkeuser,[2] Simona Helfert,[1] Romy Eichner,[1] Svetlana Hetjens,[3] Michael Neumaier,[1] and Parviz Ahmad-Nejad[4*]

CONCLUSIONS: Based on the evaluation of this long-term EQA scheme, various recommendations can be given to improve the quality of molecular genetic testing, such as the use of 2 different methods for genotyping.

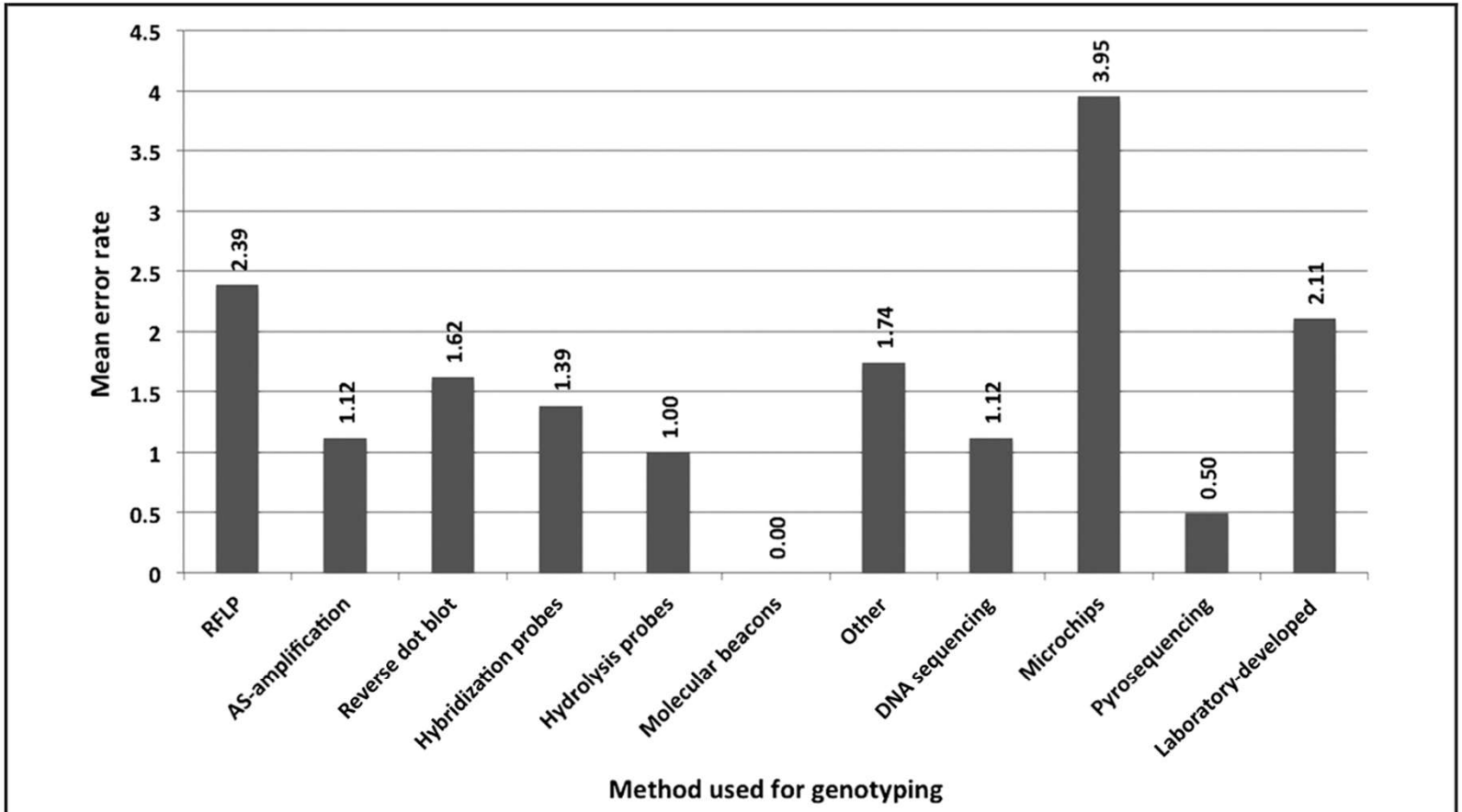


Fig. 1. Mean error rate per method used.

Data presented are based on methods reported for loci analyses between 2010 and 2014. In total, 48 795 results are considered. Displayed is the mean error rate per method. Other indicates all commercially available tests that cannot be assigned to one of the other methods; Microchips, microchip analysis.

EQA on MOLECULAR TUMOR PROFILING WITH CIRCULATING TUMOR DNA-BASED METHODOLOGIES

CLIN CHEM 2024; 70: 759-67

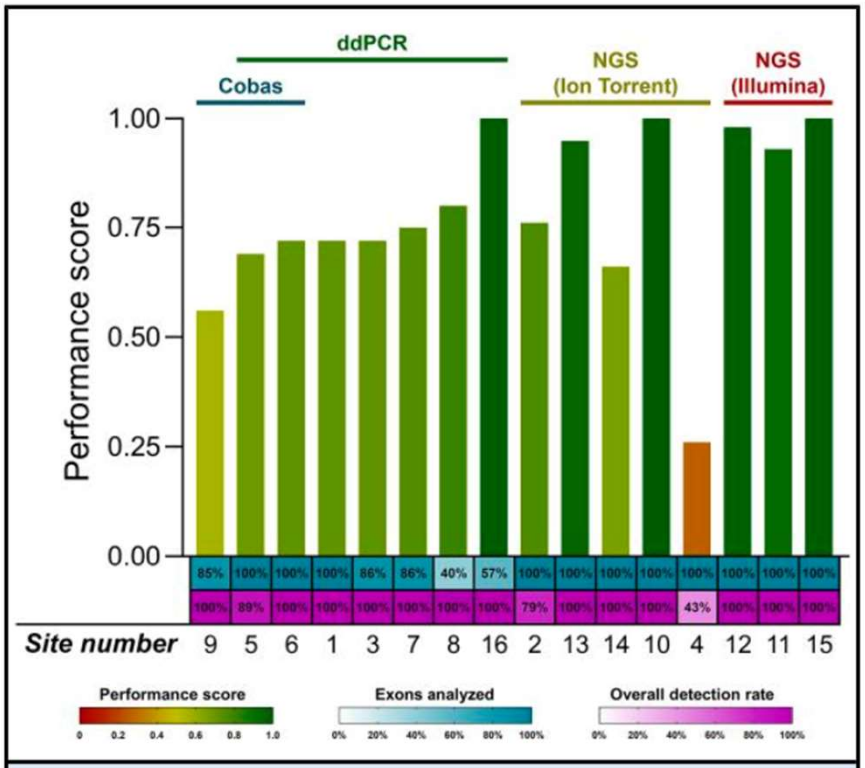
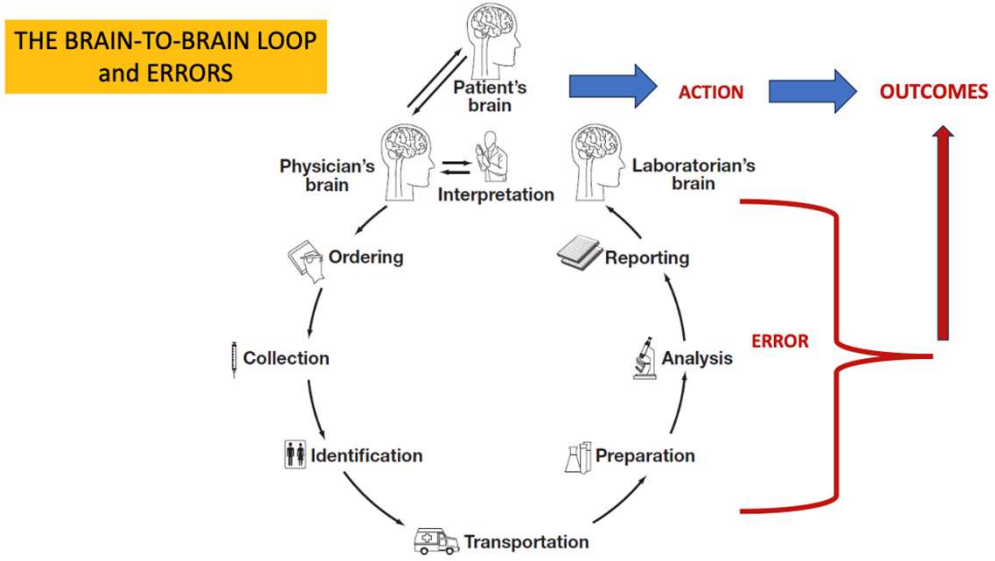
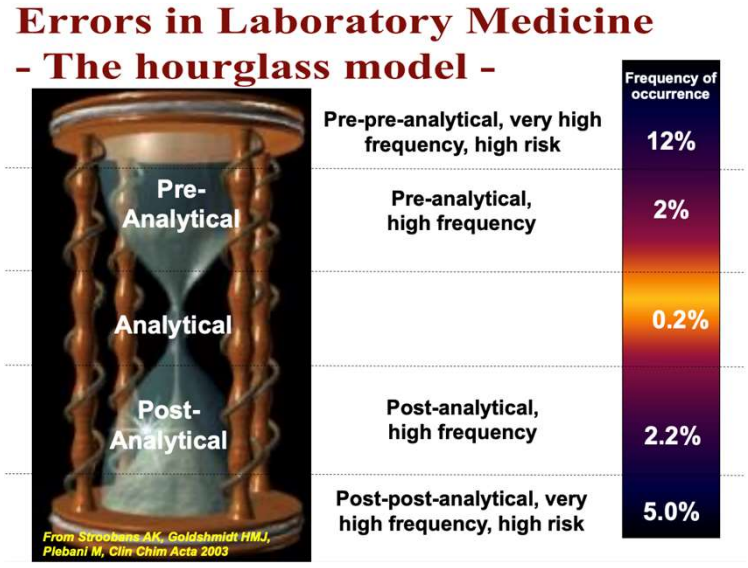


Fig. 3. Performance score, exon coverage, and overall detection rate. Performance was assessed using custom marking criteria (Supplemental Table 2). The percentage of analyzed exons is depicted based on the coverage of the applied assays. The percentage of identified variants detectable by the applied assays is expressed as the overall detection rate (also see Supplemental Table 2).

EQA: NOT ONLY ANALYTICAL PHASE

It should be noted that while External Quality Assurance (EQA) traditionally addresses analytical quality, the EQA process can equally be ***applied to other aspects of laboratory activities*** and can be used to assess both differences in other factors e.g. units, reference intervals and test names, as well as changes in response to interventions





EXTERNAL QUALITY ASSURANCE (EQA)

ANALYTICAL PHASE: well defined rules (compliance?)

PRE-ANALYTICAL: Pilot schemes

No harmonization guidelines

Only a few EQA shemes available

POST-ANALYTICAL: Measurement Units (harmonization?)

Reference intervals/decision limits

Interpretative comments

Critical values

Clin Chem Lab Med 2022; 60(1): 66–73 DE GRUYTER

Rubén Gómez Rioja*, Monserrat Ventura, María Antonia Llopis, Josep Miquel Bauça, Andrea Caballero Garralda, Mercedes Ibarz, Debora Martinez, Carolina Gómez, Paloma Salas Gómez-Pablos, Isabel García del Pino, Jose Delgado, Juan Jose Puente and Iciar Marzana

External quality assessment of serum indices: Spanish SEQC-ML program

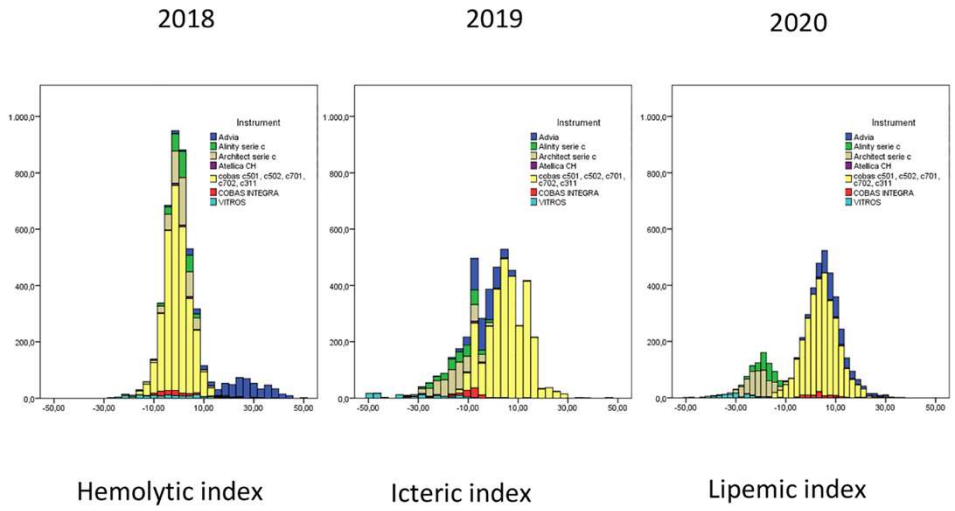
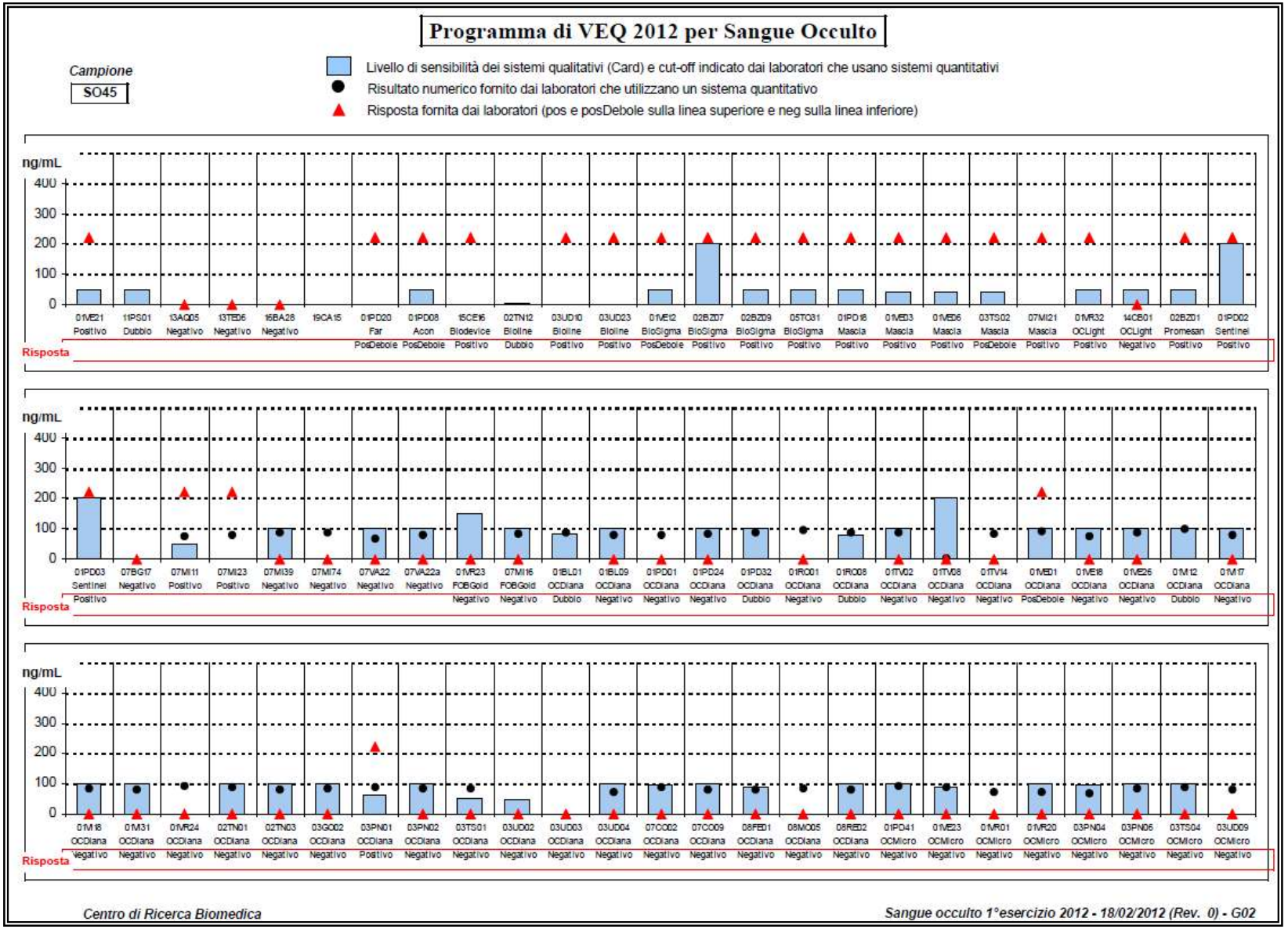


Figure 2: Percentage difference (PD%) with respect to the overall median of participants in each round. Cumulative results for years 2018–2020.

Table 2: Annual evolution of the median and 90th percentile of the percentage deviations of the participants with respect to the assigned value of their comparison group.

Indice	Percentile	2018	2019	2020
Hemolityc index	p50	3.52	3.40	2.74[a]
	p90	11.19	9.35	7.85
Icterus index	p50	5.17	4.11	5.12
	p90	15.15	16.70	12.19
Lipernic index	p50	5.72	3.88[a]	3.2[a]
	p90	19.59	11.34	9.71

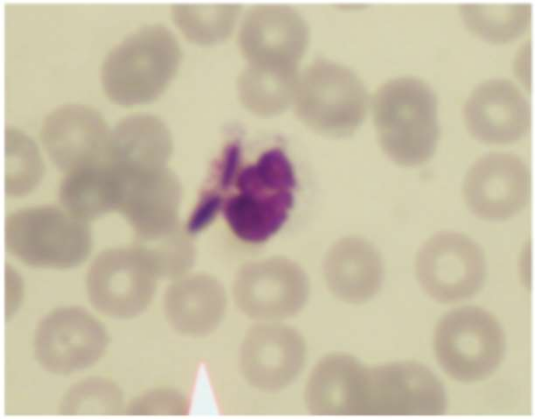
[a]$p<0.01$ with respect to the previous year in the median difference test.

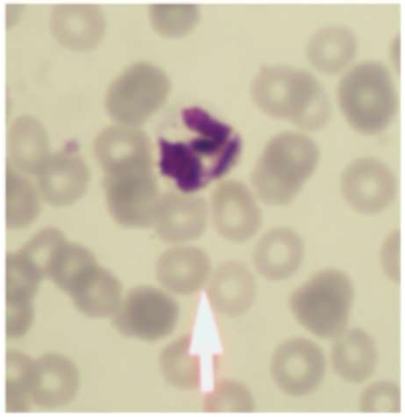


Fecal occult blood

Equivalent analytical data, but different cut-offs may lead to different clinical interpretation

ISO 15189 Accreditation: competence-based management





Morphologic description (interpretative comment) is an integral part of laboratory report s

In order to

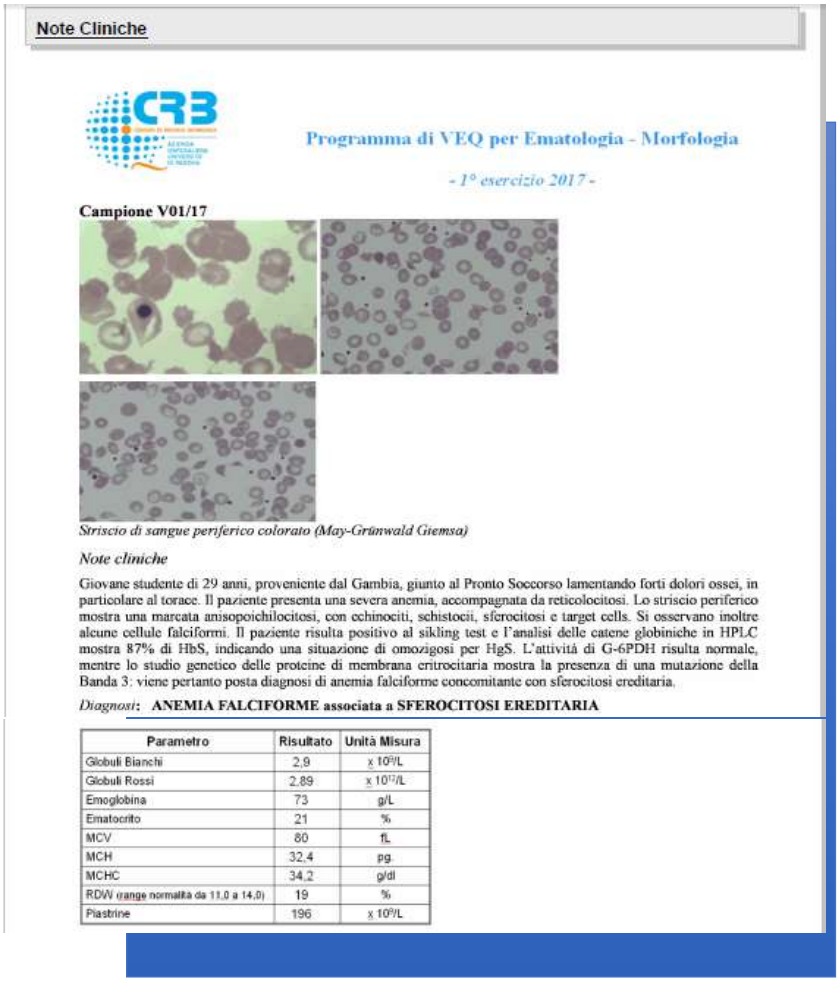
- ✓ answer to clinical question
- ✓ aid result interpretation
- ✓ Improve diagnostic value

STEPS

1. DESCRIPTION: Neutrophils containing fungi
2. INTERPRETATION: Microorganisms in blood film is observed in patients with infections/sepsis
3. COMMUNICATION: These findings should be notified as soon as possible
4. CLINICAL DECISION: Clinicians starts first-line therapy for the treatment of infection/sepsis,

EQAS on morphological evaluation of peripheral blood cell

- Assessment of competence -



Note Cliniche

Programma di VEQ per Ematologia - Morfologia

- 1° esercizio 2017 -

Campione V01/17

Striscio di sangue periferico colorato (May-Grünwald Giemsa)

Note cliniche

Giovane studente di 29 anni, proveniente dal Gambia, giunto al Pronto Soccorso lamentando forti dolori ossei, in particolare al torace. Il paziente presenta una severa anemia, accompagnata da reticolocitosi. Lo striscio periferico mostra una marcata anisopoichilocitosi, con echinociti, schistocii, sferocitosi e target cells. Si osservano inoltre alcune cellule falciformi. Il paziente risulta positivo al sikling test e l'analisi delle catene globiniche in HPLC mostra 87% di HbS, indicando una situazione di omozigosi per HgS. L'attività di G-6PDH risulta normale, mentre lo studio genetico delle proteine di membrana eritrocitaria mostra la presenza di una mutazione della Banda 3: viene pertanto posta diagnosi di anemia falciforme concomitante con sferocitosi ereditaria.

Diagnosi: **ANEMIA FALCIFORME associata a SFEROCITOSI EREDITARIA**

Parametro	Risultato	Unità Misura
Globuli Bianchi	2,9	x 10^9/L
Globuli Rossi	2,89	x 10^{12}/L
Emoglobina	73	g/L
Ematocrito	21	%
MCV	80	fL
MCH	32,4	pg
MCHC	34,2	g/dl
RDW (range normalità da 11,0 a 14,0)	19	%
Piastrine	196	x 10^9/L

All laboratory professionals that perform the morphologic evaluation in haematology, have to participate in the specific EQA Scheme.

Each operator

✓ has a confidential username and password to manage its results and visualize its reports

✓ evaluates independently the morphology of peripheral blood cells, provided by EQA Provider, and describes the morphology identified and formulates the diagnostic hypothesis

ELSEVIER

Clinica Chimica Acta 333 (2003) 209–219

www.elsevier.com/locate/clinchim

Interpretative comments and reference ranges in EQA programs as a tool for improving laboratory appropriateness and effectiveness

Laura Sciacovelli*, Lorena Zardo, Sandra Secchiero, Martina Zaninotto, Mario Plebani

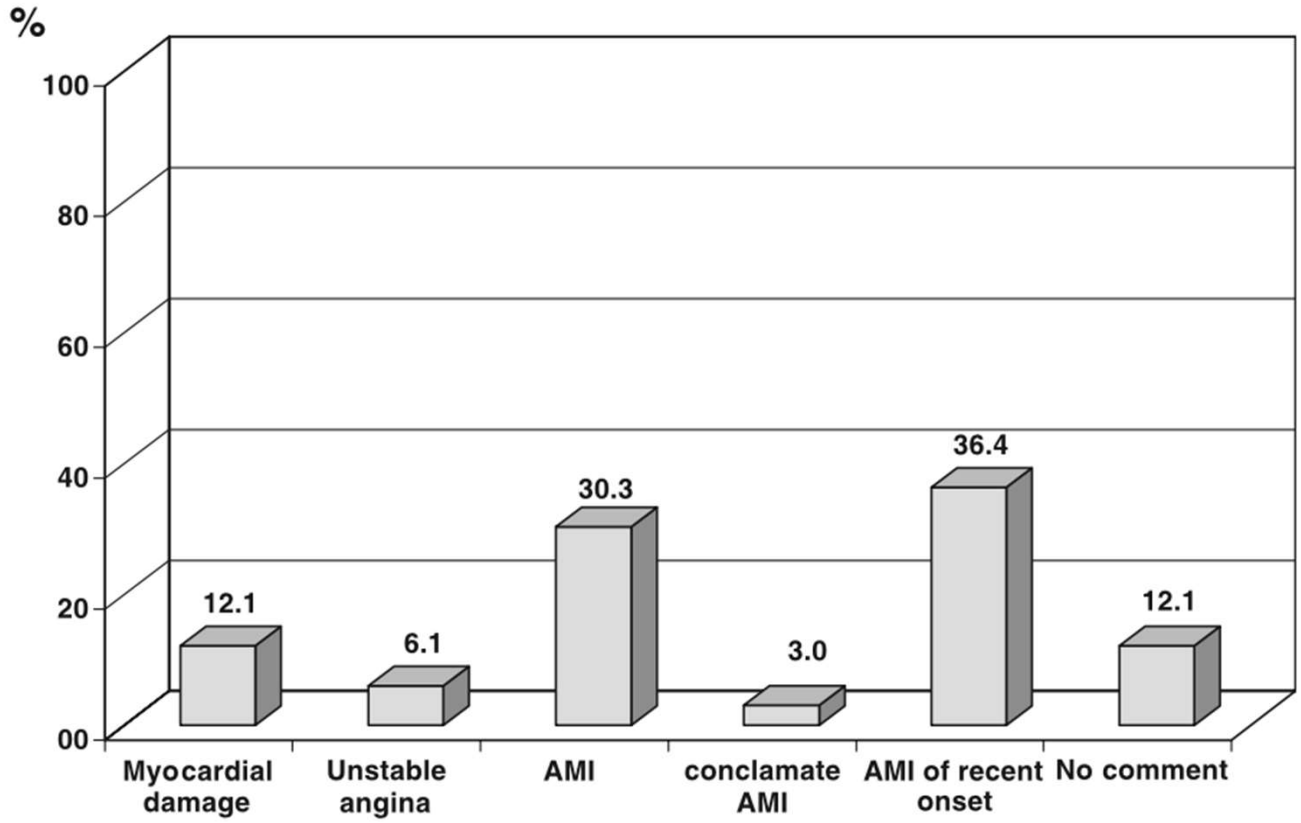


Fig. 3. Report 1: percentage of interpretative comments grouped on the basis of the diagnosis.

OUTLINE OF TALK

- Quality in laboratory medicine: ***EQA/PT and accreditation***
- Type of EQA programs: ***regulatory versus educational***
- Elements and ***categories of EQAs***
- ***Harmonization*** of EQAs and how EQAs may improve harmonization
- EQA/PT. Not only clinical chemistry and not only for analytical phase
- ***Take home messages***

EQA AND LABORATORY PROFESSIONALS

EQA/PT programs must be organized by ***third part scientific/professional organizations*** safeguarding the nature and goals of the programs

IQC and EQA are independent but ***integrated professional activities*** that should be managed by laboratory professionals

Cooperation with manufacturers is increasingly needed, but professional organizations should ensure autonomy and ***governance of the programs***

EQA AND LABORATORY PROFESSIONALS

National societies and International Federations (in particular, IFCC and EFLM) have to assure ***more and better consideration to EQA programs*** which play a fundamental role in laboratory medicine.

A ***closer cooperation*** between scientific bodies, EQA providers EQALM, manufacturers and regulators should be promoted to improve the quality and sustainability of EQA programs

There are many issues in EQA programs which require more concern, further research and harmonization

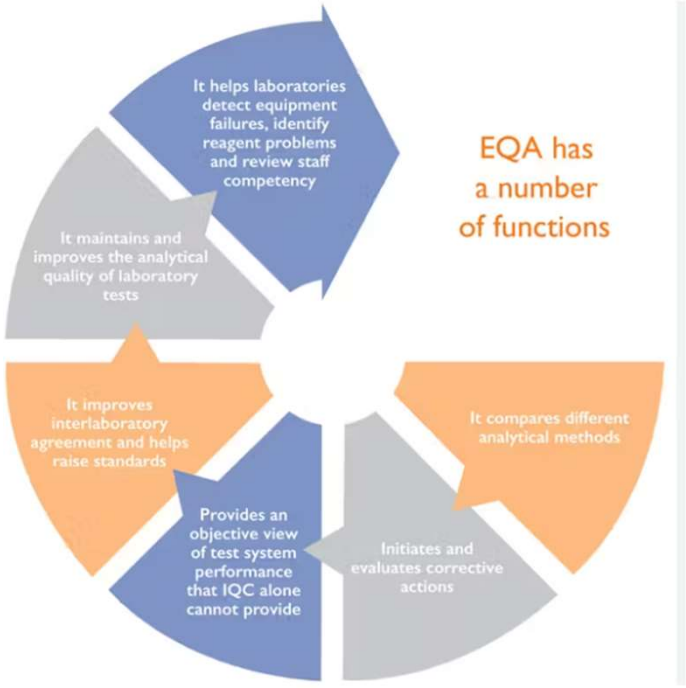
EQA and HARMONIZATION

Significant differences exist between currently available EQA/PT programs

Efforts to achieve better ***harmonization are in progress*** but further initiatives are needed to provide valuable guidelines and recommendations

Clinical laboratories have to select the EQA/PT programs that comply with the main goals which are to ***improve quality for patients*** and ***obtain accreditation***

THE FUTURE ???


It helps laboratories detect equipment failures, identify reagent problems and review staff competency
It compares different analytical methods
Initiates and evaluates corrective actions
Provides an objective view of test system performance that IQC alone cannot provide
It improves interlaboratory agreement and helps raise standards
It maintains and improves the analytical quality of laboratory tests
EQA has a number of functions


AI

TAKE HOME MESSAGES

- The most valuable ***tool for inter-laboratory comparisons***
- A fundamental ***requirement for medical laboratory accreditation*** (ISO 15189)
- A key tool for ***harmonizing*** analytical data, measurement units, reference intervals, and interpretative comments
- A valuable tool for ***sharing data*** and experiences between laboratory professionals in the same Region/Country and at an international level

Thank you for your attention!

mario.plebani@unipd.it