TBD Akademi

İç Kalite Kontrol Uygulamaları: Başarılar ve Başarısızlıklar

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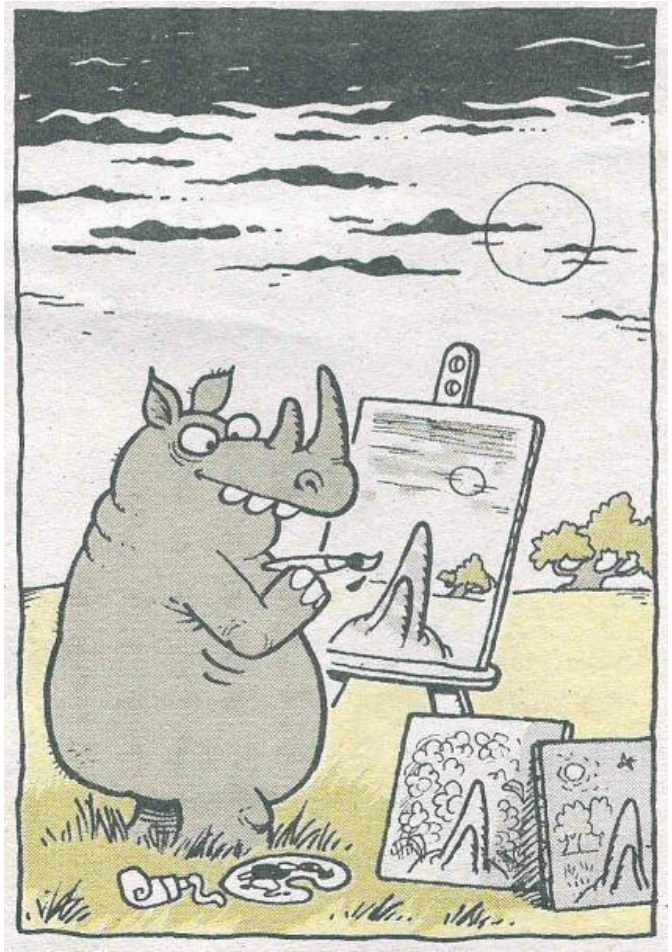
Acıbadem Üniversitesi Tıp Fakültesi
ve ClinLab Laboratuvarı

ACIBADEM UNIVERSITY MMVII

ClinLab



bu sunum bireysel görüşler içerir

Defilelerde neden giyilemez ürünler sunulur?

2018 Prada kolleksiyonu

Miuccia Prada

Teşekkürler

Fig.6. A commemorative photograph of the founders of Bio-Science Laboratories (Richard Henry is first from the left and Milton Segalove is third). These two scientists were the ones who suggested the use of control samples in clinical chemistry control charts. Henry in particular was one of the most important clinical chemists of the previous century in the fields of statistical quality control and biostatistics. He has published a plethora of relevant articles and the book Clinical chemistry: Principles and Techniques.

Fig.2 The pioneer of statistical quality control Walter Shewhart and his wife Edna. His important work was recognized through the creation of the specialized Shewhart award, honoring scientists' contribution to the field.

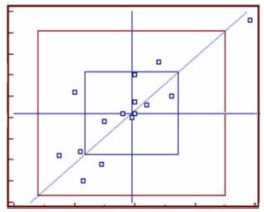


Fig.7. A picture of William Youden (1900 – 1971) from the web site of the American Statistical Association (ASA). An example of the chart named after him is also shown. Youden focused particularly on interlaboratory controls. The chart which he invented in 1959 is used in all interlaboratory control applications, as well as in external quality assessment schemes in clinical chemistry and haematology. In 1985, the ASA established the Youden award in his honor.

Fig.11. A picture of Prof. James Westgard from the web site of the University of Wisconsin, USA. Until he retired, Westgard was a clinical chemist and a professor of clinical pathology at the medical school of the University of Wisconsin. Today he is the most famous researcher on quality control for automated analyzers. He has worked mostly on computer simulations, the Decision Limit Cusum chart, power functions, quality rules for the Levey-Jennings chart (multirule method), the Operational Process Specifications Charts, method validation, and the Six Sigma theory. He has

Fig.10 A picture of Prof. George Cembrowski from the web site of the University of Alberta, Canada. Cembrowski is a clinical pathologist and he is specialized in biochemistry, statistics and medical informatics. He has been very effective in the documentation of many statistical quality control methods in collaboration with Westgard and other researchers. He has worked extensively on the moving average theory, as well as the "average of normals", the anion gap, Bull's algorithm

Fig.14. A picture of Prof. Callum Fraser from i biographical article in Clinical Chemistry. Fraser a professor of clinical chemistry at the Universit of Saint Andrews and Dundee in Scotland. He h authored papers on many subjects, most of wh are about quality control. He is one of the pionee of the theory of "quality specifications" in the fi of clinical chemistry, with significant work equations and charts which use biological va ances as a basic parameter for the selection of most suitable quality control method.

Figure 16. A picture of Dr. Carmen Ricós from James Westgard's web site. Ricós studied pharmacology at the University of Barcelona and works today in the biochemistry laboratory of the Vall d' Hebron Hospital in Barcelona. She has written many articles on the internal and external quality assessment in clinical laboratories, and is a member of quality committees for many international organizations. She is known especially for her initiative in concentrating biological variances for all substances measured at medical laboratories. These tables are used extensively today in the determination of quality specifications.

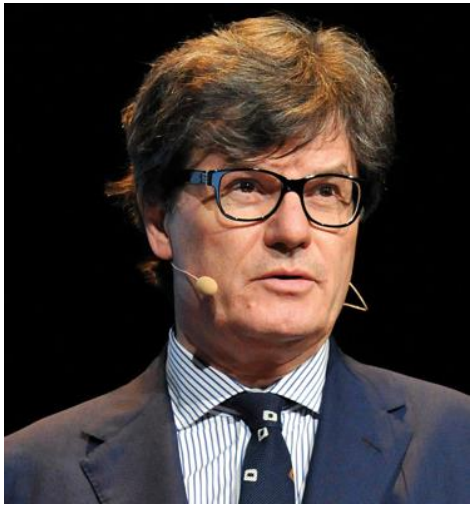
Fig.9. A picture of Prof. Brian Bull from the web site of the Loma Linda University in the USA, where Bull works as a professor of haematology. Bull's research work is extensive, but he became known mostly for his invention of a "moving average"-type equation which can be used in the quality control of haematology analyzers. This equation is used today in most haematology analyzers and is usually called "Bull's algorithm".

Fig.13. A picture of Prof. Curtis Parvin from the web site of the University of St. Lewis, USA. Parvin is a biostatistician and specialist in medical informatics and teaches these subjects at the University of Saint Lewis in Washington. He has contributed significantly to the theoretic documentation of power functions and other statistical issues concerning quality control in clinical chemistry.

Tony Badrick
PhD, CEO at RCPAA

Huub van Rossum
www.huvaros.com

Abdurrahman Coşkun



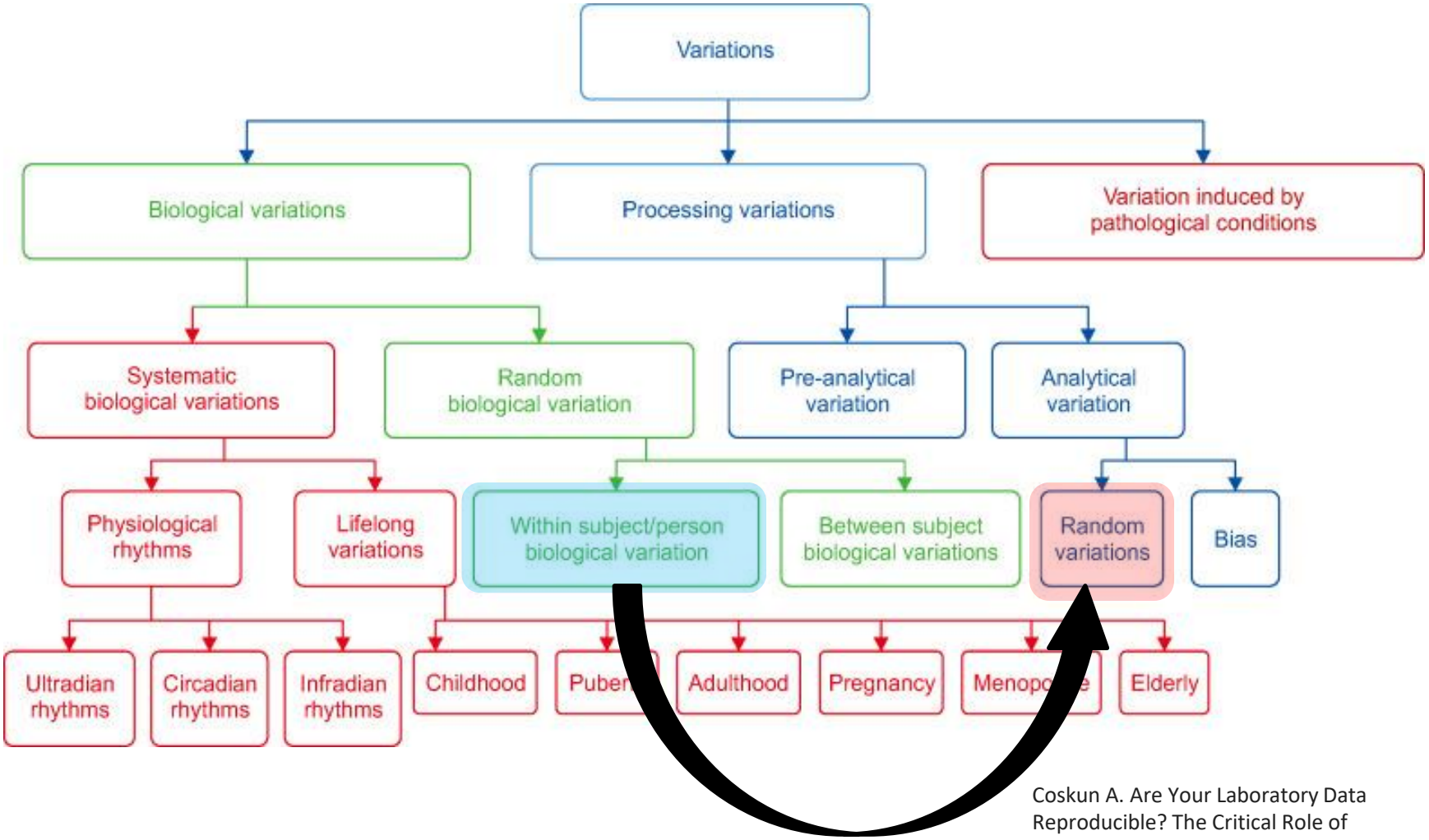
Mauro Panteghini
Chairman of JCTLM

Hikmet Can Çubukçu

Klinik Laboratuvarlarda Kalite Kontrol Alanındaki Önemli Gelişmeler

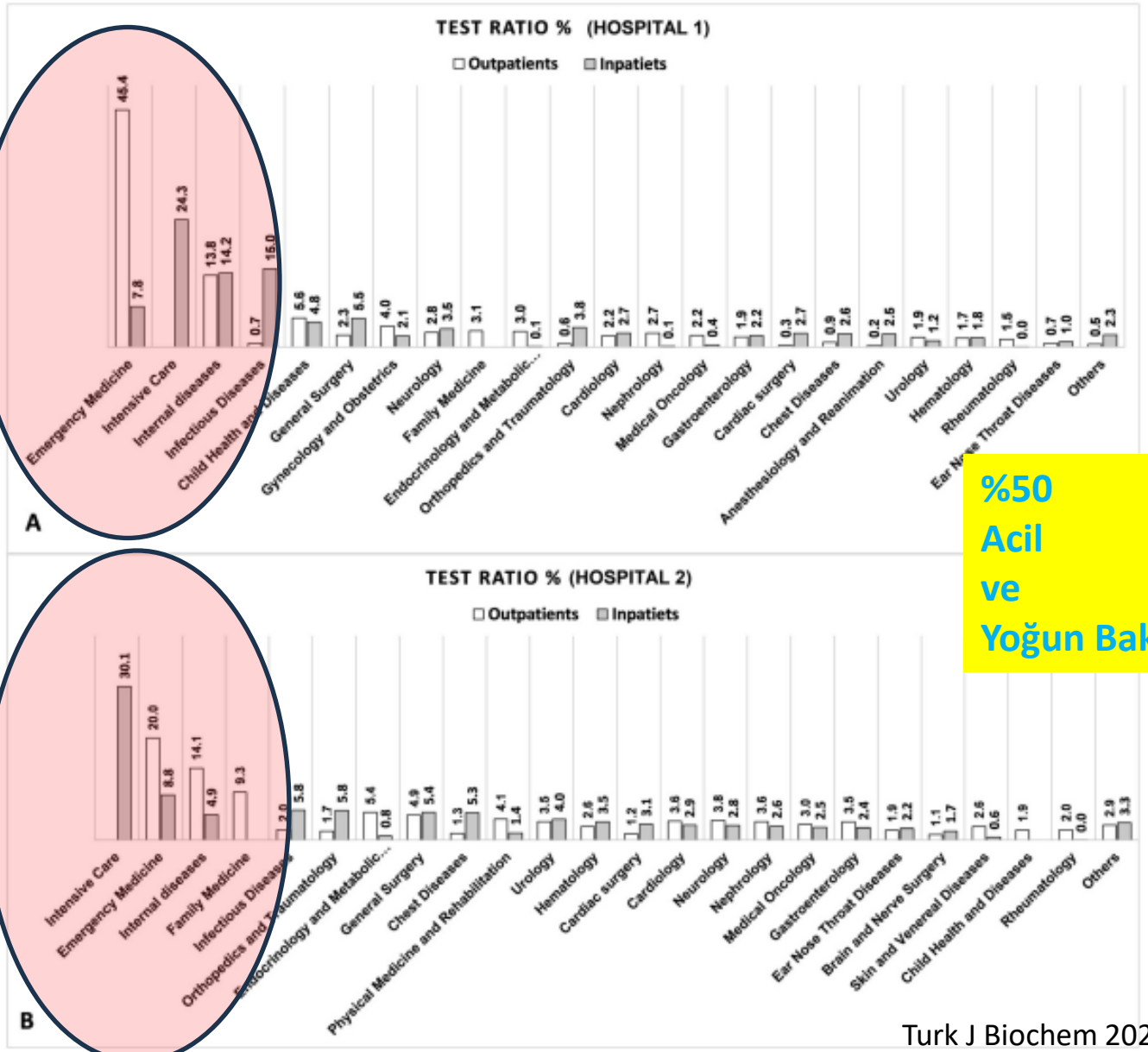
1950- Klinik laboratuvarlarda istatistiksel kalite kontrol kavramlarının uygulanması – **Levey ve Jennings**
1952- Kontrol grafiğinde bireysel KK değerinin izlenmesi – **Henry ve Sagalove**
1965- Normal ortalamalarının (Average of Normals - AoN) tanımı – **Hoffman**
1977- KK kurallarının performansının belirlenmesi – **Westgard**
1981- Birden fazla KK kuralının kullanımı – **Westgard**
1988- Cembrowski uygulamaları
1990- İzin verilebilir toplam hata (Total Error Allowable - TEa) kavramının tanıtılması
1999- Kalite gereklilikleri üzerine **Stockholm Konsensüs Konferansı**
2005- Klinik laboratuvarlara **Altı Sigma** uygulaması – **Westgard**
2010- Hasta Temelli Kalite Kontrol uygulamaları
2011- Risk yönetimine dayalı KK ile ilgili **CLSI EP23** belgesinin ilk baskısı
2012- Klinik laboratuvarlarda kalite gereklilikleri için uluslararası kılavuz olan **ISO 15189**'un ikinci versiyonu, **2022'de 3. versiyonu** yayınlandı
2014- Analitik performans spesifikasyonları (APS) üzerine **Milano Konsensüs Konferansı**
2016- İstatistiksel KK konusunda referans belge olan **CLSI C24**'ün dördüncü baskısı.
2019- IFCC Analitik komitesi **"PBRTQC"** derlemesini yayınladı
2023- Risk Temelli KK uygulaması rehberi olan **CLSI EP23 Ed2** ye yayınlandı

1. “Hasta” sonucunu etkileyen değişkenler nelerdir?



Coskun A. Are Your Laboratory Data Reproducible? The Critical Role of Imprecision from Replicate Measurements to Clinical Decision-making. Ann Lab Med. 2025 May 1;45(3):259-271.

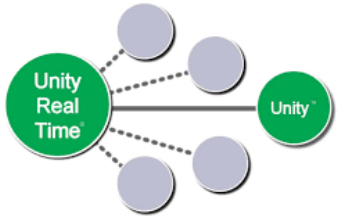
2. Laboratuvarlara en çok hangi kliniklerden örnek geliyor?



%50
Acil
ve
Yoğun Bakım

Turk J Biochem 2024; 49(3): 334–343

3. Tekrarlanabilirlik-CV% nedir?



A

Repeatability

- Measurement procedure

B

Intermediate precision

- Measurement procedure
- Instruments
- Reagents
- Operators
- Calibrations
- Operation conditions
- Others

C

Reproducibility

- Measurement procedure
- Instruments
- Reagents
- Operators
- Calibrations
- Operation conditions
- Laboratories
- Others

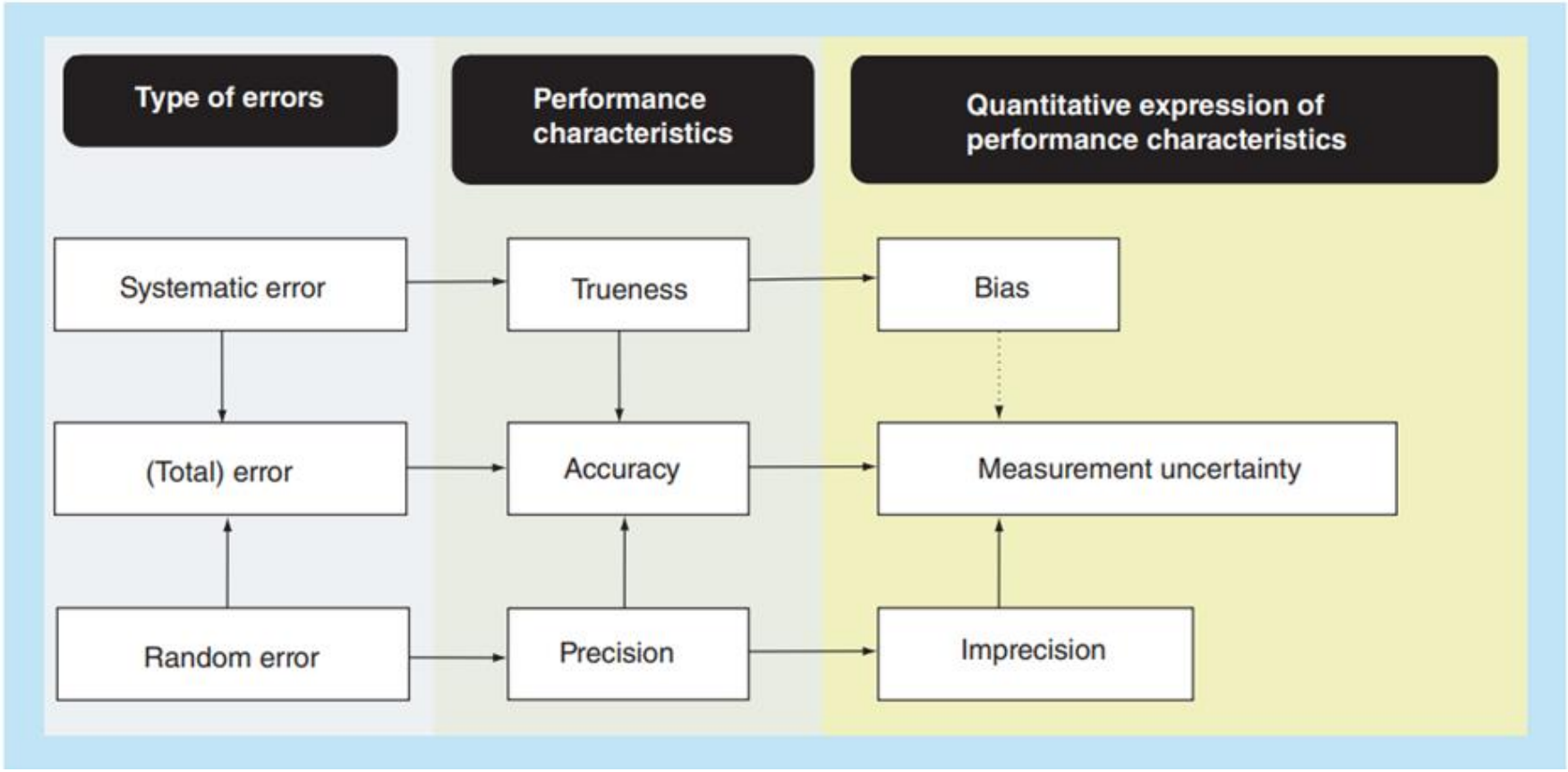
Ara değer

?

CLSI EP5
CLSI EP15

Coskun A. Are Your Laboratory Data Reproducible? The Critical Role of Imprecision from Replicate Measurements to Clinical Decision-making. Ann Lab Med. 2025 May 1;45(3):259-271.

4. Bias ve Total Hata nedir?



Theodorsson E, Magnusson B, Leito I. Bias in clinical chemistry. Bioanalysis. 2014;6(21):2855-75

4. Bias ve Total Hata nedir?

Criteria for Judging Precision and Accuracy in Method Development and Evaluation

James O. Westgard, R. Neill Carey, and Svante Wold[1]

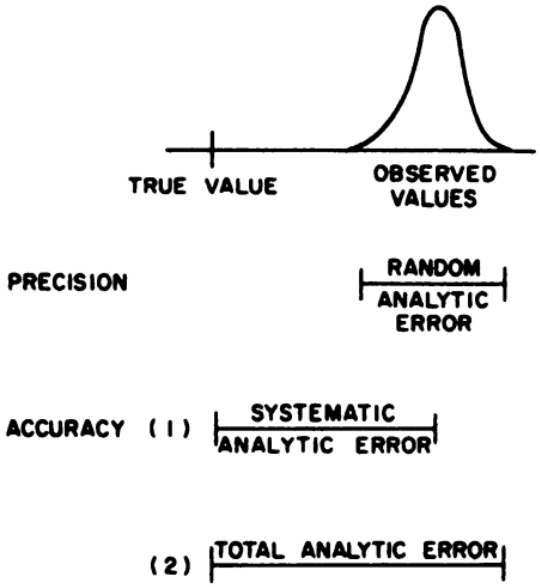
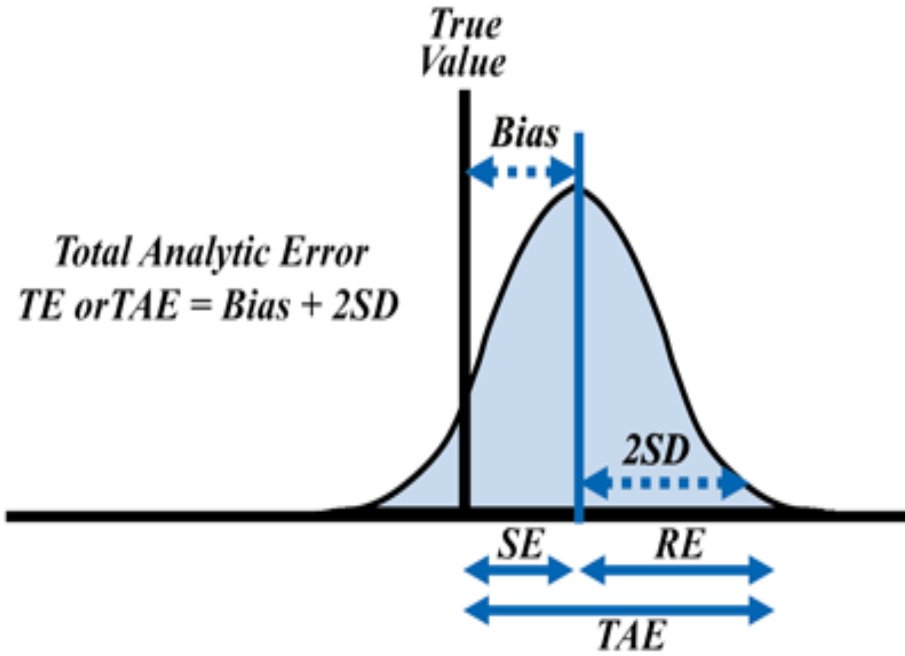
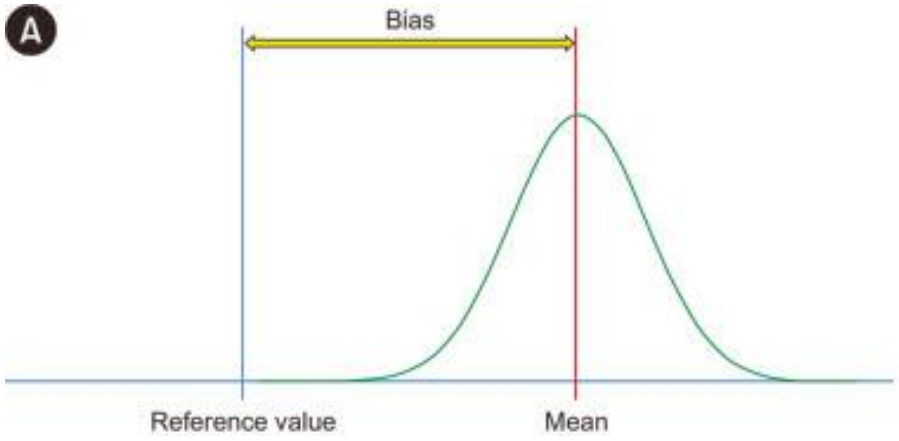


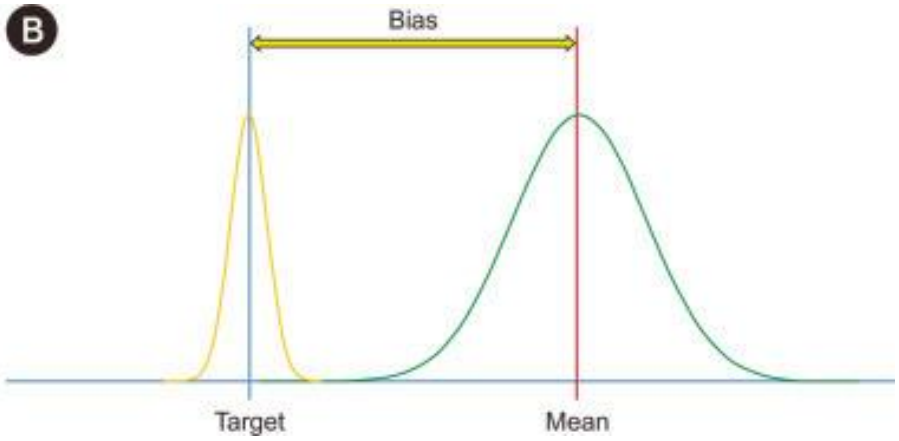
Fig. 1. Definitions of precision and accuracy in terms of random, systematic, and total analytic errors



CLIN. CHEM. 20/7, 825-833, **1974**

Bias kavramını hatalı mı kullanıyoruz!

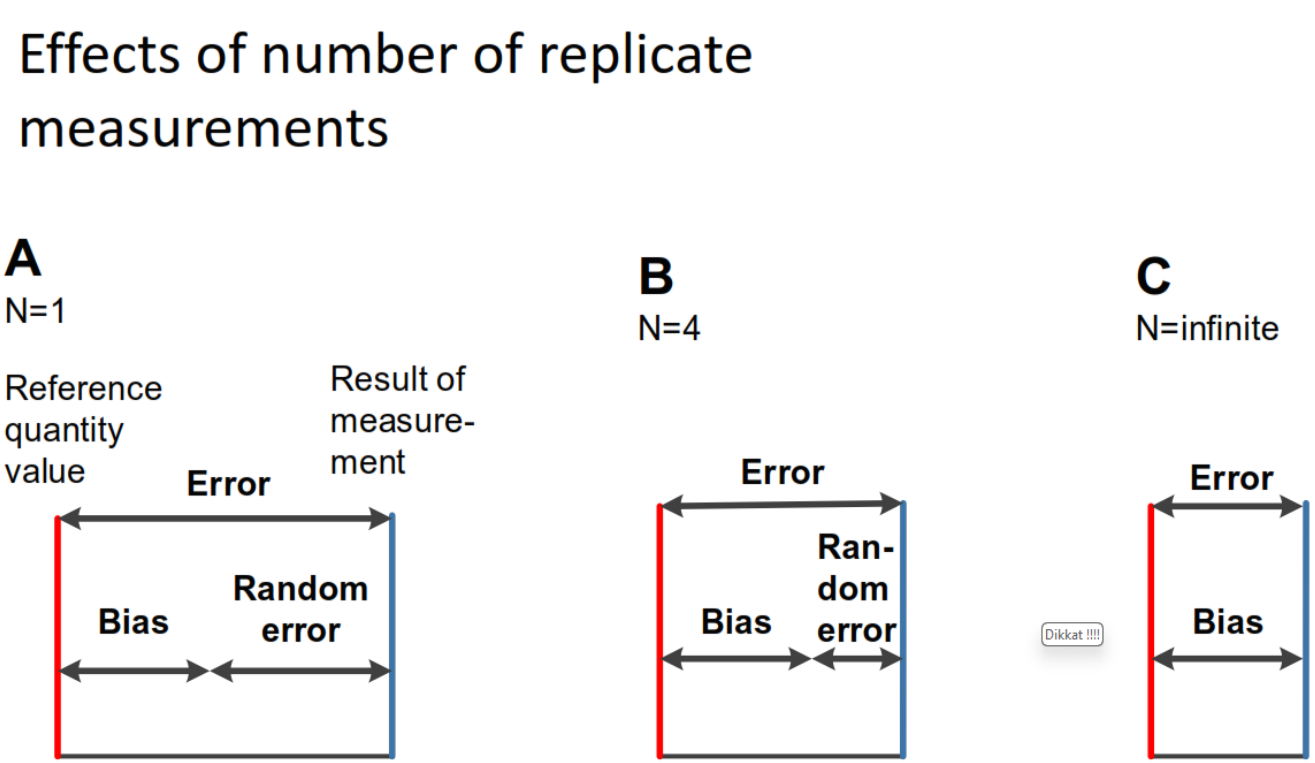




Biorad Unity !!!

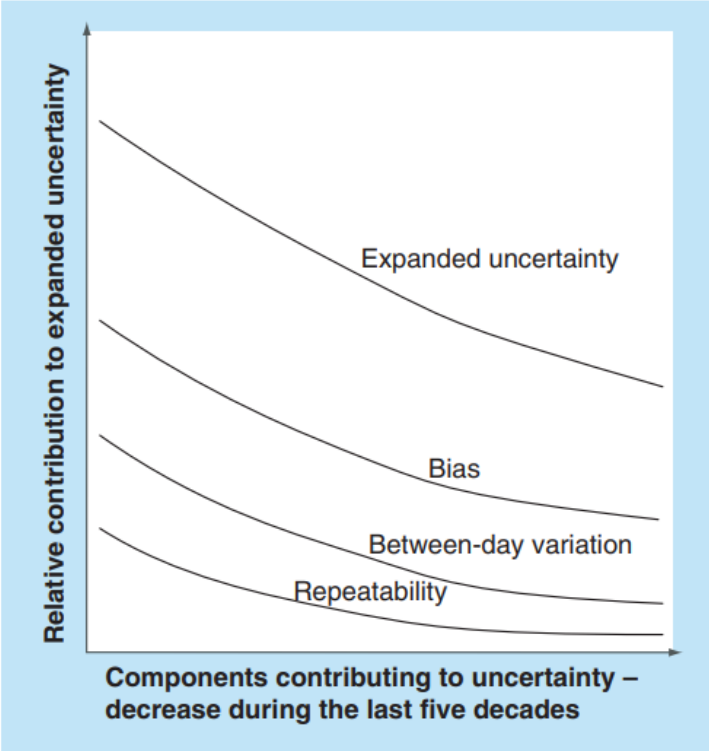
Coskun A: Ann Lab Med. 2023 Sep 4;44(1):6–20.

Tek ölçüm ile Bias hesaplanmaz



Bias in clinical chemistry. Bioanalysis. 2014;6(21):2855-75. doi: 10.4155/bio.14.249.

Bias ve Tekrarlanabilirlik bütçeleri



Theodorsson E, Magnusson B, Leito I. Bias in clinical chemistry. Bioanalysis. 2014;6(21):2855-75. doi: 10.4155/bio.14.249. PMID: 25486232.

5. ISO 15189:2022 Tıbbi Laboratuvarlar-Kalite ve Yeterlilik İçin Şartlar'I İKK ile ilgili neler ister?

7.3.7.2 İç Kalite Kontrol (IKK)

a) Genel Gereklilik:

Laboratuvar, belirlenmiş kriterlere göre, test sonuçlarının geçerliliğini **sürekli olarak izleyen bir IKK prosedürüne** sahip olmalıdır. Bu prosedür:

Hedeflenen kalite düzeyine ulaşıldığını doğrulamalı,

Sonuçların **klinik karar verme açısından tutarlı ve geçerli** olmasını sağlamalıdır.

1) Yapılan testin **klinik kullanım amacı** dikkate alınmalıdır.
2) Prosedür, **reaktif veya kalibratörlerin lotlar arası farklılıklarını** saptayabilmelidir.
   Bu farkları tespit edebilmek için: IKK materyalinde lot değişimi ile Reaktif veya kalibratör lot değişimi aynı gün/aynı çalışmada yapılmamalıdır.
3) **Üçüncü taraf (bağımsız üretici)** tarafından sağlanan IQC materyalinin kullanımı düşünülmelidir.
   Bu materyaller, cihaz ya da reaktif üreticisinin verdiği kontrol materyaline **alternatif veya tamamlayıcı** olarak tercih edilebilir.

b) IQC Materyalinin Seçimi:

Laboratuvar, kullanılacak IQC materyalini, **amacına uygun ve yeterli özelliklere sahip olacak şekilde** seçmelidir. Aşağıdaki faktörler dikkate alınmalıdır:

Ölçülmek istenen özellikler açısından **stabil** olmalı,

Materyalin yapısı, **hasta örneklerine mümkün olduğunca benzer** olmalı,

Materyal, test yöntemiyle **hasta örneğine benzer şekilde tepki vermeli**,

Materyal, test yöntemini **klinik olarak anlamlı düzeylerde zorlayabilmeli**,

Özellikle klinik karar sınırlarında yoğunluklara sahip olmalı,

Mümkünse ölçüm aralığının tamamını kapsamalıdır.

c) Uygun IQC materyali yoksa:

Eğer uygun bir kontrol materyali mevcut değilse, laboratuvar alternatif yöntemleri kullanmalıdır. Bunlar şunları içerebilir:

Hasta sonuçlarının eğilim analizi (örneğin hareketli ortalama, belli eşiklerdeki hasta sayılarının yüzdesi veya belirli tanılarla ilişkilendirme),

Hasta örneklerinin belirli aralıklarla, **alternatif bir yöntemle karşılaştırılması** (bu yöntem ISO 17511'e göre izlenebilir ve kalibre edilmiş olmalı),

Saklanan hasta örneklerinin yeniden test edilmesi.

f) IQC verilerinin değerlendirilmesi:

Elde edilen veriler, **önceden belirlenmiş kabul kriterlerine göre** düzenli ve anlamlı aralıklarla gözden geçirilmelidir.

g) IQC başarısız olduğunda yapılması gerekenler:

Eğer IQC kriterleri karşılanmaz ve bu durum **klinik açıdan önemli hata** riski taşıyorsa,

→ **Hasta sonuçları raporlanmamalı**, ilgili örnekler **hata düzeltildikten sonra yeniden analiz edilmelidir.**

IQC başarısızlığından sonra çalışılan tüm hasta örneklerinin sonuçları yeniden değerlendirilmelidir. ??

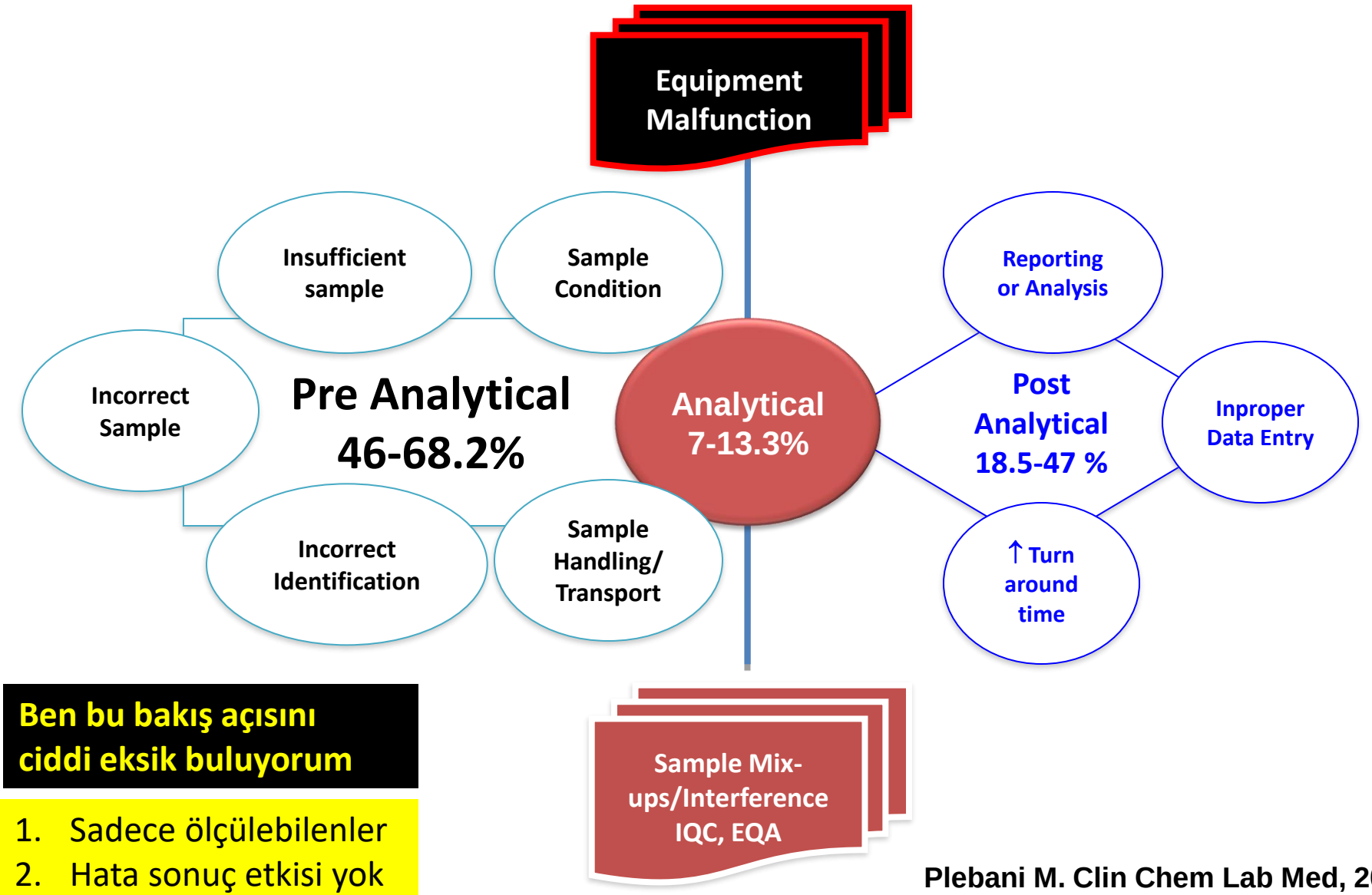
6. Analitik dönem neler kapsar? Ölçebiliyor miyiz ?

- **Standardizasyon, harmonizasyon ve stabilizasyon problemleri**
- İnterferanslar %2-8
- Personel (sayısı, yeterlilikleri)
- Uzman (sayısı, yeterlilikleri)
- İş hacmi büyüklüğü, **gereksiz hız !!!!**
- Laboratuvar çevre şartları yeterliliği
- Klinik karar eşik düzeyi ,referans aralık verifikasyonu
- Cihaz, bakım vs
- Kit ve malzeme yetersizlikleri (kalibratör, su, kontrol materyali vs)
- Yetersiz uygunsuz DKD
- **İKK yeterliliği (risk analizi, kuralları vs)**

Sınırlı

Çok Zor

Analitical error



Ben bu bakış açısını ciddi eksik buluyorum

1. Sadece ölçülebilenler
2. Hata sonuç etkisi yok
3. …

Plebani M. Clin Chem Lab Med, 2006.
Kalra J. Clin Biochem, 2004

6. Karşılaşma oranı nedir?

Clin Chem Lab Med 2023; 61(4): 688–695

Quality indicator			Laboratory results			
Code	Measurement		n	25th	50th	75th
Intra-analytical phase						
Unacceptable performances in IQC						
Intra-UnIQC	%~3 (1-6) its/total	Percentage	98	0.704 (0.025–1.648)	2.429 (1.810–2.977)	5.519 (3.341–6.866)
		Sigma		3.10 (2.99–3.33)	3.47 (3.38–3.59)	3.95 (3.63–4.98)
Unacceptable performances in EQA-PT schemes						
Intra-unac	Number of unacceptable performances in EQAS-PT schemes, per year/total number of performances in EQA schemes, per year	Percentage	22	1.192 (0.420–1.793)	1.881 (1.290–2.722)	2.863 (2.116–3.800)
		Sigma		3.40 (3.27–3.53)	3.58 (3.42–3.73)	3.76 (3.60–4.13)
Data transcription errors						
Intra-ErrTran	Number of incorrect results for erroneous manual transcription/total number of results that need manual transcription	Percentage	25	0 (0-0)	0 (0–0.004)	0.004 (0–0.009)
		Sigma		5.44 (5.24–6)	6 (5.44–6)	6 (6–6)
Intra-FailLIS	Number of incorrect results for information system problems/total number of results	Percentage	12	0 (0-0)	0 (0-0)	0 (0-0)
		Sigma		6 (5.88–6)	6 (6–6)	6 (6–6)
Pre-InsV	Number of samples with insufficient sample volume/total number of samples	Percentage	261	0.012 (0.008–0.016)	0.033 (0.027–0.039)	0.070 (0.056–0.080)
		Sigma		4.69 (4.65–4.76)	4.90 (4.86–4.96)	5.17 (5.10–5.27)
Clotted samples						
Pre-clot	Number of samples clotted/total number of samples with an anticoagulant checked for clots	Percentage	289	0.126 (0.100–0.150)	0.240 (0.220–0.280)	0.527 (0.407–0.630)
		Sigma		4.06 (3.99–4.15)	4.32 (4.27–4.35)	4.52 (4.47–4.59)

İç Kalite kontrol nedir?

- Analitik döneme ait tekrarlanabilirlik ve doğruluk (?) çalışmaları ile
- sistem problemlerini
- çevre şartlarını
- personel performansını
- değerlendiren **hata tespit** prosedürleridir.

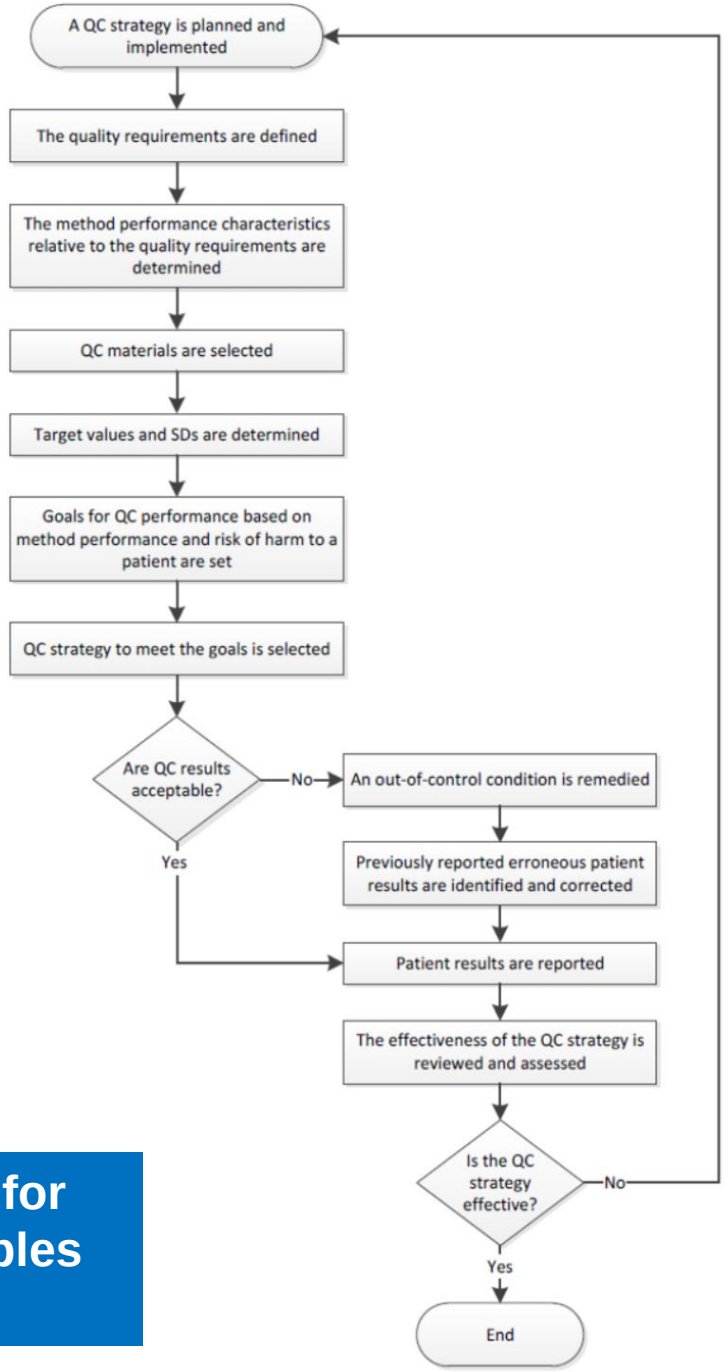
Hizmetin önceden saptanmış özellikleri taşıyıp taşımadığının ve ne ölçüde güvenilir olduğunun incelenmesi için kullanılan yöntemlerdir

Temel Basamakları

1
- Stratejini oluştur (!)
- **Analitik Performan Kriterlerini belirle**

2
- KK materyali seç
- Hedef değer ve CV Hesapla

3
- APK uygun kuralları oluştur
- **Ölç, değerlendir, kaydet ve düzelt**



CLSI C24-ED4:2016 Statistical Quality Control for Quantitative Measurement Procedures: Principles and Definitions, 4th Edition

Analitik Performans Kriterleri (APK)

Stockholm Conference -1999

'***Strategies to set global analytical quality specifications in laboratory medicine***'

Hierarchy of models:

1. Evaluation of the **effect of analytical performance on clinical outcomes** in **specific clinical settings**.

2. Evaluation of the **effect of analytical performance on clinical decisions** in **general**:

a. Data based on components of **biological variation,**

b. Data based on analysis of **clinicians' opinions**.

3. Published **professional recommendations**:

a. From national and **international expert bodies (CLIA**, Rilibak gibi)

b. From expert local groups or individuals.

4. Performance goals set by:

a. Regulatory bodies

b. Organisers of **EQA schemes**.

5. Goals based on the current **state of the art**:

a. As demonstrated by **data from EQA or Proficiency Testing schemes**,

b. As found in current **publications on methodology**.

Fraser CG. The 1999 Stockholm Consensus Conference on quality specifications in laboratory medicine. Clin Chem Lab Med. 2015 May;53(6):837-40

Milan Conference -2014

First EFLM Strategic Conference on 'Defining analytical performance goals 15 years after the Stockholm Conference on Quality Specifications in Laboratory Medicine'

Model 1. Based on the effect of analytical performance on clinical outcomes

- a. an Outcome study investigating the impact of analytical performance on clinical outcomes
- b. a Simulation study investigating the impact of analytical performance on the probability of clinical outcomes
- c. a Survey of clinicians' and/or experts' opinion investigating the impact of analytical performance on medical decisions
- These goals will be most realistic since they are based on actual medical decision-making. However, only a few tests have a direct link to medical decisions, so this model is not universally applicable to all tests.

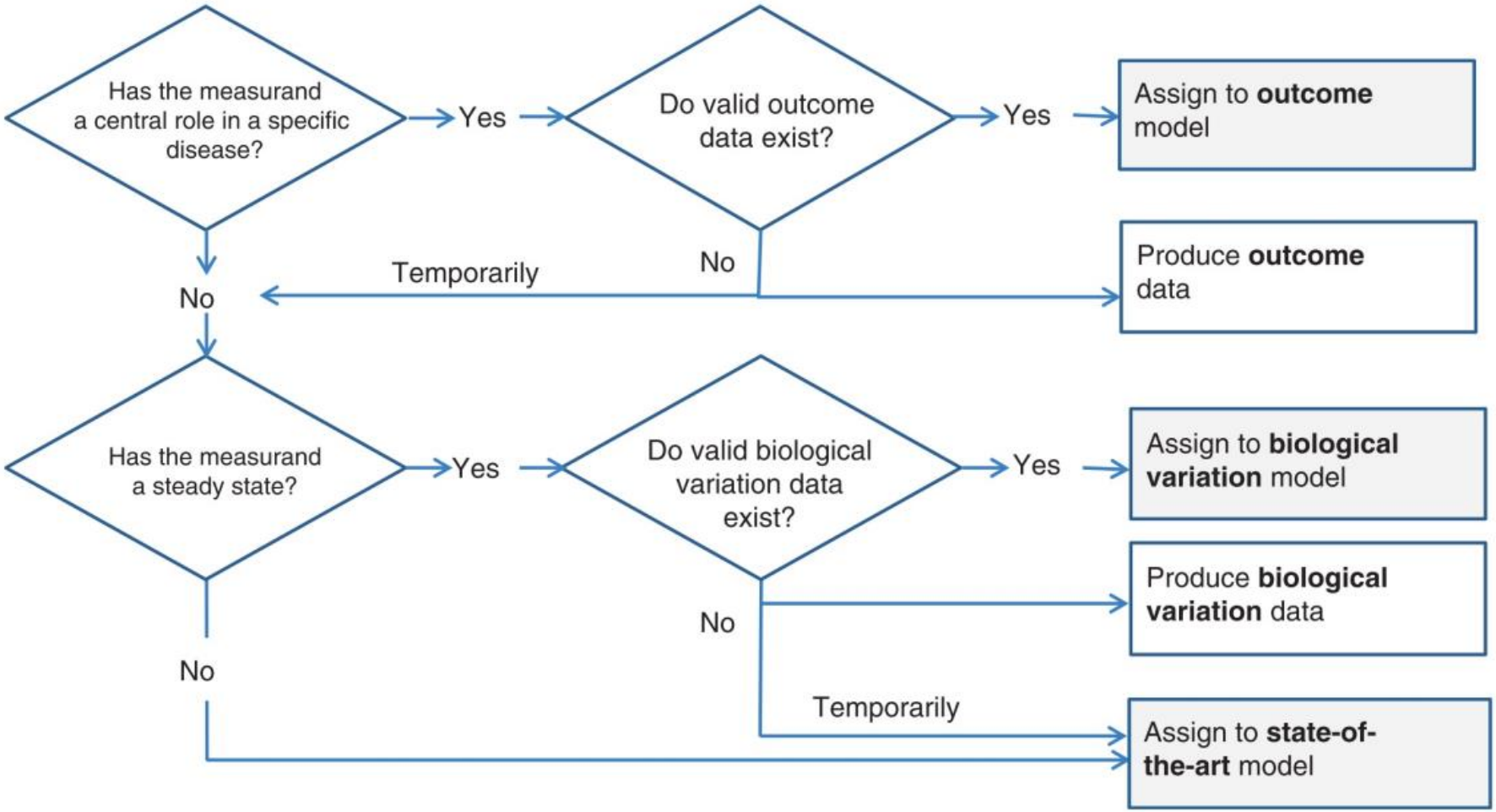
*Model 2. Based on components of biological variation of the measurand ****

- This is familiar territory. The goal here is to make sure the "**analytical noise**" does not drown out the biological signal. This works for tests where the biologic variation is not so small that the analytical specifications for noise are too stringent to be practical. However, in the new DRAFT it was pointed out that there are in fact significant limitations to this approach including the relevance and validity of the biological variation data.

Model 3. Based on state of the art

- This is least desirable model, but it based on the realistic performance "as is" of **the marketplace**. If the best laboratories can only achieve a certain quality, but cannot achieve the quality demanded by models 1 and 2, then the world will have to accept the current performance (for now). While technology is improved and (presumably) manufacturers develop better assays, the laboratory should set its specifications using this third model.

Yaklaşim nasıl olmalı?



Model 1. Based on the effect of analytical performance on clinical outcomes (A)

Table 2. Performance limits and medical utility[a] based on physicians opinions and analytic bias based on population distributions.[b]

		Medical utility, % CV			Population analytic bias limits		
Analyte	Units	Base value	Change value	Medical CV[a]	Decision limit	Bias limit[b]	Bias, CV
Bilirubin	mg/L	8	14	23.4%	11	±1	9.0%
Calcium	mg/L	90	106	7.0%	102	±1	1.0%
Cholesterol	mg/L	2100	2800	12.3%	2000	±23	1.2%
Creatinine	mg/L	10	15	17.2%	8	±1	12.5%
Glucose	mg/L	100	130	11.2%	1000	±20	2.0%
Iron	μg/L	150	100	17.2%	—	—	—
Phosphate	mg/L	350	250	14.3%	25	±1	4.0%
Potassium	mmol/L	3.8	3.4	4.8%	3.6	±0.1	2.8%
Sodium	mmol/L	125	130	1.7%	134	±1.5	1.1%
Thyroxine	μg/L	60	40	17.2%	50	±4	8.0%
Total protein	g/L	70	85	8.3%	63	±2	3.2%
Triglycerides	mg/L	1300	1900	16.1%	4000	±58	1.5%
Hematocrit	%	42	37	5.4%	35	±0.7	2.0%
Hemoglobin	g/L	150	138	3.6%	119	±3	2.5%
Leucocytes	10^9/L	6.0	3.4	16.4%	3.5	±0.2	5.7%
Erythrocyte mean cell volume	fL	95	100	3.2%	81.5	±0.7	1.0%

[a] Medical CV = 100 × [(change value − base value)/(1.645 × √2)]/[(change value + base value)/2)].
[b] Bias limit = 1 SD of change of population cumulative frequency distribution.

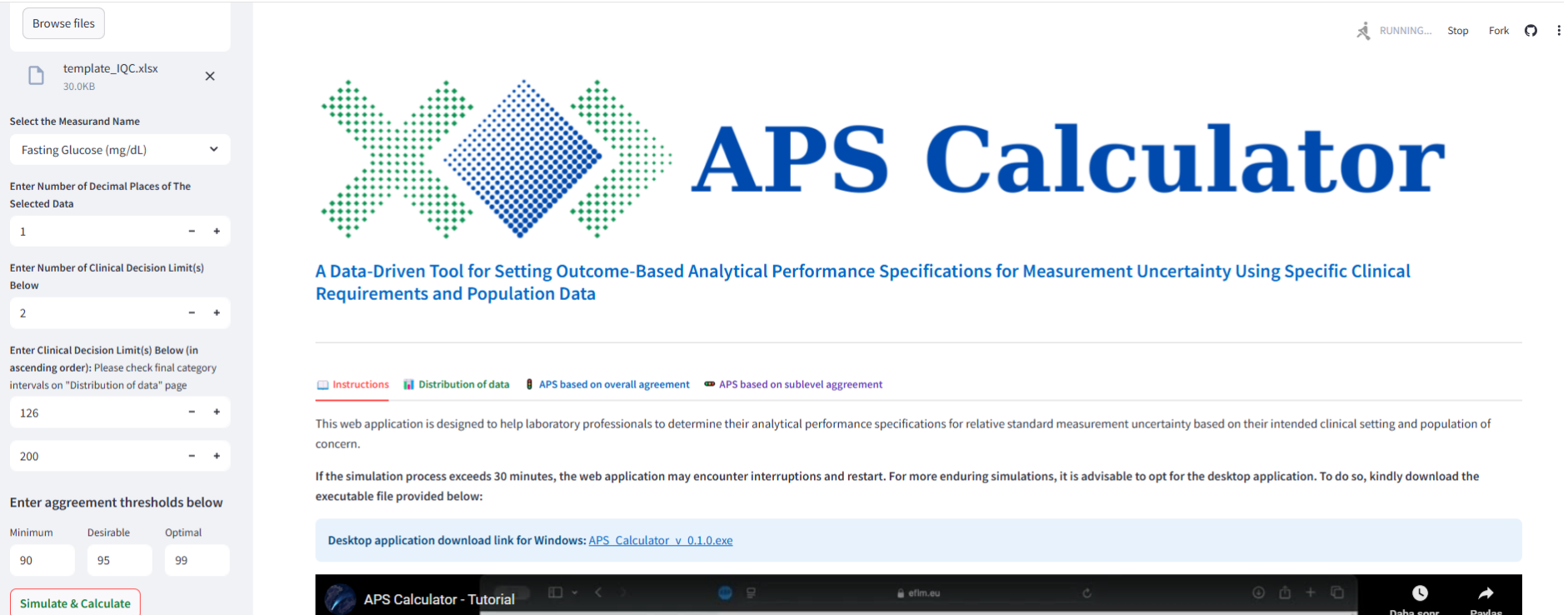
Klee, G. G. (2010). Establishment of outcome-related analytic performance goals. *Clinical chemistry*, *56*(5), 714-722.

DE GRUYTER Clin Chem Lab Med 2024; 62(4): 597–607

Opinion Paper

Hikmet Can Çubukçu*, Florent Vanstapel, Marc Thelen, Marith van Schrojenstein Lantman, Francisco A. Bernabeu-Andreu, Pika Meško Brguljan, Neda Milinkovic, Solveig Linko, Mauro Panteghini and Guilaine Boursier, on behalf of the European Federation of Clinical Chemistry and Laboratory Medicine (EFLM) Working Group Accreditation, ISO/CEN Standards (WG-A/ISO)

APS calculator: a data-driven tool for setting outcome-based analytical performance specifications for measurement uncertainty using specific clinical requirements and population data

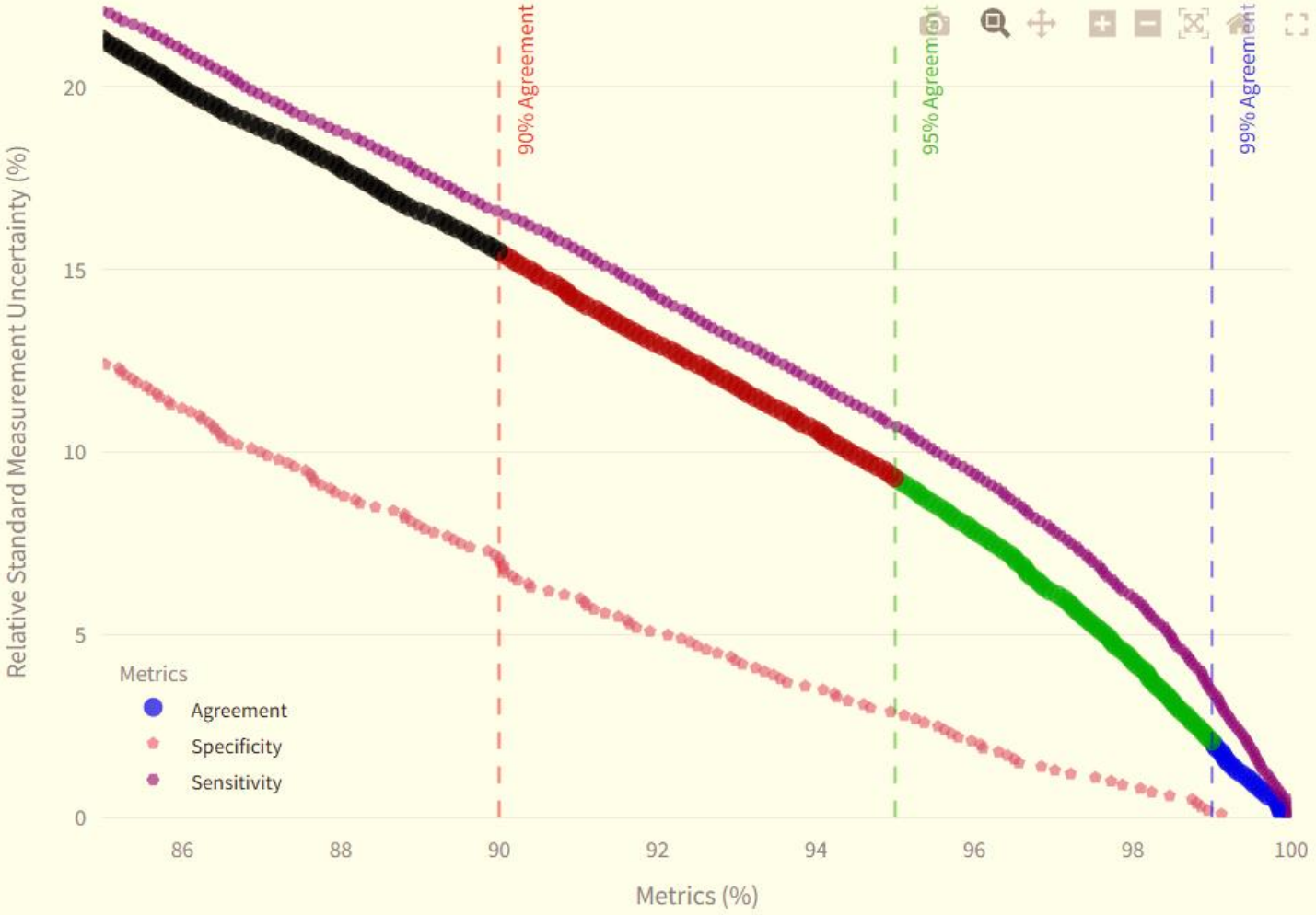


Revise your clinical decision limits if the category intervals are not appropriate

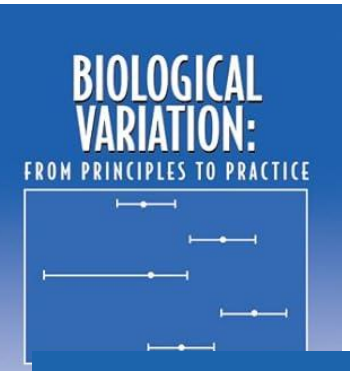
Category Intervals

APS for MU based on sublevel aggreement

APS based on sublevel: <126



APS level	MU
Minimum	15.4
Desirable	9.2
Optimal	2.0



Biyolojik Varyasyon

EFLM
EUROPEAN FEDERATION OF CLINICAL CHEMISTRY AND LABORATORY MEDICINE

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BV Data

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Search Results

Haemoglobin A1c (NGSP)

Haemoglobin A1c

Analytical Performance Specification

Matrix	BV Estimate
Whole Blood	
Whole Blood	

Colour Key for Referenc

Included In Meta Analysis Not Included In Meta A

Analytical Performance Specification Calculation

Haemoglobin A1c (NGSP)

Enter Values

% Within-subject (CVI) estimate: 1.2

% Between-subject (CVG) estimate: 5.4

Results

Specification	CVa	BIAS	MAU	Total Error
Minimum	0.9	2.1	1.8	3.6
Desirable	0.6	1.4	1.2	2.4
Optimal	0.3	0.7	0.6	1.2

There are currently three main models for calculating analytical performance specifications (APS), i.e. based on 1) direct- and indirect outcome studies, 2) biological variation, and 3) state-of-the-art

Biyolojik Varyasyon

Total allowable error (TEa)

$$< 1.65 \times (0.5 \times CVI) + 0.25 \times (CVI^2 + CVG^2)^{1/2}$$

Imprecision= $CVA < 0.5 \times CVI$

Bias = $0.25 \times (CVI^2 + CVG^2)^{1/2}$

Allowable expanded measurement uncertainty (MAU)

$$= k \times 0.5 \times CV_I$$

Fraser CG and Petersen PH, 1993
EFLM BV website

k= 2 veya 3 (95 veya 99 % sırası ile)

DE GRUYTER Clin Chem Lab Med 2024; aop

Opinion Paper

Sverre Sandberg*, Abdurrahman Coskun, Anna Carobene, Pilar Fernandez-Calle, Jorge Diaz-Garzon, William A. Bartlett, Niels Jonker, Kornelia Galior, Elisabet Gonzales-Lao, Isabel Moreno-Parro, Berta Sufrate-Vergara, Craig Webster and Aasne K. Aarsand, on behalf of the European Federation of Clinical Chemistry and Laboratory Medicine Task Group for the Biological Variation Database

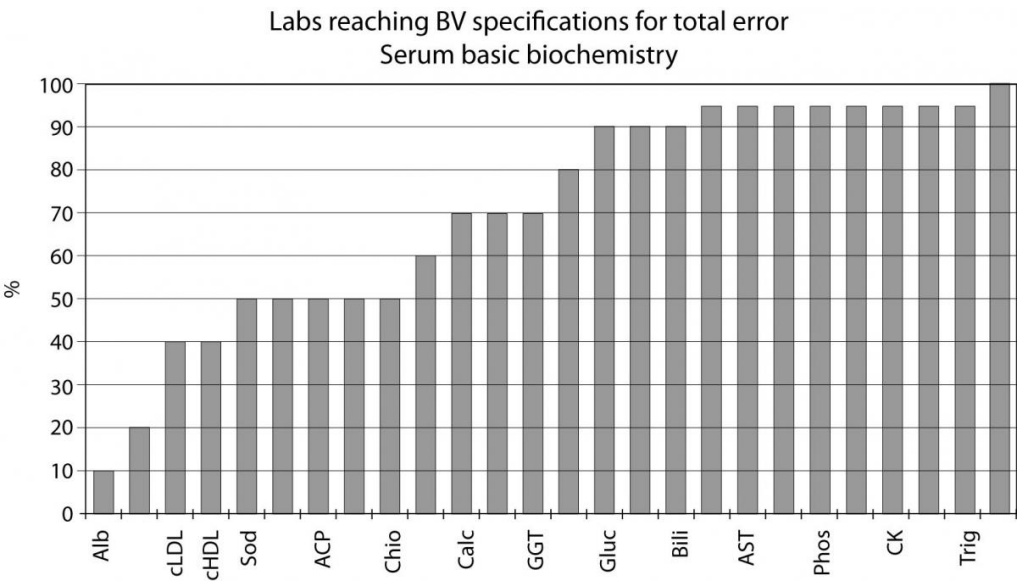
Analytical performance specifications based on biological variation data – considerations, strengths and limitations

Çok mantıklı ama

- **Sonuca göre farklı seçim kriteri belirleniyor?**
- **Bazı analitler için uygunda bazıları için neden uygun değil?**
- **Patolojik durumlar, ilaç kullanımı veya komorbiditesi olanlar dikkate alınmıyor?**
- **Gün içi farklı zamanlarda alınan örnekler için uygun olabilir mi?**
- **Tokluk durumunda durum nasıl değişiyor?**
- **Günlük , aylık, mevsimsel ritmi olan testler için ne yapacağız?**
- **Her cihaz, metot için aynı mı? ***
- **Klinik çıktıları nedir?**

Standardizayon-Harmonizasyon sağlamayabilir, karışık ve uygulaması zor

Analitik yeterlilik



- Figure 1 shows that around 10% of the laboratories participating in the external quality assurance program of the Spanish Society of Clinical Biochemistry and Molecular Pathology (SEQC) attain the specification for total error derived from BV for **albumin, 20% for HDL cholesterol, 50% for sodium and chloride and 70% for calcium**. This fact demonstrates that specifications based on biology are realistic and can be reached for routine laboratories today.

Ricós at al. Biochemia Medica 2009;19(3):250-9

Total Allowable Error Table

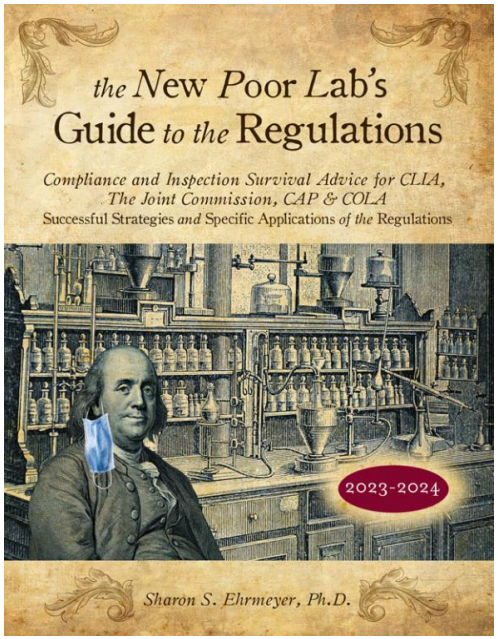
Analyte	Fluid	Method	Target Value	Source
17-Hydroxyprogesterone	Serum		5 RCPA	±2.0 nmol/L or 20% if > 10.0 nmol/L
3-Methoxytyramine (3MT)	Urine		5 RCPA	±15 nmol/L or ±15% if > 100 nmol/L
4-hydroxy-3-methoxy-mandelate, (HMMA)	Urine		5 RCPA	±6 ?mol/L or 15% if > 40 ?mol/L
5HIAA	Urine		5 RCPA	±8 ?mol/L or 20% if > 40 ?mol/L
a1-Antitrypsin (?1AT)	Serum		5 RCPA, 6 API	±0.10 g/L or 20% if > 0.5 g/L
Acetaminophen (Paracetamol)	Serum		1 CLIA, 2 WSLH, 3 CAP, 6 API	±15% or 3 µg/mL (greater)

Sources

Abbreviation	Source
1 CLIA	CLIA – Federal Register
2 WLSH	Wisconsin State Laboratory of Hygiene
3 CAP	College of American Pathologists
4 AAB	American Association of Bioanalysts
5 RCPA	The Royal College of Pathologists of Australasia and the Australasian Program
6 API	American Proficiency Institute

CLIA Acceptance Limits for Proficiency Testing

Routine Chemistry CLIA 2025		
Analyte or Test	**NEW Criteria for AP**	**OLD AP**
Alanine aminotransferase (ALT/SGPT)	**TV ± 15% or ± 6 U/L (greater)**	TV ± 20%
Albumin	TV ± 8%	TV ± 10%
Alkaline Phosphatase	TV ± 20%	TV ± 30%
Amylase	TV ± 20%	TV ± 30%
AST	**TV ± 15% or ± 6 U/L (greater)**	TV ± 20%
Bilirubin, total	**TV ± 20% or 0.4 mg/dL (greater)**	Same
Blood gas pCO2	TV ± 5 mm Hg or ± 8% (greater)	Same
Blood gas pO2	TV ± 15 mm Hg or ± 15% (greater)	TV ± 3SD
Blood gas pH	TV ± 0.04	Same
B-natriuretic peptide (BNP)	TV ± 30%	None
Pro B-natriuetic peptide (proBNP)	TV ± 30%	None
Calcium, total	TV ± 1.0 mg/dL	Same



Clinical Laboratory Improvement Advisory Committee (CLIAC)

Nisan 2024 Toplantısı (10 Nisan 2024)

- **CLIA Ücretleri ve Laboratuvar Personeli Düzenlemeleri**: CLIA 1988 düzenlemeleri kapsamında ücretler, histokompatibilite, personel gereksinimleri ve "Certificate of Waiver" laboratuvarları için alternatif yaptırımlar ele alındı.
- **Personel Gereksinimlerinin Preanalitik Testlere Uygulanabilirliği:** CLIA personel gereksinimlerinin, örnek toplama ve taşıma gibi preanalitik süreçlere nasıl uygulanacağı tartışıldı.
- **Yapay Zeka ve Makine Öğreniminin Laboratuvarlardaki Rolü:** Yapay zeka ve makine öğreniminin laboratuvar süreçlerine entegrasyonu ve potansiyel faydaları değerlendirildi.

Kasım 2024 Toplantısı (6-7 Kasım 2024)

- **Biyogüvenlik Çalışma Grubu Raporu:** Laboratuvar güvenliği ve biyogüvenlik önlemleri üzerine yapılan çalışmalar sunuldu.
- **Siber Güvenlik Gereksinimleri:** Laboratuvarlarda siber güvenlik önlemleri ve dijital altyapı güvenliği tartışıldı.
- **Proficiency Testing ve Klinik Olarak İlgili Değer Aralıkları:** Testlerin doğruluğunu değerlendirmek olarak anlamlı değer aralıklarının belirlenmesi ele alındı.
- **Uzaktan Teknoloji ile Yeterlilik Değerlendirmeleri:** Laboratuvar personelinin uzaktan eğitim ve değerlendirme yöntemleri incelendi.

Jordan Laser, MD

Total kabul edilebilir hata – Laboratuvar uygulamaları

- Laboratuvarlar arası CV < 1/3 TE

  Bias küçük olmak zorundadır

  3 Sigma

  RE=3 x SD < Total Hata (Ehrmeyer, Laessing at al Clin Chem 36, 1736-40, 1990)

- Laboratuvar içi CV arası < 1/4 TE

  4 Sigma

  RE=4 x SD < Total Hata (Westgard and Burnett, Clin Chem 36, 1629-32, 1990)

RiLiBÄK Kuralları

Richtlinien der Bundesärztekammer zur Qualitätssicherung laboratoriumsmedizinischer Untersuchungen", "Federal Alman Tabipler Birliği'nin laboratuvar tıbbi testlerinin kalite güvencesine dair yönergeleri

	Analyte	Acceptable % RMSD	Validity range			Acceptable relative deviation in interlab tests	Type of target value in interlab tests
			lower limit	upper limit	units		
1	1,25-OHs-vitamin D	25.0%	10	160	ng/L	--	--
2	25-OH-vitamin D	25.0%	5	120	ug/L	--	--
3	ACE	23.0%	10	200	U/L	--	--
4	Activated partial thromboplastin time (aPTT)	10.5%	20	120	s	18.0%	NV
5	Alanine aminotransferase (ALT)	11.5%	30	300	U/L	21.0%	RMV
			0.5	5.0	ukat/L		
6	Albumin	12.5%	20	70	g/L	21.0%	NV
7	Aldosterone (only in plasma)	25.0%	5	1,000	pg/mL	--	--
8	Alkaline phoshatase (AP)	11.0%	20	600	U/L		
			0.33				
9	alpha-Amylase	7.0%	20				
			0.33				
10	alpha-Fetoprotein(AFP)	17.0%	5				
11	ApoA1	10.0%	50				
12	ApoB	10.0%	40				
13	Aspartate aminotransferase (AST)	11.5%	20				
			0.33				
	n (total)	13.0%	>2				
			>34				
		22.0%	0.1				
			1.7				

$$\%RMSD = \frac{\sqrt{k^2(SD_{cc}{}^2) + Bias^2}}{TV}$$

SD_{cc} = standard deviation
Bias = difference of observed mean from Target Value (TV)
k = statistical "coverage factor" to account for uncertainty (1 for metric, 3 to calculate specification)
TV = Target Value for the control sample (from manufacturer)

May 30th, 2023

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)

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

Analytical performance specifications for external quality assessment – definitions and descriptions

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

RCPAQAP
The Royal College of Pathologists of Australasia
Quality Assurance Programs

Oldukça karışık

General Serum Chemsitry / Condensed Serum Chemistry

Analyte	Lower Limit	Upper Limit	Basis	Level
Albumin	+ or - 2.0 ≤ 33.0 g/L	+ or - 6% > 33.0 g/L	Total Error	Desirable
Alkaline Phosphatase	+ or - 15 ≤ 125 U/L	+ or - 12% > 125 U/L	Total Error	Desirable
ALT	+ or - 5 ≤ 40 U/L	+ or - 12% > 40 U/L	Imprecision	Optimal
Amylase	+ or - 10 ≤ 100 U/L	+ or - 10% > 100 U/L	Imprecision	Desirable
AST	+ or - 5 ≤ 40 U/L	+ or - 12% > 40 U/L	Imprecision	Desirable
Bicarbonate	+ or - 2.0 ≤ 20.0 mmol/L	+ or - 10% > 20.0 mmol/L	Total Error	Minimal
Bilirubin-Total	+ or - 3 ≤ 25 µmol/L	+ or - 12% > 25 µmol/L	Imprecision	Optimal
Bilirubin Conjugated	+ or - 3 ≤ 15 µmol/L	+ or - 20% > 15 µmol/L	Imprecision	Optimal
Calcium	+ or - 0.10 ≤ 2.50 mmol/L	+ or - 4% > 2.50 mmol/L	Imprecision	Minimal
Chloride	+ or - 3 ≤ 100 mmol/L	+ or - 3% > 100 mmol/L	Total Error	minimal
Cholesterol	+ or - 0.30 ≤ 5.00 mmol/L	+ or - 6% > 5.00 mmol/L	Imprecision	Desirable
Cholinesterase	+ or - 500 ≤ 5000 U/L	+ or - 10% > 5000 U/L	Prof. Opinion	
Creatine Kinase	+ or - 15 ≤ 125 U/L	+ or - 12% > 125 U/L	Imprecision	Optimal
CK-MB	+ or - 3 ≤ 15 U/L or µg/L	+ or - 20% > 15 U/L or µg/L	Imprecision	Desirable
Cortisol	+ or - 15 ≤ 100 nmol/L	+ or - 15% > 100 nmol/L	Prof. Opinion	

TECHNICAL SPECIFICATION **ISO/TS 20914**

First edition 2019-07

Medical laboratories — Practical guidance for the estimation of measurement uncertainty

Laboratoires médicaux — Lignes directrices pratiques pour l'estimation de l'incertitude de mesure

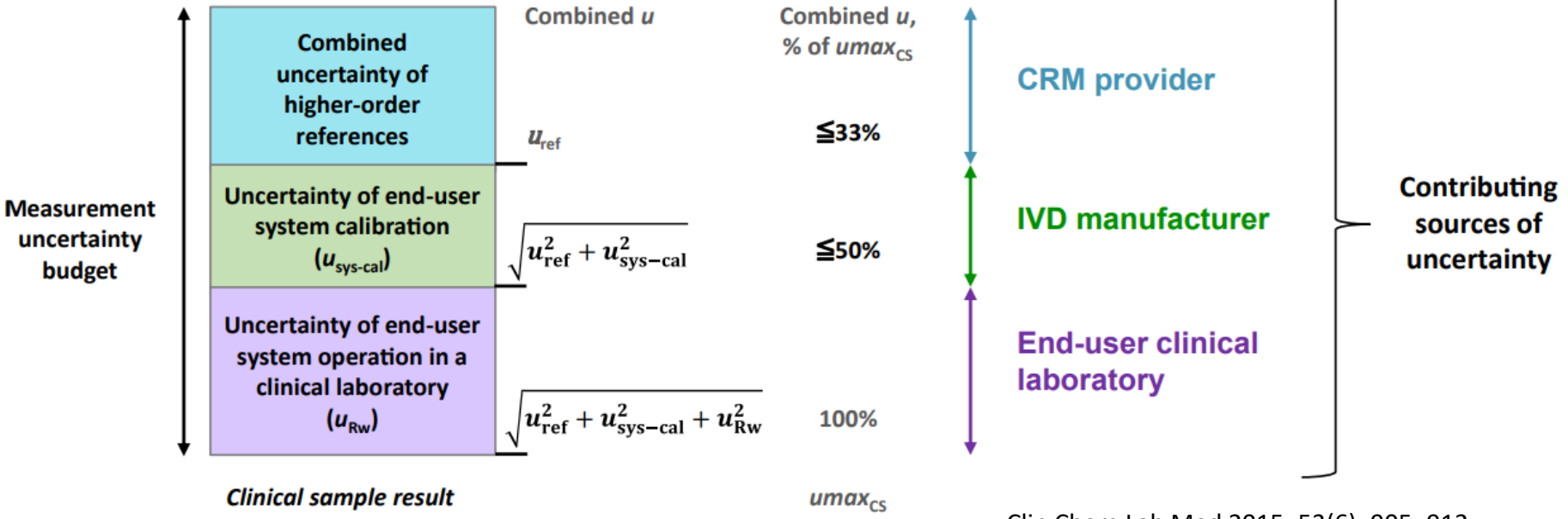
Belirsizlik

CLINICAL AND LABORATORY STANDARDS INSTITUTE

January 2012

EP29-A

Expression of Measurement Uncertainty in Laboratory Medicine; Approved Guideline



Clin Chem Lab Med 2015; 53(6): 905–912
Clin Chem Lab Med 2020; 58(9): 1407–1413
Clin Chem Lab Med 2024; 62(8): 1462–1469

Belirsilikte Bias?

TECHNICAL SPECIFICATION **ISO/TS 20914**

First edition
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Medical laboratories — Practical guidance for the estimation of measurement uncertainty

Laboratoires médicaux — Lignes directrices pratiques pour l'estimation de l'incertitude de mesure

Figure 3 — Overview — Typical pathway for estimating measurement uncertainty

Kreatinin için izlenebilirlik

Table 3: Metrological traceability and uncertainty information derived from calibrator package inserts of commercial systems measuring serum creatinine marketed by four in vitro diagnostics companies.

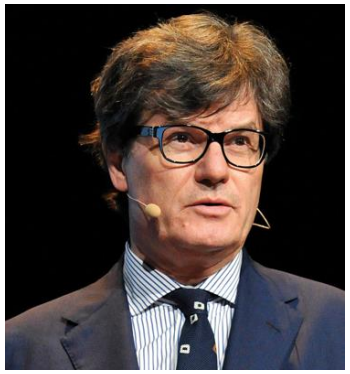
Company	Platform	Principle of commercial method	Calibrator	Declared standard uncertainty[a]	Higher order reference employed		Type of traceability chain used[b]	Combined standard uncertainty associated with the used chain[c]
					Method	Material		
Abbott	Architect	Enzymatic	Multigent clin chem calibrator	1.48%	IDMS	NIST SRM 967	A	2.12%–2.79%[d]
		ND	Multiconstituent calibrator	2.7%	IDMS	NIST SRM 967	A	2.12%–2.79%[d]
Beckman	AU	Enzymatic	System calibrator	ND	ND	NIST SRM 967	A	2.12%–2.79%[d]
		Alkaline picrate	System calibrator	ND	IDMS	NIST SRM 967	A	2.12%–2.79%[d]
		Uncompensated alkaline picrate	System calibrator	ND	ND	NIST SRM 909b L2	B	1.51%
	Synchron	ND	LX aqua calibrator	ND	IDMS	NIST SRM 914a	D	1.5%[e]
Roche	Cobas c	Enzymatic	C.f.a.s.	0.91%	IDMS	ND	D	1.5%[e]
		Alkaline picrate compensated	C.f.a.s.	1.62%	IDMS	ND	D	1.5%[e]
		Alkaline picrate rate–blanked and compensated	C.f.a.s.	1.42%	IDMS	ND	D	1.5%[e]
	Integra/Cobas c111	Enzymatic	C.f.a.s	1.06%	IDMS	ND	D	1.5%[e]
	Integra400/Cobas c111	Alkaline picrate compensated	C.f.a.s	0.30%	IDMS	ND	D	1.5%[e]
	Integra800	Alkaline picrate compensated	C.f.a.s	0.72%	IDMS	ND	D	1.5%[e]
	Modular	Enzymatic	C.f.a.s	0.91%	IDMS	ND	D	1.5%[e]
		Alkaline picrate compensated	C.f.a.s	1.38%	IDMS	ND	D	1.5%[e]
		Alkaline picrate rate-blanked and compensated	C.f.a.s	0.79%	IDMS	ND	D	1.5%[e]
Siemens	Dimension Vista	Enzymatic	ECREA calibrator A	5.08%[f]	ND	NIST SRM 914a	C	NA
			ECREA calibrator B	3.16%[f]	ND	NIST SRM 914a	C	NA
		Alkaline picrate	Chemistry calibrator	1.6%	GC-IDMS	NIST SRM 914a	D	1.5%[e]
	Advia	Enzymatic	Chemistry calibrator	0.45%	IDMS	NIST SRM 914a NIST SRM 967	A	2.12%–2.79%[d]
		Alkaline picrate rate-blanked and compensated	Chemistry calibrator	1.6%	IDMS	NIST SRM 967	A	2.12%–2.79%[d]

Clin Chem Lab Med 2015; 53(6): 905–912

Analytical performance specifications for combined uncertainty budget in the implementation of metrological traceability

Table 1: Model allocation according to the EFLM Strategic Conference consensus and proposed analytical performance specifications (APS) for standard measurement uncertainty of higher-order references (u_{ref}), *in vitro* diagnostic manufacturers' calibrators (u_{cal}), and on clinical samples (u_{result}) for measurands evaluated in the APERTURE project.

Measurand	u_{result} APS, %		u_{cal} APS, %[a]		u_{ref} APS, %[b]	
	Desirable	Minimum	Desirable	Minimum	Desirable	Minimum
Outcome-based model						
Fasting plasma glucose	2.00	3.00	1.00	1.50	0.67	1.00
Blood HbA_{1c}	3.00	3.70	1.50	1.85	1.00	1.23
Blood total hemoglobin	5.60	8.50	2.80	4.25	1.87	2.83
Serum total cholesterol	3.00	7.00	1.50	3.50	1.00	2.33
Serum HDL cholesterol	2.90	5.60	1.45	2.80	0.97	1.87
Serum triglycerides	6.10	12.4	3.05	6.20	2.03	4.13
Serum cardiac troponin	9.40	13.0	4.70	6.50	3.13	4.33
Urine albumin	9.00	17.0	4.50	8.50	3.00	5.67
Serum total folate	8.00	12.0	4.00	6.00	2.67	4.00
Serum 25-hydroxyvitamin D_3	10.0	15.0	5.00	7.50	3.33	5.00
Serum transferrin saturation	10.0	15.0	5.00	7.50	3.33	5.00
Temporarily belonging to biological variation model[c]						
Serum albumin	1.25	1.88	0.63	0.94	0.42	0.63
Plasma D-dimer	10.6	15.9	5.30	7.95	3.53	5.30
Blood platelets	4.85	7.28	2.43	3.64	1.62	2.43
Serum alanine aminotransferase	4.65	6.98	2.33	3.49	1.55	2.33
Serum creatine kinase	7.25	10.9	3.63	5.45	2.42	3.63
Serum pancreatic lipase	3.85	5.78	1.93	2.89	1.28	1.93
Serum pancreatic amylase	3.15	4.73	1.58	2.37	1.05	1.58
Biological variation model						
Serum sodium	0.27	0.40	0.14	0.20	0.09	0.13
Serum potassium	1.96	2.94	0.98	1.47	0.65	0.98
Serum chloride	0.49	0.74	0.25	0.37	0.16	0.25
Serum total carbon dioxide	2.10	3.15	1.05	1.58	0.70	1.05
Serum total calcium	0.91	1.36	0.46	0.68	0.30	0.45
Serum inorganic phosphate	3.84	5.75	1.92	2.88	1.28	1.92
Serum magnesium	1.44	2.16	0.72	1.08	0.48	0.72
Serum creatinine	2.20	3.30	1.10	1.65	0.73	1.10



Clin Chem Lab Med 2024; 62(8): 1497–1504

Opinion Paper

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

Son gelinen noktada

Karışık
Zor
Cihaz bağlmlı değişkenlik

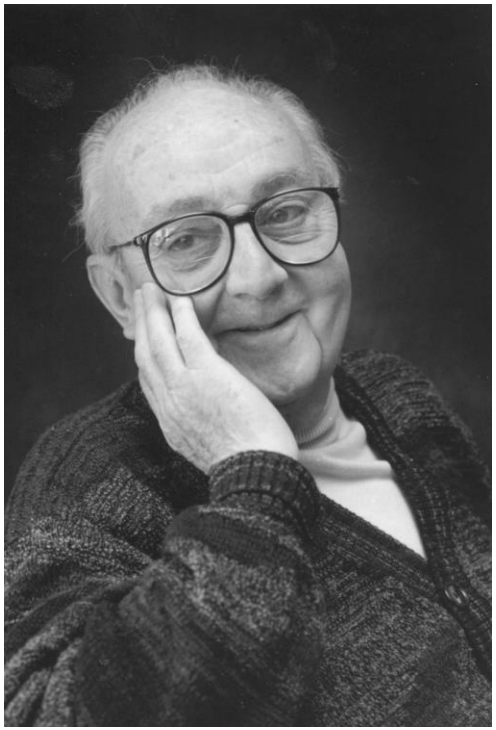
Table 1: Proposal for assignment of some commonly requested laboratory measurands to the three models for analytical performance specifications (APS) as defined in the Milan Consensus.[a]

APS model 1: outcome-based	APS model 2: biological variation	APS model 3: state-of-the-art
P-Cholesterol+ester	P-Sodium ion	U-Sodium ion
P-Cholesterol+ester in LDL	P-Potassium ion	U-Potassium ion
P-Cholesterol+ester in HDL	P-Chloride	U-Chloride
P-Triglycerides	P-Bicarbonate	U-Calcium ion
P-Glucose	P-Calcium ion	U-Magnesium ion
B-Hemoglobin A_{1c}	P-Magnesium ion	U-Phosphate (inorganic)
P-Albumin	P-Phosphate (inorganic)	U-Creatinine
P-Troponin T and P-troponin I	P-Creatinine	U-Urate
P-Thyrotropin	P-Cystatin C	
B-Hemoglobin	P-Urate	
B-Platelets	P-Proteins	
B-Neutrophil leukocytes	B-Erythrocytes	
	B-Erythrocyte volume fraction	
	B-Erythrocyte volume	
	P-Prothrombin time	
	P-activated partial thromboplastin time	

[a]Some of the measurands can also have APS from other models depending on their clinical use. P and B denotes the system blood plasma or whole blood, respectively. Measurements might be performed in different types of sample matrices, such as serum, heparin plasma, citrate plasma, etc., as appropriate for the method.

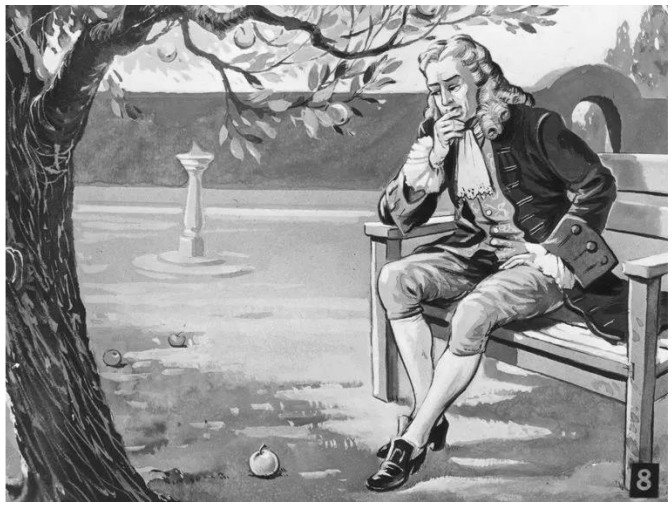
Kalite gereksinimleri neden farklıdır ?
Benim için çok karışık

Analyte	Fluid	Method	Target Value	Source
Hematocrit	WB		1 CLIA, 2 WSLH, 6 API	±4%
Hematocrit	WB		4 AAB	±6 mg/dL or 20% (greater)
Hematocrit	WB		5 RCPA	±4%
Hemoglobin	WB		1 CLIA, 2 WSLH, 6 API	±4%
Hemoglobin	WB		4 AAB	±7%
Hemoglobin	WB		5 RCPA	±5 g/L or 5% if > 100 g/L
Hemoglobin A1c (Glycohemoglobin)	WB		1 CLIA, 2 WSLH, 6 API	±8%
Hemoglobin A1c (Glycohemoglobin)	WB		4 AAB	±5%
Hemoglobin A1c (Glycohemoglobin)	WB	IFCC	5 RCPA	±4 mmol/mol or 8% if > 45 mmol/mol
Hemoglobin A1c (Glycohemoglobin)	WB	NGSP	5 RCPA	±0.4% or 6% if > 6.7%



‘All models are wrong but some are useful.’

George E.P. Box



Analitik Standardizasyon ve Harmonizasyon Komitesi

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Prof. Dr. Özkan Alataş
Prof.Dr. Diler Aslan
Dr. Ferzane Mercan

54 laboratuvardan IKK verileri alındı
24'ü değerlendirilmeye alınabildi !

- 4x
- 7x
- 8xx
- 15x
- 16xxxx
- 18xx
- 19xxx
- 20xxxx
- 21x
- 22xxxxx
- 23xxx
- 24x
- 26xxxx
- 27xxxx
- 29xx
- 30x
- 31x
- 32xxx
- 33xxxx
- 34xxxx
- 35xxxx
- 38xx
- 39x
- 41xxx------
- 45xxxx
- 46xxx
- 47x
- 52xxxxx
- 54xxxxx
- Toplu bias
- Toplu EQC bias

		Bias					CV					Total hata	
Analit		total	1	2	3	4	Total	1	2	3	4	TH MEDIAN	TH MEAN
Glikoz	Düzey 1	-2.7	-8.4	-0.9	-1.9	0.7	4.6	3.8	2.8	2.7	1.8	5.9	7.2
mg/dL	Düzey 2	-1.0	-5.9	0.2	-0.1	2.3	4.1	3.0	1.8	1.9	3.4	4.1	5.1
Üre	Düzey 1	2.8	0.9	2.2	2.4	5.7	4.0	4.2	3.4	4.0	3.1	8.4	8.8
mg/dL	Düzey2	-5.0	-6.4	-4.9	-5.2	-3.8	3.2	3.4	3.1	3.2	2.8	10.3	10.2
Kreatinin	Düzey 1	-6.1	-6.2	-5.8	-5.0	-7.9	7.8	9.6	7.2	6.0	8.2	18.7	19.0
mg/dL	Düzey2	6.0	5.4	6.0	7.3	5.3	6.3	8.3	6.0	5.1	5.1	14.8	16.1
Total Protein	Düzey 1	-1.3	0.1	-1.4	-0.4	-3.6	4.9	5.1	4.3	5.1	4.6	8.8	9.2
g/dL	Düzey2	-2.1	-0.9	-2.4	-1.0	-3.9	5.5	6.1	4.8	5.0	5.5	10.4	10.9
Albümin	Düzey 1	4.3	5.2	10.0	-2.7	5.3	5.7	2.1	4.0	5.4	2.3	10.5	10.1
g/dL	Düzey2	1.6	1.8	6.3	-4.6	3.4	5.6	2.6	4.3	5.5	2.8	8.4	8.0
Kolesterol	Düzey 1	0.9	1.8	3.6	-0.5	-1.2	2.9	1.5	2.0	3.7	1.1	3.5	4.3
mg/dL	Düzey2	-17.9	-17.9	-15.6	-19.0	-19.1	2.9	1.2	2.1	3.9	1.7	21.6	21.6
Trigliserit	Düzey 1	-0.6	-2.4	0.1	-2.1	2.2	3.5	2.5	4.2	2.8	2.3	5.4	5.4
mg/dL	Düzey2	1.0	-3.6	0.6	2.6	5.0	7.1	9.1	7.1	5.2	3.3	11.8	11.4
HDL-Kolesterol	Düzey 1	-12.8	-14.3	-12.2	-11.9	-12.5	3.2	2.4	3.8	3.3	2.5	17.1	17.7
mg/dL	Düzey2	1.3	-1.3	5.4	2.0	-0.7	3.8	4.6	2.1	2.2	1.7	4.1	5.7
AST	Düzey 1	-2.1	-5.0	-0.7	-3.3	0.6	4.1	2.8	3.2	4.2	3.2	7.3	7.7
U/L	Düzey2	2.7	2.3	3.1	1.7	3.8	2.6	2.2	2.2	2.2	3.4	6.4	6.9
ALT	Düzey 1	1.5	0.6	3.3	2.9	-0.5	5.5	4.2	4.3	5.6	6.7	10.0	10.2
U/L	Düzey2	-4.8	-4.8	-5.1	-5.0	-4.1	3.3	2.3	2.7	2.7	5.0	9.4	10.0
ALP	Düzey 1	0.5	3.1	-0.1	-1.4	0.8	7.9	6.3	7.7	9.0	8.3	13.5	13.5
U/L	Düzey2	-2.0	-4.0	-4.4	0.7	-0.8	6.9	6.8	6.5	6.7	6.2	13.3	13.0
Sodyum	Düzey 1	-2.3	-2.1	-2.0	-2.5	-2.5	1.5	0.9	1.4	2.3	1.2	4.5	4.7
mmol/L	Düzey2	-2.4	-2.4	-2.2	-2.3	-2.7	1.8	1.3	1.6	2.6	1.5	5.0	5.3
Potasyum	Düzey 1	-1.0	-1.3	-0.7	-1.0	-0.8	2.7	2.5	2.2	3.4	2.6	5.1	5.3
mmol/L	Düzey2	0.9	0.5	1.6	1.1	0.4	2.7	2.6	2.4	2.9	2.9	5.3	5.3
Klorür	Düzey 1	-0.5	0.8	-0.2	-1.4	-1.4	3.0	1.6	2.4	3.5	3.4	5.6	5.0
mmol/L	Düzey2	-1.0	-0.9	-1.6	-1.1	-0.5	3.0	1.7	3.3	3.5	3.1	6.3	5.8
HbA1c	Düzey 1	-0.3	1.9	2.8	-1.8	-4.3	3.8	2.4	3.4	2.7	2.1	4.2	4.7
%	Düzey2	0.3	0.1	3.0	-0.6	-1.0	2.7	2.2	2.6	2.2	1.7	3.9	4.0
LDH	Düzey 1												
U/L	Düzey2												

Örnek 1

Kurum Adı:
Tıbbi Biyokimya Sorumlu Uzmanı Ad-Soyad:

Analit		4/1/2014	4/2/2014	4/3/2014	4/4/2014	4/7/2014	4/8/2014	4/9/2014	4/10/2014	4/11/2014	4/14/2014	İç Kalite Kontrol Hedef Değer	İç Kalite Kontrol Minimum-Maksimum
Glikoz	Düzey 1	102	100	104	98	99	101	102	102	97	100	98.2	90,2-106,2
mg/dL	Düzey 2	*	*	*	*	*	*	*	*	*	*	*	*
Üre	Düzey 1	40	44	36	43	35	38	38	36	38	37	38.4	33,9-42,9
mg/dL	Düzey2	*	*	*	*	*	*	*	*	*	*	*	*
Kreatinin	Düzey 1	1.4	1.4	1.3	1.11	1.3	1.2	1.4	1.4	1.3	1.3	1.45	1,11-1,79
mg/dL	Düzey2	*	*	*	*	*	*	*	*	*	*	*	*
Total Protein	Düzey 1	5.26	5.47	5.46	4.92	5.86	5.53	5.21	5.24	5.14	5.17	5.38	4,85-5,91
g/dL	Düzey2	*	*	*	*	*	*	*	*	*	*	*	*
Albümin	Düzey 1	3.6	3.7	3.6	3.5	3.6	3.5	3.7	3.6	3.6	3.8	3.93	3,43-4,43
g/dL	Düzey2	*	*	*	*	*	*	*	*	*	*	*	*
Kolesterol	Düzey 1	153	147	151	149	144	144	145	147	146	152	149	135-163
mg/dL	Düzey2	*	*	*	*	*	*	*	*	*	*	*	*
Trigliserit	Düzey 1	91	90	91	86	86	84	87	87	87	90	86.9	77,9-95,9
mg/dL	Düzey2	*	*	*	*	*	*	*	*	*	*	*	*
HDL-Kolesterol	Düzey 1	43	45	46	48	43	44	42	44	40	44	43.7	38,2-49,2
mg/dL	Düzey2	*	*	*	*	*	*	*	*	*	*	*	*
AST	Düzey 1	42	43	42	49	47	43	51	47	41	46	46.4	39,9-52,9
U/L	Düzey2	*	*	*	*	*	*	*	*	*	*	*	*

Tek düzey

Her zaman Firmanın önerisi olan aralık kullanımı

Örnek 2

Analit	7/8/2014	7/9/2014	7/10/2014	7/11/2014	7/14/2014	7/15/2014	7/16/2014	7/18/2014	7/21/2014	7/22/2014	7/23/2014	7/24/2014	7/25/2014	7/31/2014	İç Kalite Kontrol	
															Hedef Değer	Minimum-Maksimum
Glikoz	76	76	75		76	74		76		76	75		75	75	73.6	66,1-81,1
mg/dL	281			276			277		287	277		276			283.5	266-301
BUN	19		20	19	19			20		19		20	19	19	20	18,5-21,5
mg/dL		51	52				52		51	51	53		53		53.1	50,1-56,1
Kreatinin	1		1				1	1.1		1		1			1.07	0,95-1,19
mg/dL		5.4		5.4		5.7		5.7		5.2		5.7		5.5	5.59	5,19-5,99
Total Protein	3.8		3.8		3.7		3.6		3.8	3.8			3.8	3.8	3.71	3,21-4,21
g/dL	6.9	6.9		6.9		7		7		6.9	6.9	7			6.89	6,39-7,39
Albümin	2.2		2.2		2.3		2.2		2.3	2.1			2.3	2.2	2.25	1,95-2,55
g/dL	4.3			4.3	4.4		4.3		4.4	4.3	4.4				4.49	3,99-4,99
Kolesterol	137		136		137		136	137		136	137		136		136	123-149
mg/dL		229		223				229	226	223		229			227.8	211,8-243,8
Trigliserit	112		114	116		115			112	116		115		112	121	104-138
mg/dL	242		245	238		248			244	248		247		245	262.5	235,5-289,5
HDL-Kolesterol	47		48	48		47			47	48		48		47	48.3	43,6-53

Bazı günler düzey 1
Bazı günler düzey 2
3 düzeyin değişen 2 düzey seçimi

Analitik standardizasyon ve harmonizasyon komitesi ön çalışma sonuçları

						1. çalışm		2. çalışma	Öneri								Biolojik varyasyon		
	N	75.0	90.0	95.0	97.5	99	95.0	95.0	Türkiye		Spain 1	Spain 2	USA	Germany	Australasia	Switzerland	TE	CVa	Ba
Albumin (Alb)	3736	5	8	10	12	14	11	10	15	Switzerland	13	14	10	20	6	15	3.9	1.6	1.3
Alanin aminotransferase (ALT)	3966	7	13	18	25	36	17	18	20	CLIA	20	23	20	23	12	18	32.1	12.2	2
Alkaline phosphatase (ALP)	3637	10	18	26	34	40	27	26	30	CLIA	28	31	30	21	12	21	11.7	3.2	6.4
Aspartate aminotransferase (AST)	3941	6	11	16	22	30	15	16	20	CLIA	19	21	20	21	12	21	15.2	6	5.4
Chloride (Cl)	3541	3	6	8	10	12	8	8	9	Switzerland	8	9	5	8	3	9	1.5	0.6	0.5
Cholesterol(Cho)	3664	4	8	11	14	19	9	11	11	CLIA	10	11	10	13	6	10	9	3	4.1
Creatinine (Cre)	3883	7	14	19	23	28	20	19	20	Spain	28	20	15	20	8	20	6.9	2.2	3.4
Glucose (Glu)	3899	5	8	11	15	20	13	11	11	spain	10	11	10	15	8	10	7.9	3.3	2.3
HDL cholesterol (HDLC)	3529	10	18	24	29	33	26	24	30	CLIA	34	33	30	No	12	30	11.1	3.6	5.2
Lactate dehydrogenase (LDH)	3563	7	14	21	29	35	22	21	21	Switzerland	25	26	20	18	8	21	11.4	4.3	4.3
Potassium (P)	3624	4	6	9	11	15	8	9	9	Switzerland	7	8	NC	8	5	9	5.8	2.4	1.8
Protein (Prot)	3474	4	7	9	11	13	9	9	10	CLIA	10	12	10	10	5	12	3.4	1.4	1.2
Sodium (Sod)	3588	2	4	6	7	9	5	6	6	Switzerland	5	5	N C	5	2	6	0.9	0.4	0.3
Triglyceride (Tri)	3526	5	9	12	15	18	13	12	15	TÜRKİYE	15	18	25	16	12	20	27.9	10.5	10.7
Urea (Ure)	3748	6	10	14	20	41	13	14	15	TÜRKİYE	17	19	9	20	12	20	15.7	6.2	5.5
HbA1c	722	6	10	13	16	19	13	13	15	TÜRKİYE				18			..	2.8	..

Henüz yeterli sayıda verimiz oluşmamıştır. Buna rağmen veriler önceki çalışmalar ile uyumludur.

Ricos ve ark çalışması incelendiyse Probe error çalışması için laboratuvar sayısının veri olarak verilmesi gerekir. Ancak şu an için gerekli olmadığını düşünüyoruz.

Dışlama oranı **%1.55** dir. Bu konuda eğitimlere devam edilmelidir.

Bu verilere göre Mustafa hocanın yaptığı gibi iç kalite kontrol bütcesinin belirleme çalışılmaları yapılmalıdır. Bu konuda bir arkadaşı görevlendirmeliyiz.

Çalışmaya 56926 veri alınmış. Yanlış yazılım olduğu düşünülen 104 veri çıkrılmıştır. Bunlar ekte verilmiştir.

Çalışmaya göre 3SD dışındaki veriler dışlanması yapılmıştır. 781 veri çıkarılmıştır.

54 farklı laboratuvar iç kalite kontrol ve dış kalite değerlendirme sonuçları ile tekrar değerlendirme yapıldı

Research Article

Ferzane Mercan, Muhittin A. Serdar*, Mehmet Senes, Dildar Konukoglu, Tamer Cevat İnal, Özkan Alatas, Asli Pinar, Özlem Savci, Muhammet Güven, Mehmet Gündüz, Ertuğrul Eğin, Yasal Önder Tipioğlu, Ahmet Tekin and Doğan Yucel

National External Quality Assessment follow-up: 2010–2017 Turkish experience

Ulusal Dış Kalite Değerlendirme İzlemi: 2010–2017 arası Türkiye Deneyimleri

Table 4: Distribution of reasons for unconformity by years.

The reason for unconformity	2015 (%)	2016 (%)	2017 (%)
Data entry errors (target or own results of the laboratory values)	22.2	18.04	8.27
Erroneous definition of methods	1.7	0.97	2.22
Erroneous definition of units	0.2	0.69	1.06
Erroneous preparation of samples (especially dilution)	5	6.37	11.4
EQA sample problems (inappropriate transfer or storage conditions)	2.7	0.97	0.15
Technical errors (probe, lamp, electrode, etc.)	7.9	4.58	3.76
Error concerning the reagent (past expiry date, waited too long on the device, insufficient collection by probe due to small amount)	4.6	4.09	3.07
Problems concerning the deionised water system	1.8	1.02	1.61
No problem detected. Patient and IQC practices checked and found to be conformant. Subsequently control observed to be conformant	44.9	53.8	59.5
Other reasons	9.0	9.47	8.96

Analitik standardizasyon çalışma sonuçları ve ilgili rehberin hazırlanması

T.C.
SAĞLIK BAKANLIĞI
Sağlık Hizmetleri Genel Müdürlüğü

SAĞLIK HİZMETLERİ GENEL MÜDÜRLÜĞÜ - TIBBİ LABORATUVAR HİZMETLERİ DAİRE BAŞKANLIĞI
13/10/2016 14:08 - 95966346 - 010.06.02 - E.02-827
00031589149

Sayı : 95966346
Konu : İzin Verilen Toplam Hata Sınırları

GENELGE
2016/47

Tıbbi laboratuvarların, 09/10/2013 tarihli ve 28790 sayılı Resmi Gazete'de yayımlanan Tıbbi Laboratuvarlar Yönetmeliği ve kalite standartları çerçevesinde uygun periyotlarda, iç kalite kontrol programını yapılandırması ve dış kalite değerlendirme programına dâhil olması zorunludur.

Kalite kontrol işlemleriyle amaçlanan, belirlenen analitik kalite hedeflerine ulaşılmasıdır. Belirlenen analitik kalite hedefleri daha çok **İzin Verilen Toplam Hata** (Allowable Total Error, TAH) olarak ifade edilmektedir.

Toplam analitik hata (TAH), bir test sonucuna yansıyan **Rastlantısal Hata** ve **Sistematik Hatanın** toplamı olur. **Hasta güvenliği bakımından toplam analitik hatanın, izin verilen toplam hata sınırını aşmaması gerekmektedir.**

Sağlık Bakanlığı Sağlık Hizmetleri Genel Müdürlüğü Tıbbi Laboratuvar Hizmetleri Daire Başkanlığı tarafından oluşturulan Standardizasyon ve Harmonizasyon çalışma grubu tarafından, on beş parametreye ait izin verilen toplam hata sınırları Tablo 1'de belirlenmiştir.

Tıbbi biyokimya laboratuvarları tarafından İzin Verilen Toplam Hata Sınırları belirlenen testler için;

1. Tıbbi Laboratuvarlar Yönetmeliği'nin 27inci maddesinin 2inci fıkrası gereğince, iç kalite kontrol çalışması yapması gerekmektedir. Bu çalışma Tablo 1'de bildirilmiş parametreler için ilgili testin çalışıldığı günlerde, en az bir defa ve en az iki seviye olmalıdır.
2. İç kalite kontrol ve dış kalite değerlendirme bulgularından elde edilen bilgilerle varyasyon katsayısı (% CV) ve izin verilen toplam hata (% TAH) hesaplanmalı ve Tablo 1'de bildirilen değerleri aşmamalıdır. Aşılırsa düzeltici önleyici faaliyetler (DÖF) başlatılmalı ve kayıt altına alınmalıdır.
3. Bu çalışmanın nasıl yapılacağına yönelik "İzin Verilen Toplam Hata Hedeflerine Göre Kısa Rehber" ekte sunulmuştur.

İş bu genelgenin ilinizde faaliyet gösteren kamu, üniversite ve özel sağlık kuruluşlarına tebliği ile uygulamanın Tıbbi Laboratuvarlar Yönetmeliği ve Genelge esaslarına göre yürütülmesinin takibini önemle rica ederim.

Prof. Dr. Eyüp GÜMÜŞ
Bakan a.
Müsteşar

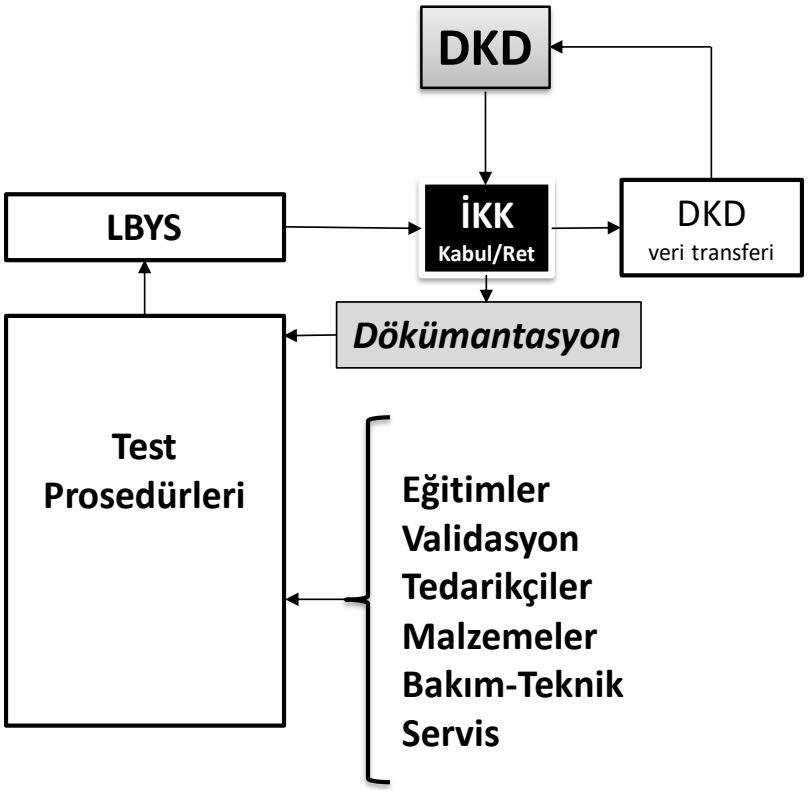
Ek:
Ek-1 İzin Verilen Toplam Hata Hedeflerine Göre Kısa Rehber

Dağıtım:
81 İl Valiliği (İl Sağlık Müdürlüğü)
Türkiye Halk Sağlığı Kurumu
Türkiye Kamu Hastaneleri Kurumu
Türkiye İlaç ve Tıbbi Cihaz Kurumu
Yükseköğretim Kurulu

Analit	İzin Verilen Toplam Hata (%)	Acceptable limits of performance for RIQAS	İzin Verilen En Yüksek Varyasyon Katsayısı (%CV)
Albümin	15	9,1	7,5
Alanin Aminotransferaz	20	14,9	10
Alkalen Fosfataz	30	20,6	10
Aspartat Aminotransferaz	20	14,6	10
Klorür	9	4,6	5
Kolesterol	11	8,6	5
Kreatinin	20	11,8	10
Glikoz	11	8,1	5
HDL Kolesterol	30	21	10
Laktat Dehitrogenaz	21	14,9	10
Potasyum	9	5,4	5
Total Protein	15	8,2	7,5
Sodyum	9	3,6	5
Trigliserit	15	13,2	7,5
Üre	15	11,1	7,5

İKK ve DKD

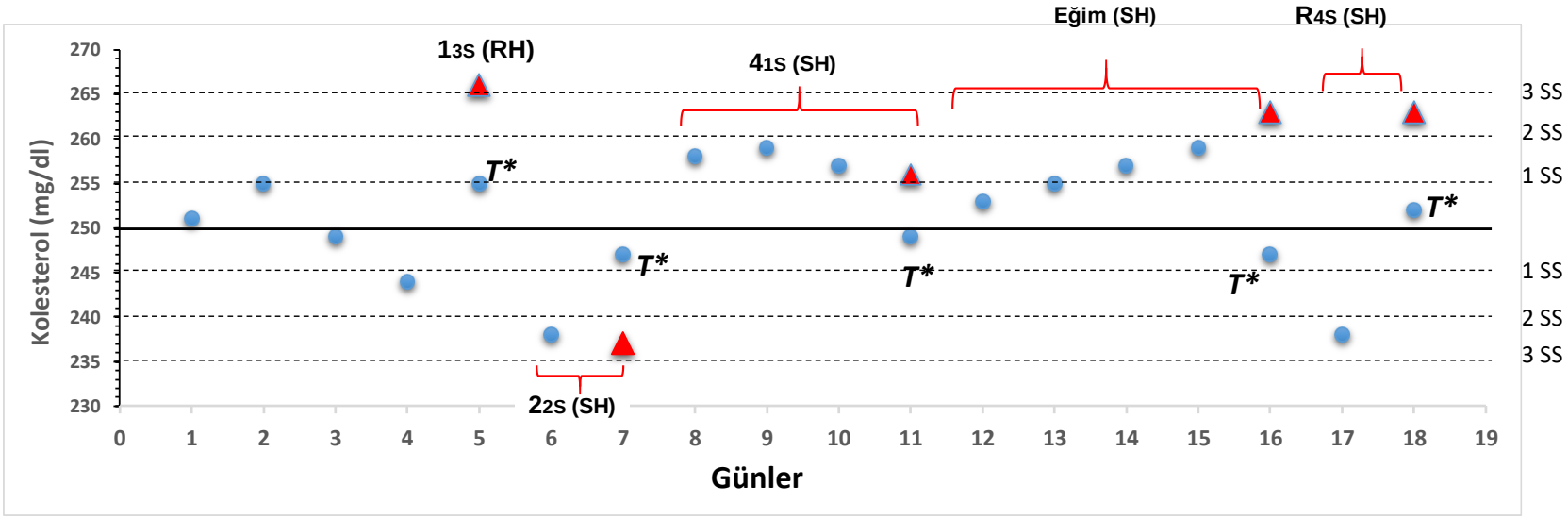
- Son yıllarda farklı uygulama teknikleri olsa da temel olarak iki çeşit kalite kontrol uygulaması vardır.
- **İç Kalite Kontrol (İKK) :** Laboratuvarın kendi içinde değeri bilinen veya bilinmeyen örneklerle yapılan temel olarak tekrarlanabilirlik çalışmalarıdır
- **Dış Kalite Değerlendirme (DKD):** Laboratuvar dışında yeterliliğe sahip bağımsız bir grup tarafından yapılan daha çok doğruluk temelli çalışmalardır. DKD hükümetler tarafından yönetilir ve değerlendirilirse "Yeterlilik Testi" olarak da tanımlanmaktadır.
- İKK ve DKD analitik dönemde diğer unsurlarla iç içe değerlendirilmeli ve laboratuvar işleyiş prosedürünün, indikatörlerinin göstergelerinden biri olarak değerlendirilmelidir



IKK uygulamaları

- **Klasik İKK (CLSI C24 ED4)**
- **Risk Temelli İKK (CLSI EP23 ED2)**
- **Hasta verileri ile İKK**
- **Spesifik uygulamalar (Rilibak gibi)**
- **Gerçek zamanlı klasik İKK (Biorad Unity, Accusera gibi)**

Klasik İKK ve çoklu kurallar

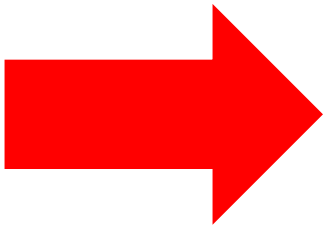


Analitik sistemin üreticisi tarafından sağlanan kontrol materyalleri kullanıldığında, CV ve hedef değerin, analitik olarak stabil koşullarda (aynı reaktifler, aynı teknisyen vb.) **10–20 gün boyunca yapılan** en az **10–20 ölçüm ile** hesaplanması önerilir. Ayrıca bu bilgilerin daha uzun bir süre sonra **(6–12 ay) güncellenmesi tavsiye** edilir.

Kontrol materyallerinin aynı lotu kullanıldığı sürece, gözlemlenen ortalamaların sağlayıcı tarafından belirlenen hedef değer aralığıyla uyumunun izlenmesi iyi bir uygulamadır.

Kuralları yıllardır inceliyoruz

- **Hangilerini kullanıyorsunuz?**



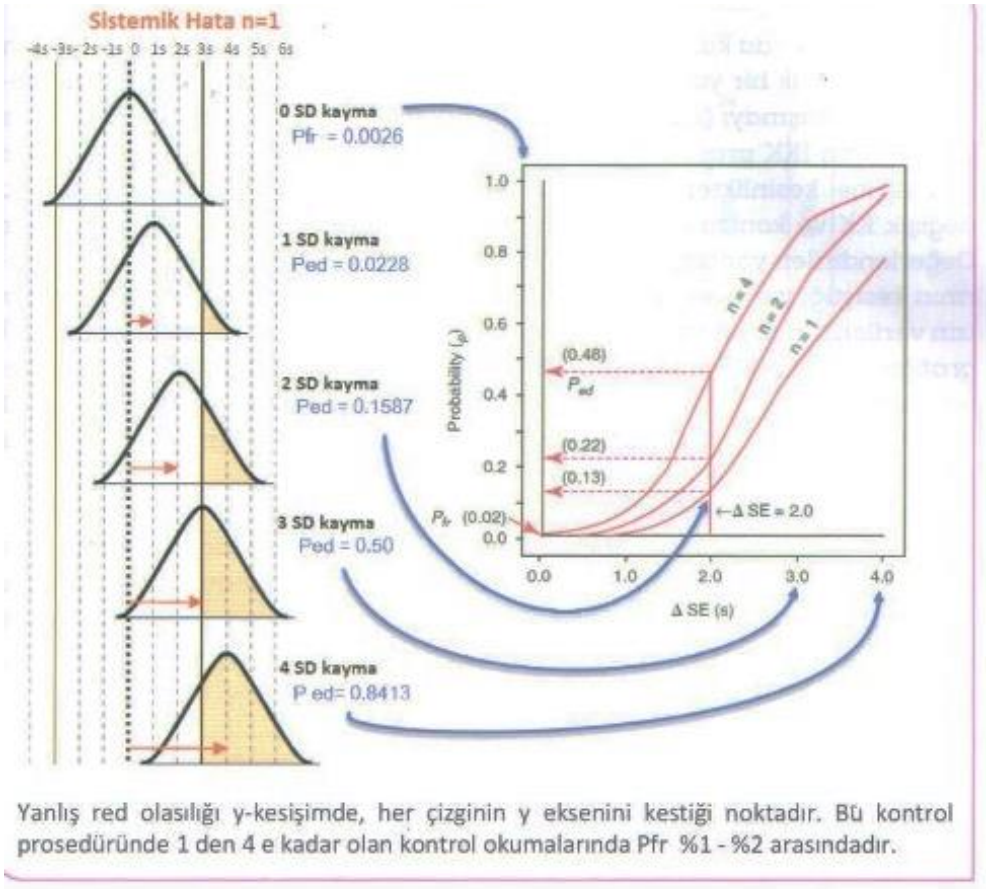
Tab. 2.7: Statistical rules used in clinical laboratory QC.

QC rules	Interpretation	Sensitivity to	Possible error cause
1_{3s}	QC failure occurs when one QC result is ±3 SD limits	Random error	– Clogged pipettors – Obstructed rinsing needles – Air bubbles in reagent – Insufficient mixing of reagent – Incorrect fitting of disposable tips – Variation of power supply
1_{ks} ($1_{3.5s}$, 1_{4s}, 1_{5s})	QC failure occurs when one QC result is ±k SD limits		
R_{4s}	QC failure occurs when there is a 4 SD difference between two consecutive control measurements		
2_{2s}	QC failure when 2 successive QC results exceed the same +2 or −2 SD limits	Systematic error	– Deterioration of QC material – Reagent lot change – Calibration bias – Evaporation of reagent of calibrator – Reagent cross-contamination – Alteration of light source – Change in environmental conditions (increase or decrease in temperature and humidity) – Deterioration of water quality
2 of 3_{2s}	QC failure when two out of three consecutive QC results are located + or −2 SD from the mean		
3_{1s}, 4_{1s}	QC failure when 3 (3_{1s}) of 4 (4_{1s}) consecutive QC results exceed the same +1 or −1 SD		
7t	QC failure when 7 consecutive QC results move upwards or downwards		
8x, 10x, 12x	QC failure when 8 (8×), 10 (10×), or 12 (12×) consecutive QC results are located on the same side of the mean		
1_{2s}	QC failure occurs when one QC result is +/−2 SD limits	Random and systematic errors	All random or systematic causes
1_{2s}, single repeat	QC failure occurs when the first QC result is +/−2 SD limits and repeat testing of the same QC is also +/−2 SD		

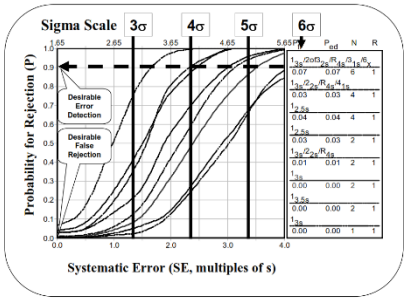
CLSI C24-ED4:2016 Statistical Quality Control for Quantitative Measurement Procedures: Principles and Definitions, 4th Edition

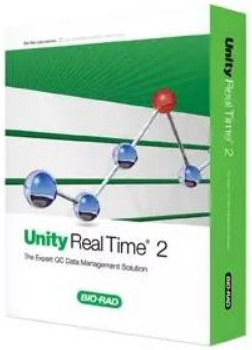
Doğru saptama > %90

Yanlış red <%5



Yanlış red olasılığı y-kesişimde, her çizginin y eksenini kestiği noktadır. Bü kontrol prosedüründe 1 den 4 e kadar olan kontrol okumalarında Pfr %1 - %2 arasındadır.



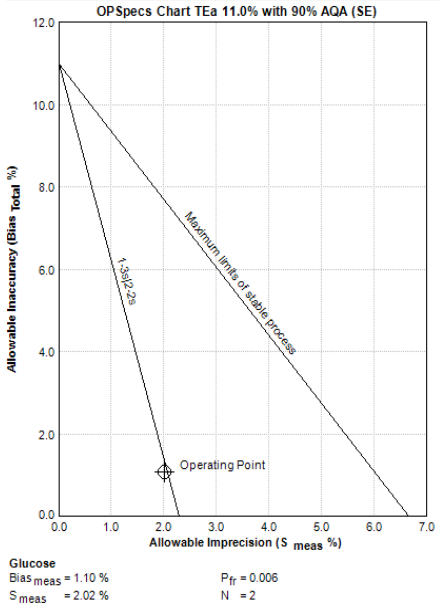


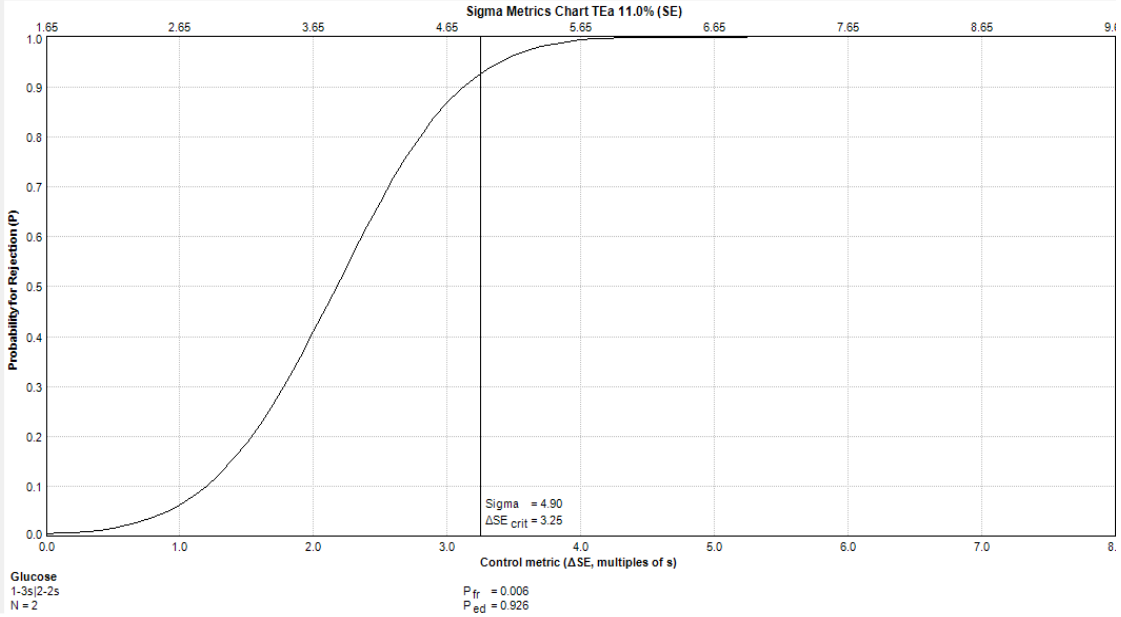
Güç fonksiyon grafikleri

Suggested Rules	N	Ped	Pfr
1-3s|2-2s	2	0.926	0.006
1-3s|2-2s|R-4s	2	0.926	0.010
1-3s|2-2s|R-4s|4-1s	2	0.989	0.012
1-3s|2-2s|R-4s|4-1s|10-X	2	0.999	0.013
1-3s|2-2s|R-4s|4-1s|8-X	2	0.999	0.019
1-2.5s	2	0.949	0.025
1-2s	2	0.988	0.091
1-3.5s	2	0.639	0.001

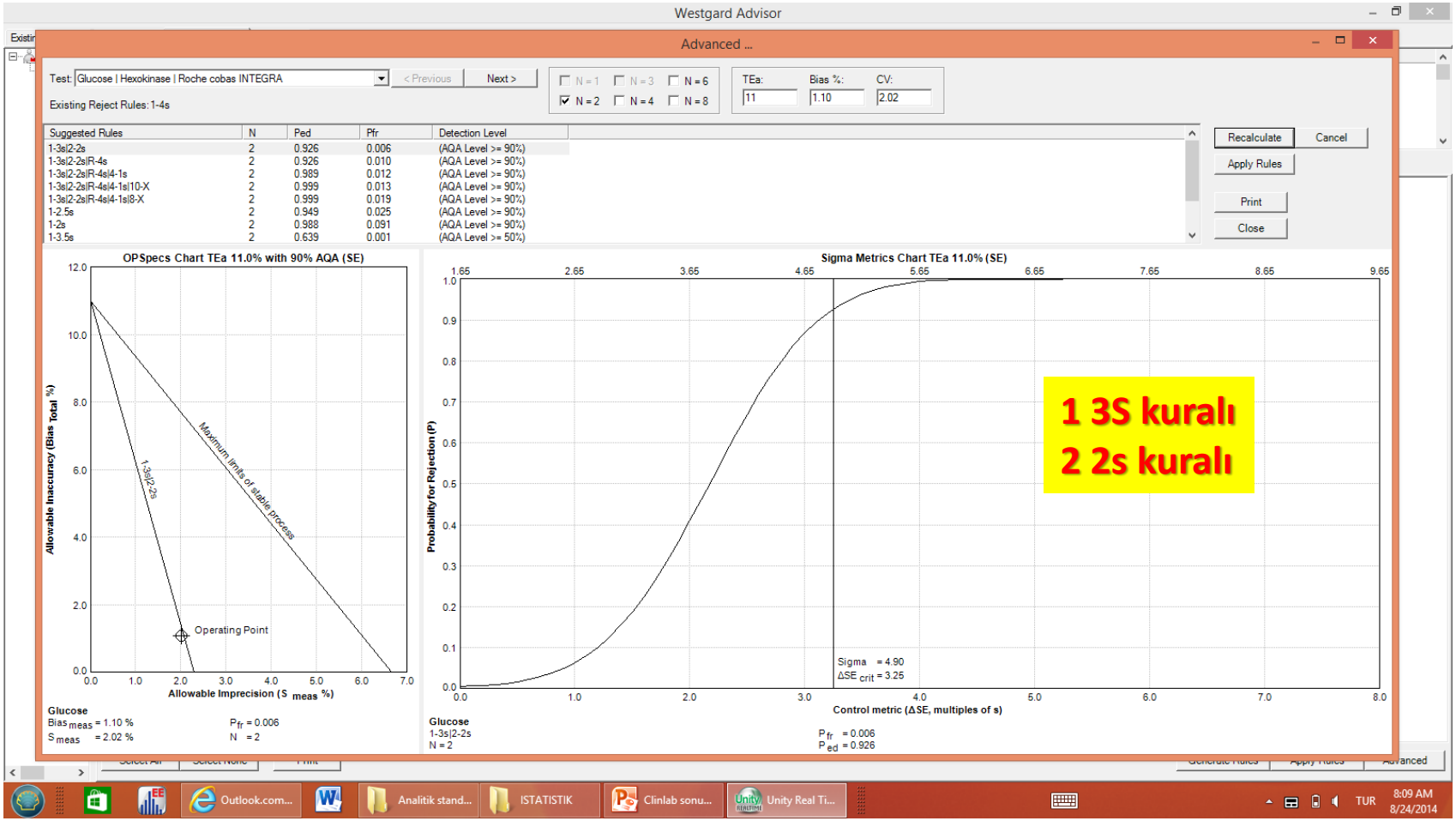
OPSpecs Chart TEa 11.0% with 90% AQA (SE)

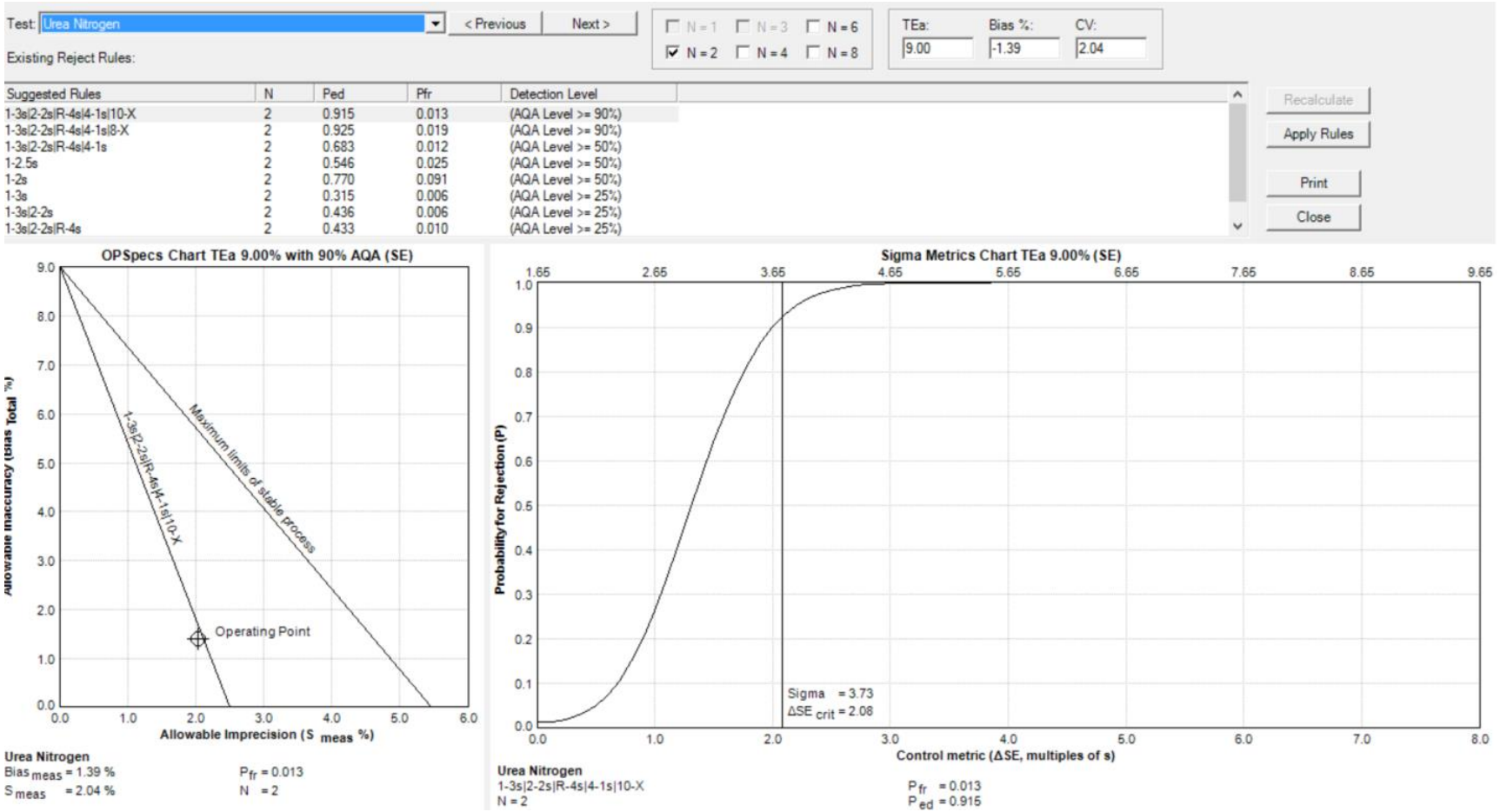
TEa: 11 Bias %: 1.10 CV: 2.02





Kolesterol TE:11, Bias:1.10, Pre:2.02

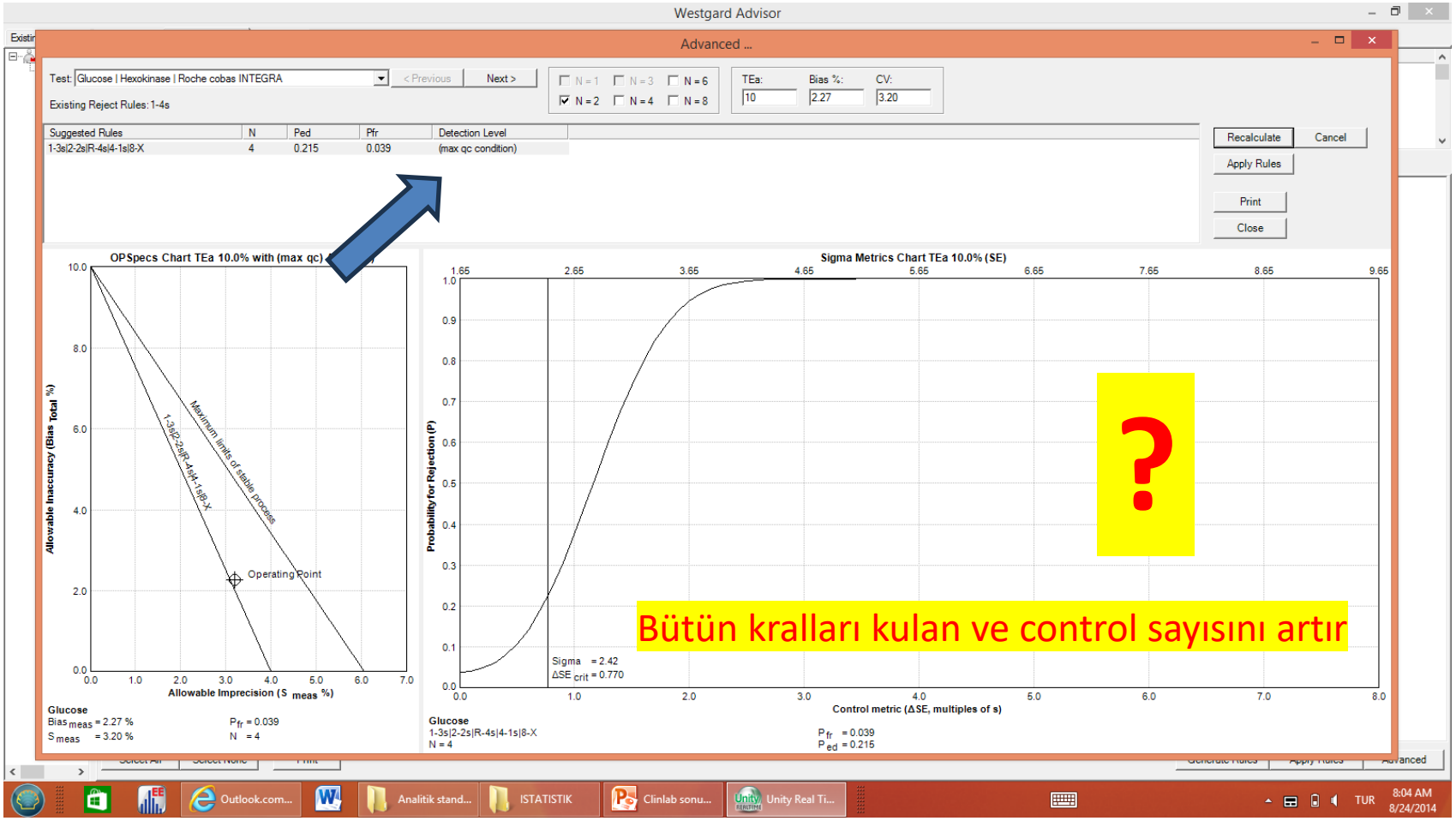




Üçüncü Parti Kontrol Kullanılarak Analitik Performansın Değerlendirilmesine Bir Örnek: **Üre**

Nilhan Nurlu Ayan, Ayşegül Keleş, Aybala Özerdem, N. Özden Serin

Albumin TE:10, Bias:2.27, Pre:3.20



Başka yazılımlar var mı?

Home
Levey Jennings Chart
Moving Averages Charts for IQC
Method Decision Charts
Risk-based QC Parameters Single rule
Risk-based QC Parameters Multi rule
Patient Based Quality Control
Optimizer for PBQC

QC Constellation

Developed by Hikmet Can Çubukçu, MD, MSc, EuSpLM
hikmetcancubukcu@gmail.com

Fork

QC Constellation

Welcome to QC Constellation, a pioneering web-based application designed to revolutionize quality control practices in clinical laboratory environments. The tool is intricately crafted to navigate the complexities of modern quality control, enabling laboratory professionals to implement contemporary risk-based quality control practices with precision and confidence.

Quality control in clinical laboratories is a multifaceted domain, where error detection spans routine quality control rules to sophisticated methods like moving averages. Tools such as sigma-metric measurements and method decision charts play a crucial role in evaluating analytical procedures. QC Constellation leverages these tools, ensuring their optimal use based on the specific performance of analytical methods and the associated patient risks.

QC Constellation incorporates traditional Westgard rules, trend detection methods like EWMA and CUSUM, and the Six Sigma methodology for comprehensive performance evaluation. Furthermore, moving averages charts adapted for patient-based QC and its optimization tool are both available. Our application's core lies in its ability to make these sophisticated practices accessible and actionable for laboratory professionals in a risk-based manner.

Please cite: *Çubukçu HC. QC Constellation: a cutting-edge solution for risk and patient-based quality control in clinical laboratories. Clin Chem Lab Med. 2024 May 31. doi: 10.1515/cclm-2024-0156. Epub ahead of print. PMID: 38814734.*

Calculate MRS based on custom patient risk factor

- Home
- Levey Jennings Chart
- Moving Averages Charts for IQC
- Method Decision Charts
- Risk-based QC Parameter
- Risk-based QC Parameter
- Pati
- Opti

E(Nuf) value vs Systematic Error(%) Plot

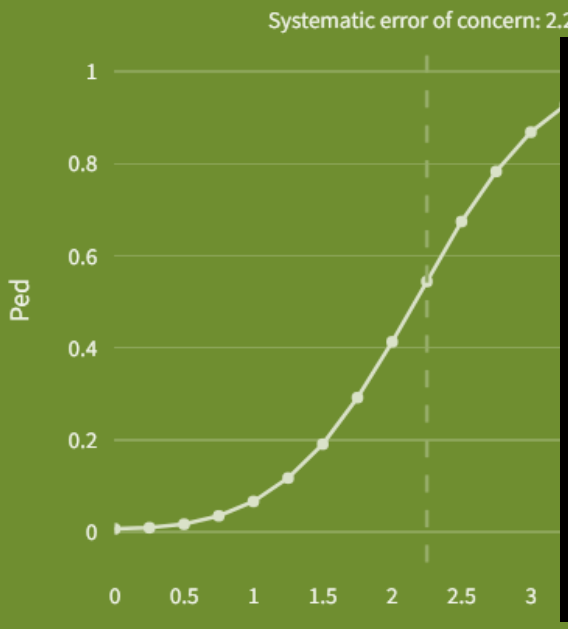
E(QCE) value and U(nR)% vs. Systematic Error(%) Plot

E(Nuf)
E(Nuc)
E(QCE)
UnR (%)
E(Nuc)
UnR (%)
9.9997
4.74974
9.49983
4.24991
9
92
95
74

Risk based QC Parameters

Parameter	*Value*
Probability of false rejection (%)	0.7

Power Function Plot



Parameter	*Value*
Probability of harm	0.000003156383
Acceptable probability of harm	0.000100
Risk management index	0.031564
Systematic error (%) at Max RMI	4.5
Systematic error (as multiples of SD) at Max RMI	2.25

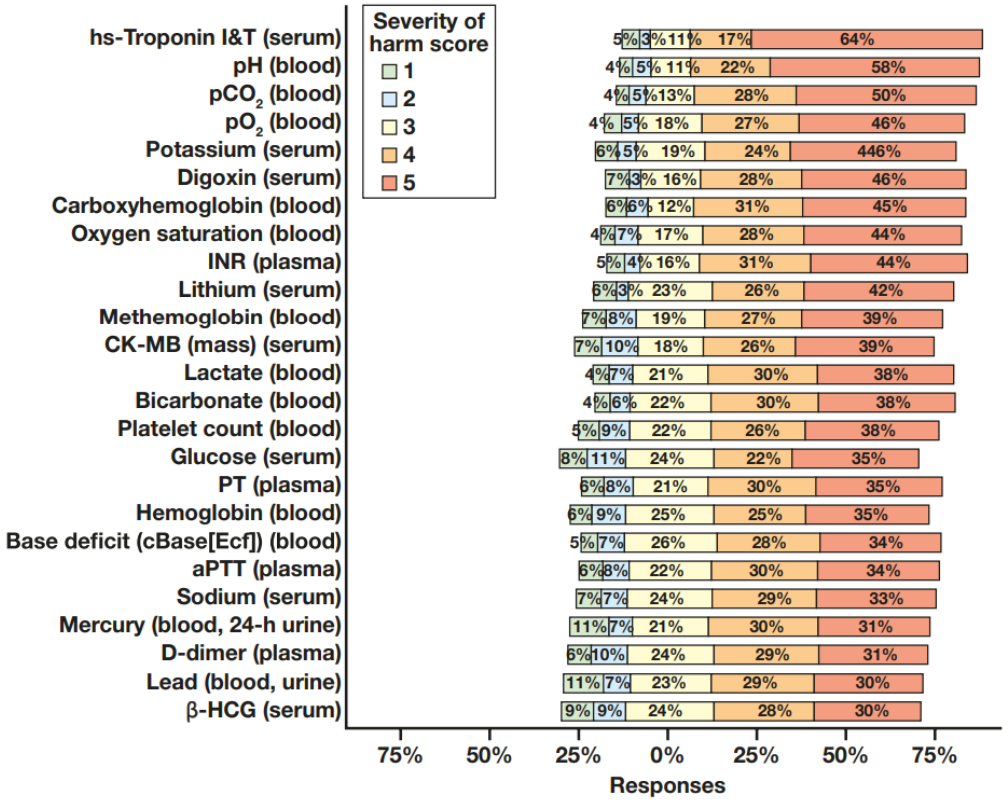
Testlere ait şiddet puanının nereden bulabilirim?

AJCP | ORIGINAL ARTICLE

Measuring the impact

Severity of harm from laboratory errors in 195 tests

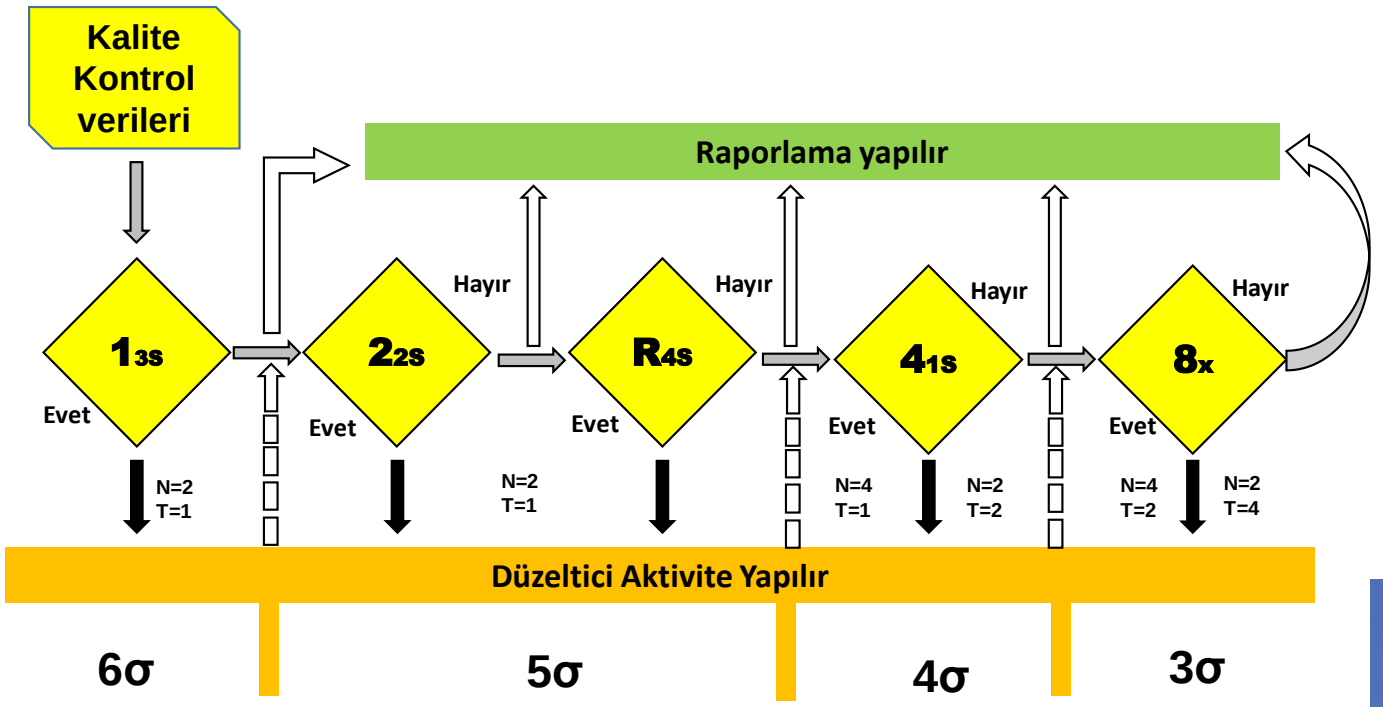
Hikmet Can Çubukçu, MD, MSc,[1] Murat Cihan, MD,[2] Hamit Hakan Alp, PhD,[3] Serkan Bolat, MD,[4] Oğuzhan Zengi,[5] Kamil Taha Uçar, MD,[5] Deniz İlhan Topcu, MD, PhD,[6] Muhammed Fevzi Kılınçkaya, MD,[7] Habib Özdemir, MD,[8,9] Murat Gülşen, MD,[1] Hayri Canbaz, MD,[10] Doğan Yücel,[11] Muhittin Abdulkadir Serdar, MD[12]



TBD Akademi

Çubukçu HC, Cihan M, Alp HH, Bolat S, Zengi O, Uçar KT, Topcu Dİ, Kılınçkaya MF, Özdemir H, Gülşen M, Canbaz H, Yücel D, Serdar MA. Measuring the impact: Severity of harm from laboratory errors in 195 tests. Am J Clin Pathol. 2025 Mar 8;163(3):453-463. doi: 10.1093/ajcp/aqae144.

Sıralı ve Sigmametrik kurallar



Ensuring internal quality control practices in medical Laboratories: IFCC recommendations for practical applications based on ISO 15189:2022

Jean-Marc Giannoli [a], Anne Vassault [b], Anna Carobene [c,*], Armand Perret Liaudet [d], Ivan M Blasutig [e,f,g], Pradeep Kumar Dabla [h], Ji Lin [i], Annette Thomas [j], José Antonio Tesser Poloni [k], Qing H Meng [l], Egon P Amann [m], on behalf of the International Federation of Clinical Chemistry, Laboratory Medicine Task Force on Global Lab Quality TF-GLQ

Identification and Management of Analytical Risks in Internal Quality Control (IQC).

Risk	Identification of risk and potentially erroneous result	Recommendations: suppliers or best practices	Limitations of these recommendations	Effectiveness of correction	Other possible actions (master plan)	Residual risk	Indicators
8	Deviations over time (drift). Gradual changes in test results due to instrument wear, reagent degradation, calibration drift, or environmental influences, potentially leading to clinically significant errors if not detected in time.	– Implement a structured IQC strategy tailored to reagent and analyte stability. – Define appropriate IQC frequency based on analytical robustness and clinical risk. – Utilize *Westgard rules* or advanced statistical methods to identify systematic trends. – Establish acceptable control limits aligned with method performance and clinical decision-making needs.	– IQC intervals may not always capture subtle trends in real-time. –Frequency too low. – Wide acceptable limits may delay drift detection. – Inadequate *Westgard rules*.	Partial.	–Use advanced statistical techniques for drift analysis. – IQC with acceptable limits adapted to the actual performance of the analyser and clinical needs. – Visual assessment of drift and trend control charts. – Monitoring of CVs according to relevant specifications. – 6 Sigma calculation; – Monitoring of patient mean values. – If several analysers,	Acceptable.	– Frequency of long-term CV monitoring by analyte and instrument. – Percentage of IQC failures attributed to drift. – Conformity of CVs with established APS. – Number of corrective actions initiated due to detected drift.

Clinica Chimica Acta 571 (2025) 120240

DE GRUYTER Clin Chem Lab Med 2025; aop

THE WAR ON SCIENCE

Opinion Paper

Hikmet Can Çubukçu*, Marc Thelen, Mario Plebani and Mauro Panteghini

IFCC recommendations for internal quality control practice: a missed opportunity

IFCC'nin IQC rehberi, risk temelli bir yaklaşım sunsa da güncel olmayan kavramlar, eksiklikler ve hatalar içermektedir.

Daha sistematik, güncel ve kanıta dayalı bir yaklaşımın benimsenmesi gerektiğini savunmaktadır.

1. **Metrolojik İzlenebilirlik Çağında IKK Tasarımı:** Rehber, geleneksel istatistiksel kontrollere odaklanmakta ancak metrolojik izlenebilirlik, hasta zararı ve ölçüm sistemi hızı gibi diğer yaklaşımları yeterince dikkate almamaktadır. Önerilen iki bileşenli IKK yaklaşımı (izlenebilirliği kontrol eden IQC-I ve rastgele hataları değerlendiren IQC-II) göz ardı edilmiştir.
2. **IKK Kabul Limitlerinin Tanımlanması:** Kabul limitlerinin istatistiksel dağılıma göre belirlenmesi önerilirken, klinik olarak uygun Analitik Performans Spesifikasyonları (APS) ile uyumlu olması gerektiği vurgulanmaktadır. Biyolojik varyasyon ve EQA (Harici Kalite Değerlendirmesi) limitleri gibi modellerin yetersizliği eleştirilmiştir.
3. **Ölçüm Belirsizliği (MU) Tahmini:** Rehber, MU'nun nasıl hesaplanacağı konusunda yetersiz ve kafa karıştırıcı bilgiler içermektedir. Toplam hata (TEA) ile MU arasındaki fark net bir şekilde açıklanmamıştır. Ayrıca, sistematik hataların kaynakları ve yönetimi yeterince ele alınmamıştır.
4. **Farklı Analizörler Arasındaki Sonuçların Karşılaştırılabilirliği:** Aynı laboratuvarda kullanılan farklı analizörlerin sonuçlarının karşılaştırılabilirliği konusunda net bir rehberlik sunulmamıştır. Metrolojik izlenebilirliğin doğrulanması ve klinik olarak eşdeğer sonuçların sağlanması gerektiği belirtilmiştir.

Sigma-Metrik değerlendirme İKK kuralları

- Sigma metric = (Quality specifications – |Bias|)/Test variation)

or

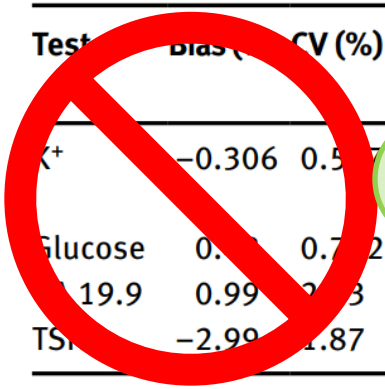
- Sigma metric = (TEa – |**Bias**|)/CV

Definition of QC rules according to Sigma metrics.

Sigma metric	Category	Proposed QC rule	Proposed QC frequency	Additional action
>6	Excellent tests	$1_{3,5s}$	One QC per day	None
4–6	Tests that are suited for purpose	$1_{2.5s}$	Two levels of QC per day	None
3–4	Poor performers	$1_{3s}\,2_{2s}\,R_{4s}\,4_{1s}$ 10×	Two levels of QC two times a day	None
<3	Problematic tests	$1_{3s}\,2_{2s}\,R_{4s}\,4_{1s}$ 10×	Three levels of QC three times a day	Consider testing patient specimens in duplicate

Impact of TEa selection on Sigma metrics.

Test	Bias (%)	CV (%)	TEa #1	TEa #1 (%)	Sigma #1	TEa #2	TEa #2 (%)	Sigma #2	TEa #3	TEa #3 (%)	Sigma #3
K+	−0.306	0.5	BV des	5.61	10.3	BV opt	2.8	4.82	IPH Belgium	4.8	8.7
Glucose	0.	0.7	2	6.96	8.62		3.48	3.99	RCPA	8	10
19.9	0.99	2	3	46.2	16.6		23.1	8.1	RiliBäk	14	4.8
TSI	−2.99	1.87		23.7	11.1		11.9	4.78	GOST	28.5	13.7



Hasta Bazlı Gerçek Zamanlı Kalite Kontrol (PBRTQC)

"bir kültür değişimidir"

Karakteristik	PBRTQC	İstatistiksel IQC
QC frekansı	Sürekli	Planlanmış
Değiştirilebilirlik	Gidilebilir	Ortaklaştırılamazlık riski
Kontrol edilebilir teşhis aşamaları	Preanalitik aşama ve analitik aşama	Analitik aşama
Kalite kontrol seviyesi	Hasta popülasyonuna ve MA ortamlarına bağlı bir seviye	Çoklu seçilebilir seviyeler
Hata algılama	Önyargı (kesinsizlik daha az sıklıkta)	Önyargı ve kesinsizlik
Optimizasyon	Deneme ve hata/güç fonksiyonları/TE_a [b] tespiti simülasyon/ANP_{ed}/bias algılama eğrileri	Klasik SD/σ metriklerine/riske dayalı
Doğrulama	Güç fonksiyonu/MA doğrulama çizelgeleri/yanlılık tespiti simülasyonları	Güç fonksiyonu analizi/ istatistiksel modelleme
Sonuçların grafiksel sunumu	Doğruluk grafiği/Levey-Jennings grafiği	Levey-Jennings arsası
Sonuçları yayınlamak için kullanın	Sonuçlara hükmetme ve hükmetme (kuruluma ; arkadan serbest bırakma)	Sonuçların kesinleşmesi ve açıklanması
Operasyonel maliyetler	Her analiz için uygulama sırasında önemli zaman; MA QC alarm çalışması	QC malzemeleri, QC analizi ve QC alarm çalışması

[a] van Rossum ve Kemperman'dan (20) uyarlanmıştır.

[b] TE_a, izin verilen toplam hata.

HUVAROS

Rutin uygulanabilir mi?

Table 1: Optimized MA procedures and assay characteristics.

Analyte	MA settings						Test characteristics		
	Truncation limits	Batch size	Control limits		Units	MA alarms Sept–Dec 2013 data set	Average daily number of tests[a]		Sigma
			Lower	Upper			Analyzer 1	Analyzer 2	
Alkaline phosphatase	≤ 1000	50	85	196.5	U/L	2	92.3	67.6	6.2
Alanine aminotransferase (ALT)	≤ 50	50	17.1	27.8	U/L	2	107.1	74.4	9.4
Albumin	≥ 20	25	29.16	43.6	g/L	4	56.7	38.6	1.6
Aspartate aminotransferase (AST)	≤ 50	50	22.6	31.7	U/L	1	83.8	61.5	8.7
Bicarbonate	None	50	21.9	27	mmol/L	3	19.8	14.2	1.0
Bilirubin (total)	≤ 50	50	8	18	µmol/L	1	57.3	46.3	12.7
Calcium	None	50	2.2	2.54	mmol/L	9, strange peaks and dips	42.8	32.0	1.0
Chloride	None	50	102.71	110.66	mmol/L	4, strange peaks and dips	22.5	23.5	1.9
Cholesterol	None	25	4.1	6.1	mmol/L	4, at least 1 due to technical failure	32.9	23.9	5.8
Creatine kinase	≤ 500	50	80	175	U/L	1	32.0	27.8	21.4
Creatinine	40–150	50	65.1	91.84	µmol/L	5	188.6	150.6	3.2
γ-glutamyltransferase (γGT)	≤ 200	25	22	90	U/L	2	87.4	61.8	14.4
Glucose	≤ 10	50	5.36	7.55	mmol/L	0	93.3	73.9	2.3
HDL-Cholesterol	None	25	1.05	1.59	mmol/L	2	28.6	21.2	5.3
Lactate dehydrogenase	≤ 500	25	180	300	U/L	1	77.5	56.0	5.0
Magnesium	≤ 2.0	25	0.67	1.02	mmol/L	3	40.9	38.1	3.4
Phosphate	≤ 3	25	0.91	1.5	mmol/L	3	37.5	29.8	6.3
Potassium	≤ 6	50	3.8	4.43	mmol/L	6	161.6	138.1	4.5
Protein (total)	None	25	60	77.5	g/L	0	15.2	11.2	6.9
Sodium	None	25	133.48	140.72	mmol/L	14, about 50% due to technical failure	142.9	124.2	1.1
Transferrin	None	25	1.76	2.98	g/L	0	8.8	5.3	2.1
Triglycerides	≤ 10	50	1.36	2.6	mmol/L	2	62.7	27.2	15.1
Urea	≤ 20	50	5.3	9.9	mmol/L	3	113.0	99.5	6.9
Uric acid	None	50	0.27	0.38	µmol/L	1	10.2	7.3	7.9

[a]Average daily number of tests were obtained using the September–December 2013 data sets.

http://login.huvaros.com/

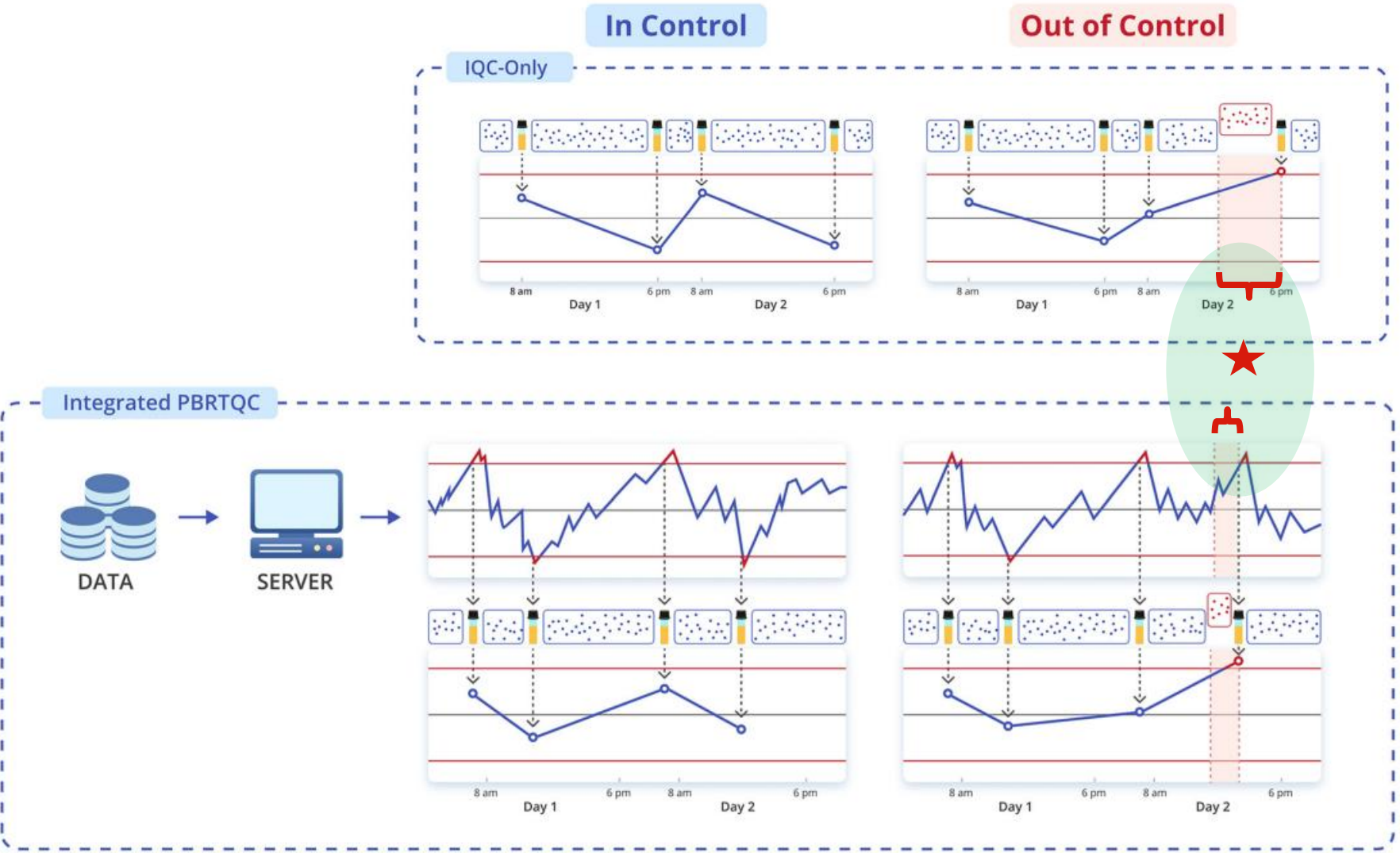
Clin Chem Lab Med 2017; a

Xincen Duan, Tony Badrick, Wenqi Shao, Andreas Bietenbeck, Xiao Tan, Jing Zhu, Wenhai Jiang, Ying Zhao, Chunyan Zhang, Baishen Pan*, Beili Wang* and Wei Guo*

Improving the efficiency of quality control in clinical laboratory with an integrated PBRTQC system based on patient risk

- Risk Based Regression-adjusted real-time quality control (RARTQC)

https://doi.org/10.1515/cclm-2025-0163



Xincen Duan, Tony Badrick, Wenqi Shao, Andreas Bietenbeck, Xiao Tan, Jing Zhu, Wenhai Jiang, Ying Zhao, Chunyan Zhang, Baishen Pan*, Beili Wang* and Wei Guo*

Improving the efficiency of quality control in clinical laboratory with an integrated PBRTQC system based on patient risk

https://doi.org/10.1515/cclm-2025-0163

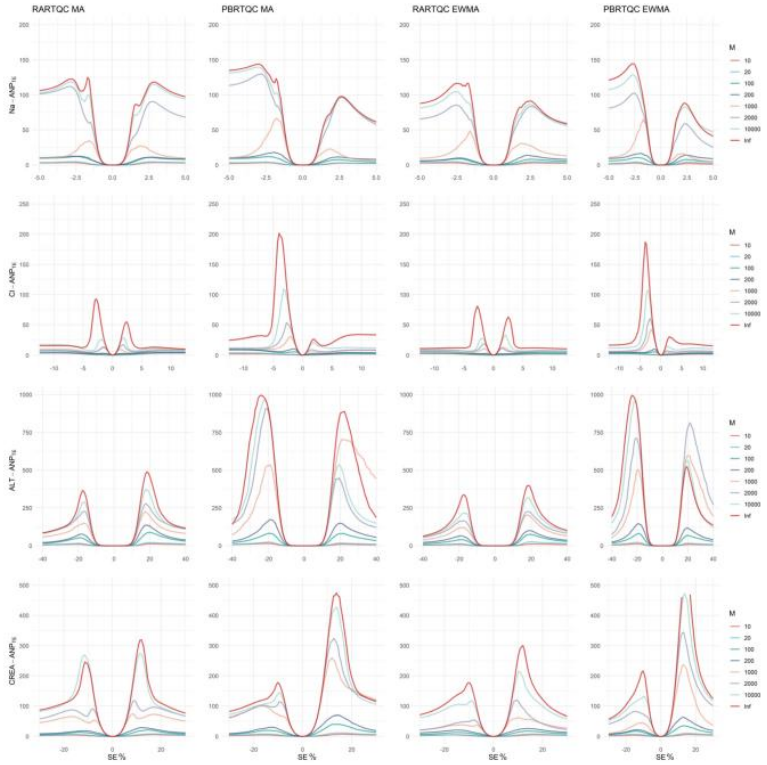


Figure 3: The ANP_{TE} curves for four analytes across four algorithms at various DFAR levels.

Table 1: Summary of descriptive statistics and the IQC performance metric of the four analytes.

Analyte	Na	Cl	ALT	CREA
Total number of tests	387,280	387,281	617,215	975,813
Average daily testing volume	1,061	1,061	1,691	2,673
Mean	140.6	103.2	35.5	81.6
SD	3.7	4.2	84.4	56.3
Median	140.8	103.5	20.1	72.9
2.5th	132.65	94.01	6.93	42.99
97.5th	146.65	110.48	156.81	172.97
Skewness	0.18	−0.16	24.16	9.73
Mean of nearest QC level	136.5	96.5	28.2	83.2
Analytical SD	0.925	0.769	0.862	1.34
Analytical CV	0.68 %	0.8 %	3.06 %	1.61 %
TEa	2	5	16	12
Sigma metric	2.94	6.25	5.23	7.45
Number of QC events per day	2	2	2	2
Number of observations at a QC event	3	3	3	3
Average number of patient results between each QC event (M)	530.5	530.5	845.5	1,336

Are we there yet?—why is the adoption of patient-based real-time quality control taking so long?

Paul Dean[1], Joel Smith[2,3], Tony Badrick[4]

Henüz ulaşamadık mı?—Hasta bazlı gerçek zamanlı kalite kontrolün benimsenmesi neden bu kadar uzun sürüyor

- PBRTQC'yi duymuş olan çoğu laboratuvarcı algoritmaları ve bunların **hasta popülasyonları için nasıl optimize edileceğini anlamıyor**. Birçok farklı algoritma mevcut ve her izlenen analiz farklı bir hesaplamaya daha uygun olabilir.
- PBRTQC algoritmaları ve parametreleri simülasyon kullanılarak optimize edilmelidir. Optimal algoritma için uygun **PBRTQC parametrelerini (blok boyutu, dışlama, kesme ve hata tespiti sınırları) hasta popülasyonlarına göre belirlenmelidir.**
- Hasta **popülasyonundaki dalgalanmaların PBRTQC'yi nasıl etkileyebileceği konusunda bilgi eksikliği vardır.** (kreatinin gibi cinsiyete bağlı ölçümler, hemoliz gibi preanalitik sorunlar ve yatan hastalar, klinikler ve yoğun bakım hastalarındaki varyasyon gibi)
- Laboratuvarın, **hasta popülasyonlarını, analiz sistemlerini ve laboratuvar yazılımının** sınırlarını iyi anlaması gerekir.

ÖNERİ

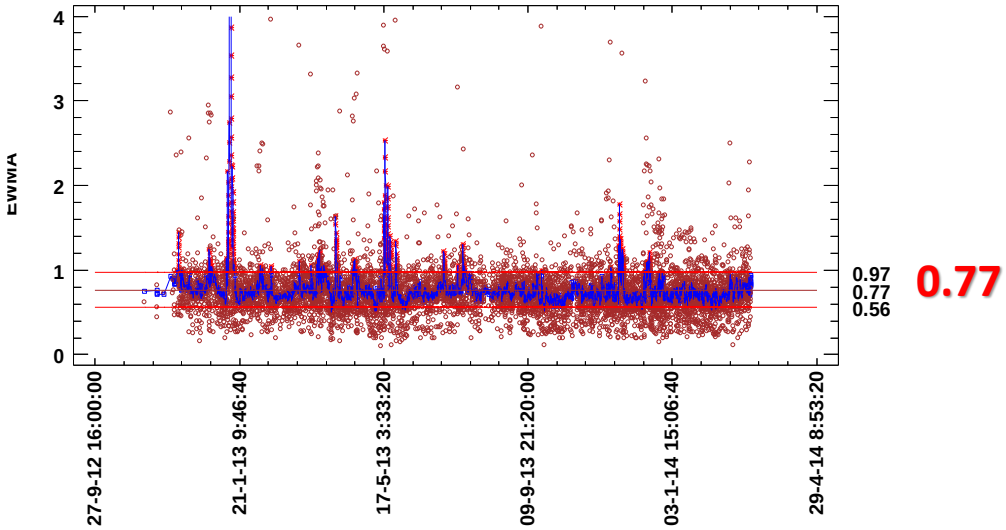
PBRTQC'nin uygulanmasını için **Potasyum, kalsiyum veya sodyum** gibi sıkı biyolojik kontrole sahip birkaç ölçümle başlamak en iyisidir.

Yaş, cinsiyet ve mevsimsel değişim az biyolojik varyasyona sahip ölçümleri seçmek.

Journal of Laboratory and Precision Medicine, 2025

Hasta verilerinin incelenmesi rutin laboratuvar uygulamalarımızda geriye yönelik uygulama açısın çok önemli

Cihaz 1



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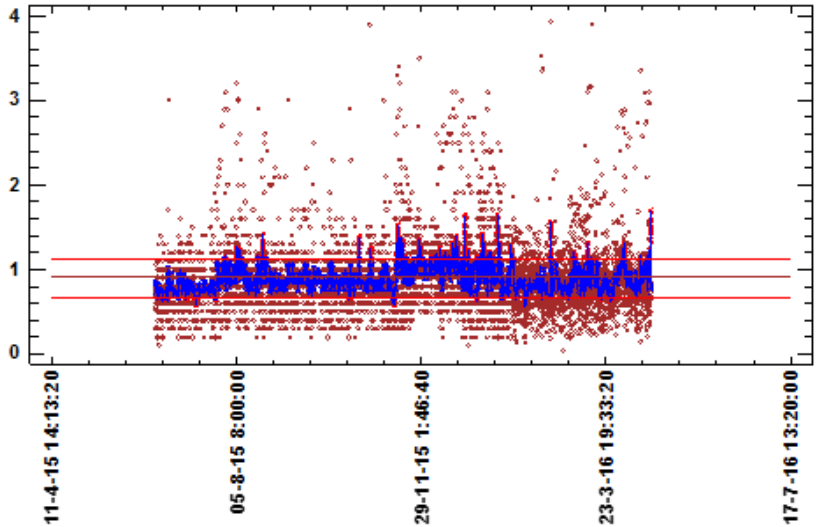
Cihaz 2



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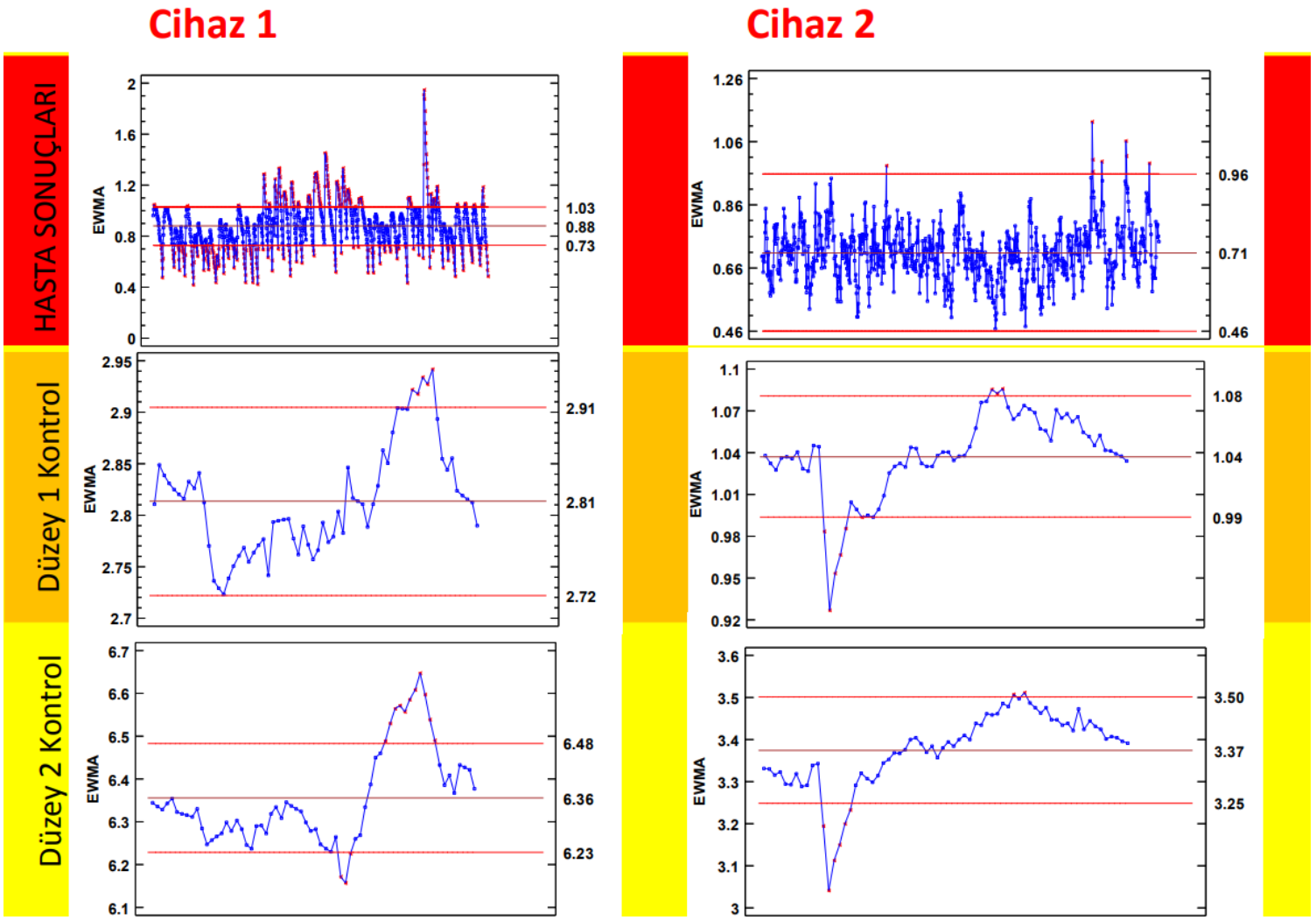
İKK sonuçları ile hasta sonuçları parallel mi?



Quality Control Practices for Chemistry and Immunochemistry in a Cohort of 21 Large Academic Medical Centers

American Journal of Clinical Pathology, 150, Issue 2, **2018,** Pages 96–104

Barnes-Jewish Hospital/Washington University, St Louis
Brigham and Women's Hospital
Cedars-Sinai Medical Center
Duke University Hospital
Hospitals of the University of Pennsylvania–Penn Presbyterian
Houston Methodist Hospital
Johns Hopkins Hospital
Massachusetts General Hospital
Mayo Clinic
Mount Sinai Hospital
New York-Presbyterian Columbia
New York-Presbyterian Cornell
Northwestern Memorial Hospital
Ronald Reagan UCLA Medical Center
Stanford Health Care–Stanford Hospital
The Cleveland Clinic
Tisch Hospital, NYU Langone Health
University of California, San Francisco Medical Center
University of Colorado Hospital
University of Michigan Hospitals and Health Centers
UPMC Presbyterian Shadyside, Pittsburgh

Hospital	Chemistry	Immunochemistry
A	Roche	Roche
B	Siemens	Siemens
C	Roche	Roche, Abbott
D	Siemens	Siemens
E	Roche	Roche
F	Roche, Beckman Coulter	Abbott, Roche, Beckman Coulter
G	Ortho	Ortho, Roche, Abbott
H	Beckman Coulter	Beckman Coulter, Roche
I	Beckman Coulter	Beckman Coulter, Siemens
J	Beckman Coulter	Roche, Abbott, Beckman Coulter, Siemens
K	Abbott	Abbott
L	Roche	Roche
M	Roche	Roche
N	Roche	Roche, Beckman Coulter, Siemens
O	Roche	Roche, Siemens, Beckman Coulter
P	Beckman Coulter	Beckman Coulter
Q	Roche	Roche, Abbott, Beckman Coulter
R	Siemens	Siemens
S	Siemens	Siemens
T	Roche	Roche, Siemens, Bio-Rad, Abbott, Beckman Coulter
U	Beckman Coulter	Beckman Coulter

%90'I Bio-Rad

Hangi Kontrol Materyali?

Hospital	Chemistry	Immunochemistry
A	MAS Chemtrak	Bio-Rad
B	Bio-Rad	Bio-Rad
C	Bio-Rad	Bio-Rad
D	Bio-Rad	Bio-Rad
E	Bio-Rad, manufacturer when necessary	Bio-Rad, manufacturer QC when necessary
F	Bio-Rad	Bio-Rad
G	Bio-Rad	Bio-Rad
H	Bio-Rad	Bio-Rad
I	Predominantly Bio- Rad QC and some manufacturer supplied (if available)	Predominantly Bio-Rad QC and some manufacturer supplied (if available)
J	Bio-Rad, MAS Chemtrak	Automatic laboratory: manufacturer supplied when possible, third party when necessary (Bio-Rad). Special chemistry laboratory: Bio-Rad when possible, manufacturer when necessary; supplemented with patient pools
K	Bio-Rad	Bio-Rad, manufacturer QC when necessary
L	Bio-Rad	Bio-Rad, Roche, Randox
M	MAS ChemTrack	Manufacturer, third party when needed (Bio-Rad)
N	Mostly Bio-Rad, also Stanbio, Thermo TDM, UTAK, Elsohly	Mostly Bio-Rad, manufacturer control where necessary
O	Bio-Rad, very few manufacturers or laboratory made	Bio-Rad, very few manufacturers
P	Bio-Rad	Bio-Rad
Q	Bio-Rad, some Beckman Coulter, Abbott, and in-house prepared	Bio-Rad, some Beckman Coulter, Abbott, and in-house prepared
R	Bio-Rad	Bio-Rad
S	Bio-Rad	Bio-Rad, some Beckman Coulter, Abbott, and in-house prepared
T	Bio-Rad, some Roche	Bio-Rad, some Roche, Abbott
U	Bio-Rad, very few manufacturers	Bio-Rad, very few manufacturers

American Journal of Clinical Pathology, 150, Issue 2, **2018,** Pages 96–104

%95'I 2SD

Hangi Kurallar kullanıyorsunuz?

Hospital	Chemistry	Immunochemistry
A	±2 SD	±2 SD
B	±2 SD	±2 SD
C	±2 SD	±2 SD
D	±2 SD, some ±2.5 SD and ±3 SD	±2 SD
E	±2 SD	±2 SD
F	±2 SD	±2 SD
G	±2 SD	±2 SD
H	±2 SD	±2 SD
I	Variable (1-3S, 1-3.5S, 1-4S, 1-5S, 2-2S, 2 of 3-2S, R-4S, 3-1S, 4-1S, or N-x, 1-2S, 1-2.5S)	Variable (1-3S, 1-3.5S, 1-4S, 1-5S, 2-2S, 2 of 3-2S, R-4S, 3-1S, 4-1S, or N-x, 1-2S, 1-2.5S)
J	±2 SD	±2 SD
K	±2 SD	±2 SD
L	±2 SD	±2 SD
M	±2 SD	±2 SD
N	±2 SD	±2 SD
O	±2 SD	±2 SD
P	±2 SD	±2 SD
Q	3 SD	3 SD
R	±2 SD	±2 SD
S	2-2S, 1-3S, R-4S, 10x	2-2S, 1-3S, R-4S, 10x
T	2 or 3 SD	Some 2 or 3 SD;
U	±2 SD	±2 SD

IKK uygulma sıklığı nedir?

			QC Events/d				
Hospital	CHEM	IM	Stat IM	CHEM	IM	Tn	hCG
A	2-3 Lv qd (electrolytes q8h)	2-3 Lv qd	2-3 Lv qd, negative QC q8h for Tn and hCG	3	1	3	3
B	2-3 Lv q8h	2-3 Lv q8h	2-3 Lv q8h	3	3	3	3
C	1 Lv (alternating) q2h	2-3 Lv q8h	cTn 4 Lv qd, 2 Lv alternating q2h, hCG 2 Lv q8h	12	3	12	3
D	2 Lv q12h	2 Lv q12h	2 Lv q8h	2	2	3	3
E	2 Lv q8h	2 Lv qd	2 Lv qd	3	1	1	1
F	2 Lv q8h	2 Lv qd	2 Lv qd	3	1	1	1
G	High control q12h, low control qd	2-3 Lv qd (medium Lv q12 for Lv 3 tests) or high Lv q12h/low Lv qd	Tn/CKMB/NT-proBNP: 2 Lv q12h; hCG: high q12h, low qd	2	2	2	2
H	2-3 Lv q12h	2-3 q12h	2-3 q12h	2	2	2	2
I	2-3 Lv q8h or qd	2-3 Lv qd	2-3 Lv qd	3	1	1	1
J	2 Lv q8h (q4h for electrolytes)	2-3 qd, 1 Lv (alternating) second/third shift	2-3 Lv day shift, 1 Lv (alternating) second/third shifts	6	3	3	3
K	2 Lv qd	2-3 Lv qd	Tn/hCG: 3 Lv qd	1	1	1	1
L	2 Lv q6h, 2 Lv startup/shutdown	2-3 Lv q12h	5 Lv q8h; hCG 2-3 Lv q12h	6	2	3	2
M	2 Lv at startup, 1 Lv (q4h alternating)	2-3 Lv at startup, 1 Lv at shutdown	Tn/hCG 2/3 Lv at startup, 1 Lv (alternating) q4h	7	2	7	7
N	3 Lv startup/shutdown, then 2 levels QC q2h	3 Lv startup/shutdown, plus 2 levels q8h	3 Lv q8h	12	4	3	3
O	3 Lv qd	2-3 Lv qd	Core laboratory: Tn/hCG 3 Lvq12h/q24 hours; ED laboratory: Tn/hCG 2 Lv qd	1	1	2	1
P	2-3 Lv q12h	2 Lv q8h	2 Lv q8h	2	3	3	3
Q	3 Lv day shift, 2 Lv other shifts	3 Lv day shift, 2 Lv other shifts	3 Lv qd, 2 Lv q12h	3	3	2	2
R	2 Lv q12h	2 Lv q12h	3 Lv q12h	2	2	2	2
S	2-3 q12h	q12h, certain tests once at start up	q12h, some qd	2	2	2	2
T	2 Lv qd	2 Lv qd	2 Lv qd	1	1	1	1
U	3 Lv q8h	3 Lv qd	3 Lv qd	3			

American Journal of Clinical Pathology, 150, Issue 2, **2018,** Pages 96–104

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BASIC QC PRACTICES

Leading Laboratories Lag Behind in QC Practices

A new survey of 21 Large Academic Medical Centers in the USA has revealed some sobering facts. We assume that QC processes have evolved from the antique practices of the 1950s and 1960s, particularly since the introduction of "Westgard Rules" in 1981 and other evidence-based optimization techniques in subsequent decades. The reality appears to be the opposite. QC practices may be regressing, not evolving.

Leading Laboratories? They Lag Behind in QC Practices

Sten Westgard, MS
July 2018

ABD'deki 21 Büyük Akademik Tıp Merkezi'nde yapılan yeni bir araştırma, bazı gerçekleri ortaya çıkardı. QC süreçlerinin, özellikle 1981'de "Westgard Kuralları"nın ve sonraki on yıllarda diğer kanıta dayalı optimizasyon tekniklerinin getirilmesinden bu yana, 1950'ler ve 1960'ların antika uygulamalarından evrimleştiğini varsayıyoruz.

Gerçek tam tersi gibi görünüyor. QC uygulamaları evrimleşmiyor, geriliyor olabilir.

Sten Westgard tarafından 2017 ve 2021 yıllarında beş kıtadan 700-900 laboratuvara IQC protokolleriyle ilgili iki anket yapıldı

Worldwide surveys concerning the IQC model applied

IQC model	2017	2021
Control limits		
Laboratory standard deviation	63	58
Manufacturer control insert	43	57
Peer group standard deviation	20	24
Operative control run		
1_{2s}	**55**	**59**
Multi-rule for all measurands	–	**23**
Multi-rule for some measurands	–	**64**
Control sample origin		
Instrument manufacturer	64	67
Third party, liquid, assayed	44	43
Third party, lyophilized	35	31
Third party, liquid, unassayed	30	20
Average of normals	11	14
Frequency		
Once per day	49	54
Several times per day	41	46
Staff criterion	38	38
According to patient risk	14	NR
Beginning and end work day	13	NR
Patient groups (i.e., every 100patients)	9	NR

Worldwide surveys concerning the immediate management after an out-of-control warning.

Management	2017	2021
Out-of-control measurement procedure		
To search for reasons before repeating patient samples	78	79
To repeat control sample	78	68
To prepare a new control sample	64	55
To recalibrate the instrument	16	20
To immediately notify the manufacturer	2	4
Retesting patient samples		
Only determined groups	33	31
All daily patients	32	33
Only abnormal results	20	24
Only those near the control failed	13	14
Releasing patient results when control failed		
Never	54	48
Few times (<10/month)	30	30

Ricós C, Fernandez-Calle P, Perich C, Westgard JO. Internal quality control - past, present and future trends. Adv Lab Med. 2022 May 23;3(3):243-262. doi: 10.1515/almed-2022-0029.

İKK problem çözümü

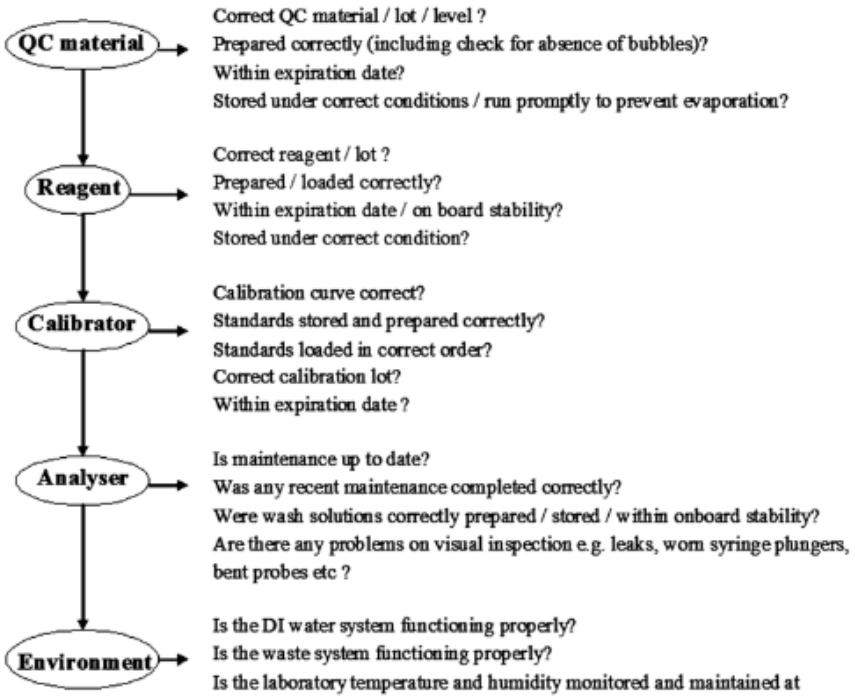


Figure 1 Troubleshooting internal quality control (IQC) failure. Based on typical manufacturer guidelines.

RILIBAK

2.1 Internal quality assurance

2.1.1 Procedures

(1) The manufacturer's requirements are to be observed with regards to type and frequency of internal quality assurance.
Independently of this, internal quality assurance is to be performed in terms of frequency:
a) In accordance with Table B 2-1 for the tests listed therein
b) Adequately and regularly as consistent with medical necessity and with the required testing frequency of patient samples, if the tests are not listed in Table B 2-1.
The requirements of Paragraph (1) Sentence 2 are considered to be met if corresponding controls, which ensure the accurateness of the results, are integrated with the applied analysis system.
(2) In addition, internal quality assurance is to be performed after disruptions to the testing procedure. Disruptions to the testing procedure include:
a) Restarting the device after it has been switched off completely
b) Calibration by the user
c) Repair or maintenance work on devices relevant to the test results
d) Changing reagent lots *[This also includes changes to the composition of the reagents, such as the production of dilutions or, in the case of in-house production, repeated preparation of reagents.]*
(3) The control samples must be as similar to the patient samples being investigated as possible. Identical control and calibration material may not be used in the same testing procedure.
(4) Control samples are to be used which have a known result that is within the measurement ranges relevant for making medical decisions.
(5) When unit-of-use reagents and their corresponding analytical systems are used in point-of-care laboratory testing, the requirements of Paragraph (1) Sentence 2 and Paragraph (2) Sentence 2 (a) do not need to be met if process control measures, which show the output of erroneous test results, are integrated in the test.

CLSI C24-ED4:2016 Statistical Quality Control for Quantitative Measurement Procedures: Principles and Definitions, 4th Edition

Table 1. Examples of Possible Causes for Out-of-Control Conditions

Possible Cause	Type of Error	Nature
Clot or debris in pipette	Systematic or random error	Transient or Persistent
Inadequate wash	Systematic or random error	Transient or Persistent
Incorrect liquid transfer volumes	Systematic or random error	Transient or Persistent
Temperature control	Systematic or random error	Persistent
Electronic noise	Systematic or random error	Transient or Persistent
Calibration problem	Systematic error	Persistent
Calibrator deterioration	Systematic error	Persistent
Reagent deterioration	Systematic error	Persistent
Deterioration of QC material	Systematic error	Persistent
Lack of calibration following major maintenance	Systematic error	Persistent

Trend nedenleri

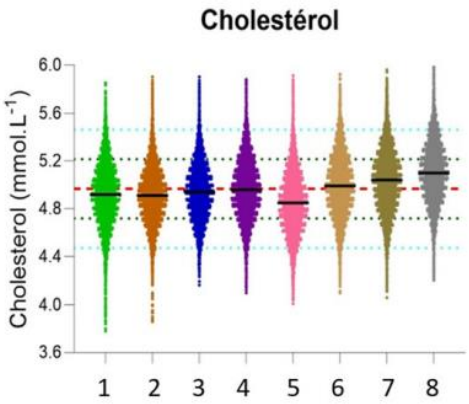
- Cihaz ışık kaynağının bozulması
- Numune/reaktif tubinglerinde kademeli olarak birikinti birikmesi
- Elektrot yüzeylerinde kademeli olarak birikinti birikmesi
- Reaktiflerin kademeli bozulması
- Kontrol malzemelerinin kademeli olarak bozulması
- İnkübasyon esnasında sıcaklığının kademeli olarak bozulması (yalnızca enzimler)
- Işık filtresi bütünlüğünün kademeli olarak bozulması
- Kalibrasyonun kademeli olarak bozulması

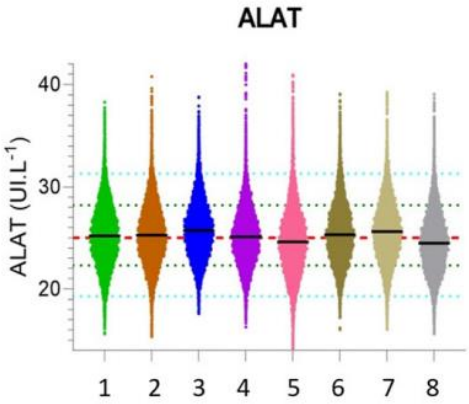
Shift nedenleri

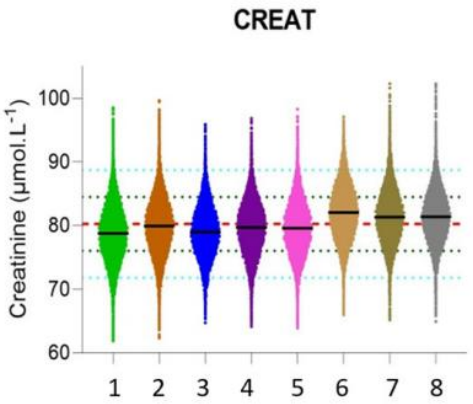
- Işık kaynağında ani arıza veya değişiklik
- Reaktif LOT değişikliği
- Cihazın ana bakımının yapılamaması
- İnkübasyon sıcaklığında ani değişiklik (yalnızca enzimler)
- Oda sıcaklığında veya neminde değişiklik
- Örnekleme sisteminde başarısızlık
- Reaktif dağıtım sisteminde arıza
- Hatalı kalibrasyon/yeniden kalibrasyon

Çoklu cihazda tek hedef kullanılır mı?

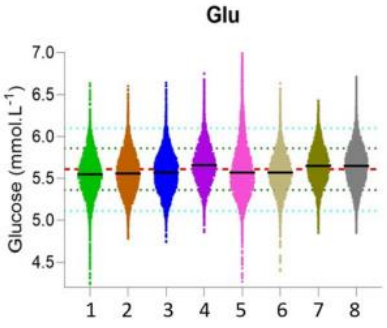
Biorad unity bir çözüm olabilir mi?

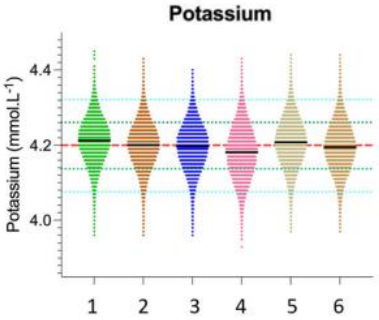






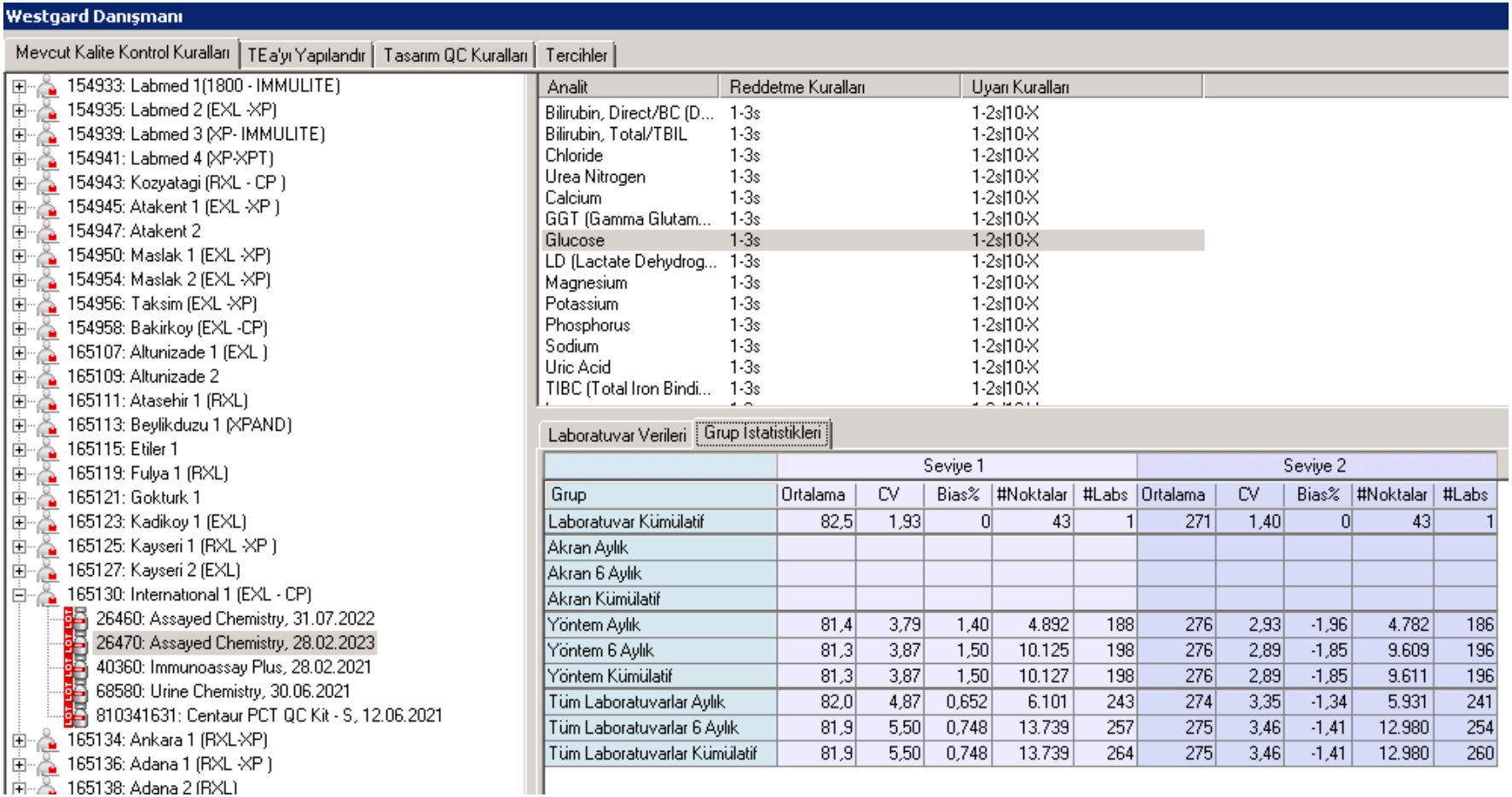
13s/22s/R4s





Badrick T., Giannoli J.M. Managing the quality control of multiple instruments. Clin. Chem. Lab. Med. 2024;62:e62–e64.
Clin Chem Lab Med 2024; 62(5): 853–860

Biorab Unity



	Seviye 1					Seviye 2				
Grup	Ortalama	CV	Bias%	#Noktalar	#Labs	Ortalama	CV	Bias%	#Noktalar	#Labs
Laboratuvar Kümülatif	82,5	1,93	0	43	1	271	1,40	0	43	1
Akran Aylık										
Akran 6 Aylık										
Akran Kümülatif										
Yöntem Aylık	81,4	3,79	1,40	4.892	188	276	2,93	-1,96	4.782	186
Yöntem 6 Aylık	81,3	3,87	1,50	10.125	198	276	2,89	-1,85	9.609	196
Yöntem Kümülatif	81,3	3,87	1,50	10.127	198	276	2,89	-1,85	9.611	196
Tüm Laboratuvarlar Aylık	82,0	4,87	0,652	6.101	243	274	3,35	-1,34	5.931	241
Tüm Laboratuvarlar 6 Aylık	81,9	5,50	0,748	13.739	257	275	3,46	-1,41	12.980	254
Tüm Laboratuvarlar Kümülatif	81,9	5,50	0,748	13.739	264	275	3,46	-1,41	12.980	260

Biorad Unity ile öğrendiklerim

Lab Data | Group Statistics

	Level 1					Level 2				
Group	Mean	CV	Bias %	# Points	# Labs	Mean	CV	Bias %	# Points	# Labs
Lab Cumulative										
Peer Monthly	119	3,41	N/A	253	13	96,6	2,92	N/A	258	12
Peer 6 Months	119	3,33	N/A	282	14	96,6	2,90	N/A	286	13
Peer Cumulative	119	3,33	N/A	282	14	96,6	2,90	N/A	286	13
Method Monthly	106	7,68	N/A	6.535	232	87,8	6,87	N/A	6.542	227
Method 6 Months	105	7,07	N/A	16.723	266	87,2	6,26	N/A	16.860	262
Method Cumulative	105	7,05	N/A	16.989	267	87,2	6,22	N/A	17.134	263
All Labs Monthly	104	7,47	N/A	8.375	314	86,9	6,54	N/A	8.332	308
All Labs 6 Months	104	6,81	N/A	21.415	353	86,5	5,90	N/A	21.500	348
All Labs Cumulative	104	6,81	N/A	21.415	355	86,5	5,90	N/A	21.500	350

Cihazlar ve Kontrol materyali uyumlulukları

Unity verilerini ile bizim verilerimizin karşılaştırılması

Farklı amaçlar için kullanımı

Unity™ Worldwide Report

Assayed Chemistry • Lot 14480 • Exp 31–May–2017

Creatinine Alkaline picrate–kinetic mg/dL

Siemens Dimension Series

	Level 1 Mon	Level 1 Cum	Level 2 Mon	Level 2 Cum
Mean	2.80	2.73	6.26	6.17
SD	0.141	0.140	0.222	0.247
CV	5.0	5.1	3.5	4.0
# Points	1058	23427	997	22373
# Labs	33	135	33	131

Unity % 5.1 % 4

Bu değerlerin yaklaşık 3SD ile aralıklar belirleniyor

Bizim verilerimiz

% 2.59 % 2.84

Creatinine Alkaline picrate–kinetic, IFCC–IDMS Standardized mg/dL

Abbott AEROSET/ARCHITECT (c, i, ci models)

	Level 1 Mon	Level 1 Cum	Level 2 Mon	Level 2 Cum
Mean	2.77	2.78	6.31	6.30
SD	0.109	0.116	0.139	0.188
CV	3.9	4.2	2.2	3.0
# Points	2918	38205	2812	37799
# Labs	69	146	69	146

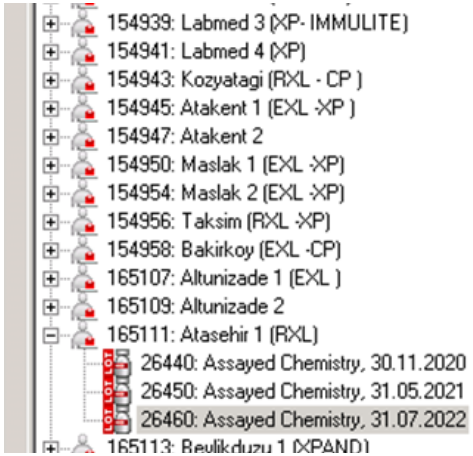
Beckman Coulter AU 400/480/600/640/680/2700/5400/5800

	Level 1 Mon	Level 1 Cum	Level 2 Mon	Level 2 Cum
Mean	2.22	2.21	5.53	5.49
SD	0.071	0.086	0.149	0.182
CV	3.2	3.9	2.7	3.3
# Points	1282	15825	1269	15504
# Labs	37	68	37	69

Roche cobas 6000/8000/c 311

	Level 1 Mon	Level 1 Cum	Level 2 Mon	Level 2 Cum
Mean	2.19	2.18	5.37	5.36
SD	0.112	0.129	0.178	0.194
CV	5.1	5.9	3.3	3.6
# Points	2039	27246	1970	26635
# Labs	75	111	72	110

Biorad Unity ile öğrendiklerim

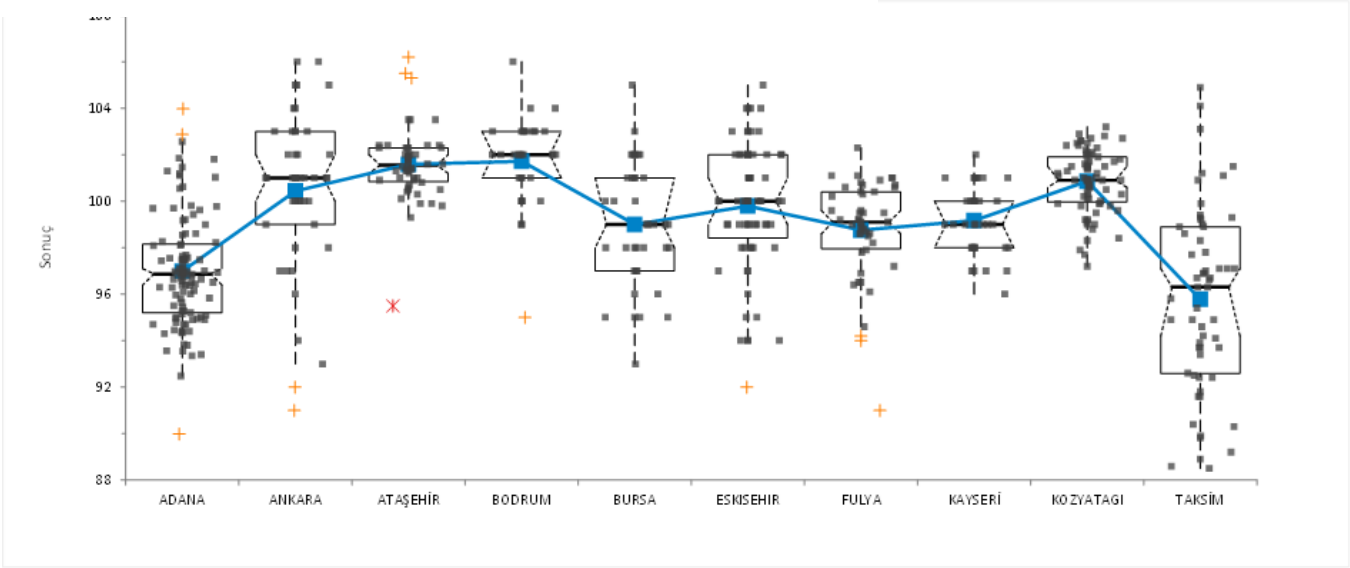


Protein, Total, Serum	1-3s	1-2s|10-X
Sodium	1-3s	1-2s|10-X
Uric Acid	1-3s	1-2s|10-X
Chloride	1-3s	1-2s|10-X

Lab Data | Group Statistics

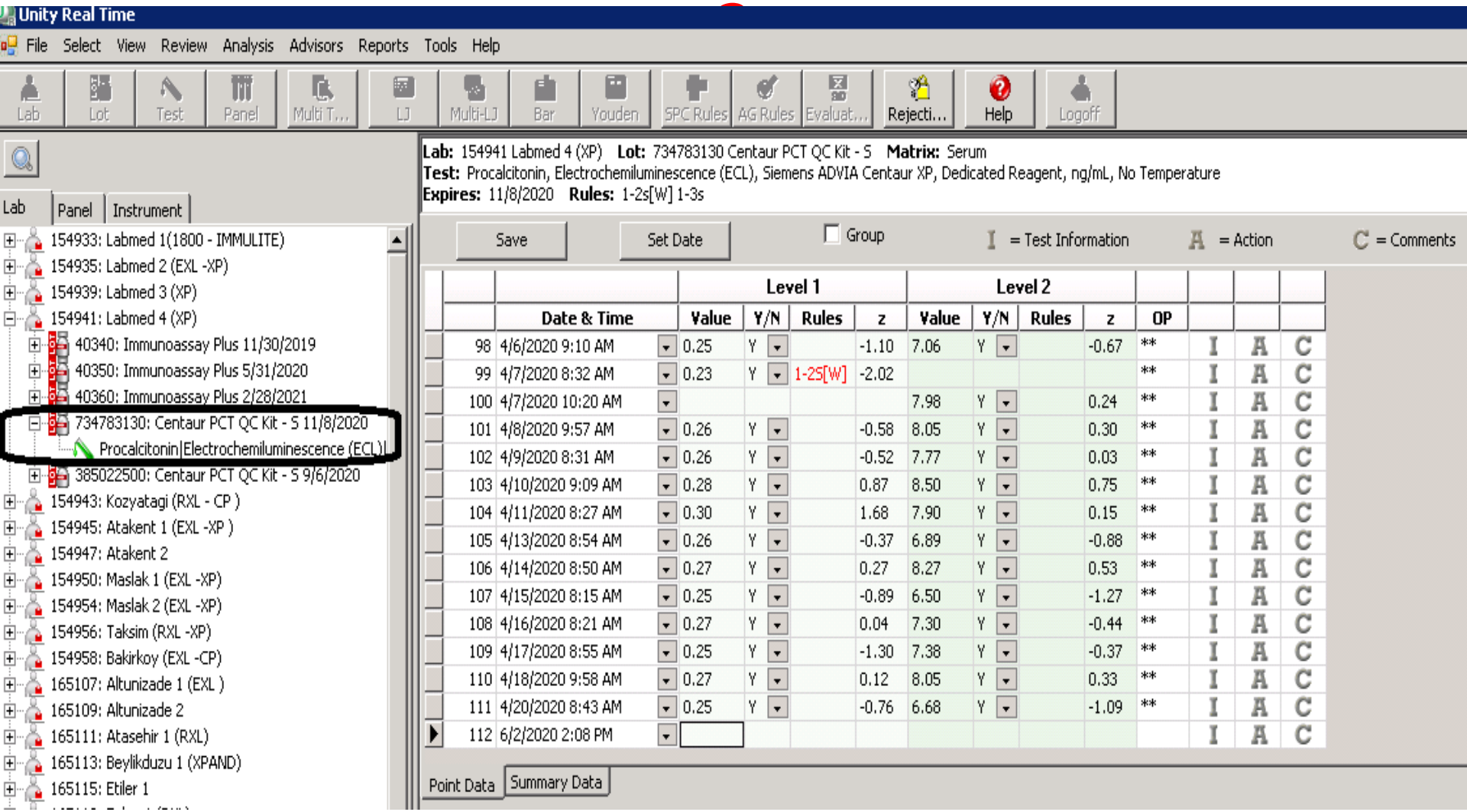
	Level 1					Level 2				
Group	Mean	CV	Bias %	# Points	# Labs	Mean	CV	Bias %	# Points	# Labs
Lab Cumulative										
Peer Monthly	119	3,41	N/A	253	13	96,6	2,92	N/A	258	12
Peer 6 Months	119	3,33	N/A	282	14	96,6	2,90	N/A	286	13
Peer Cumulative	119	3,33	N/A	282	14	96,6	2,90	N/A	286	13
Method Monthly	106	7,68	N/A	6.535	232	87,8	6,87	N/A	6.542	227
Method 6 Months	105	7,07	N/A	16.723	266	87,2	6,26	N/A	16.860	262
Method Cumulative	105	7,05	N/A	16.989	267	87,2	6,22	N/A	17.134	263
All Labs Monthly	104	7,47	N/A	8.375	314	86,9	6,54	N/A	8.332	308
All Labs 6 Months	104	6,81	N/A	21.415	353	86,5	5,90	N/A	21.500	348
All Labs Cumulative	104	6,81	N/A	21.415	355	86,5	5,90	N/A	21.500	350

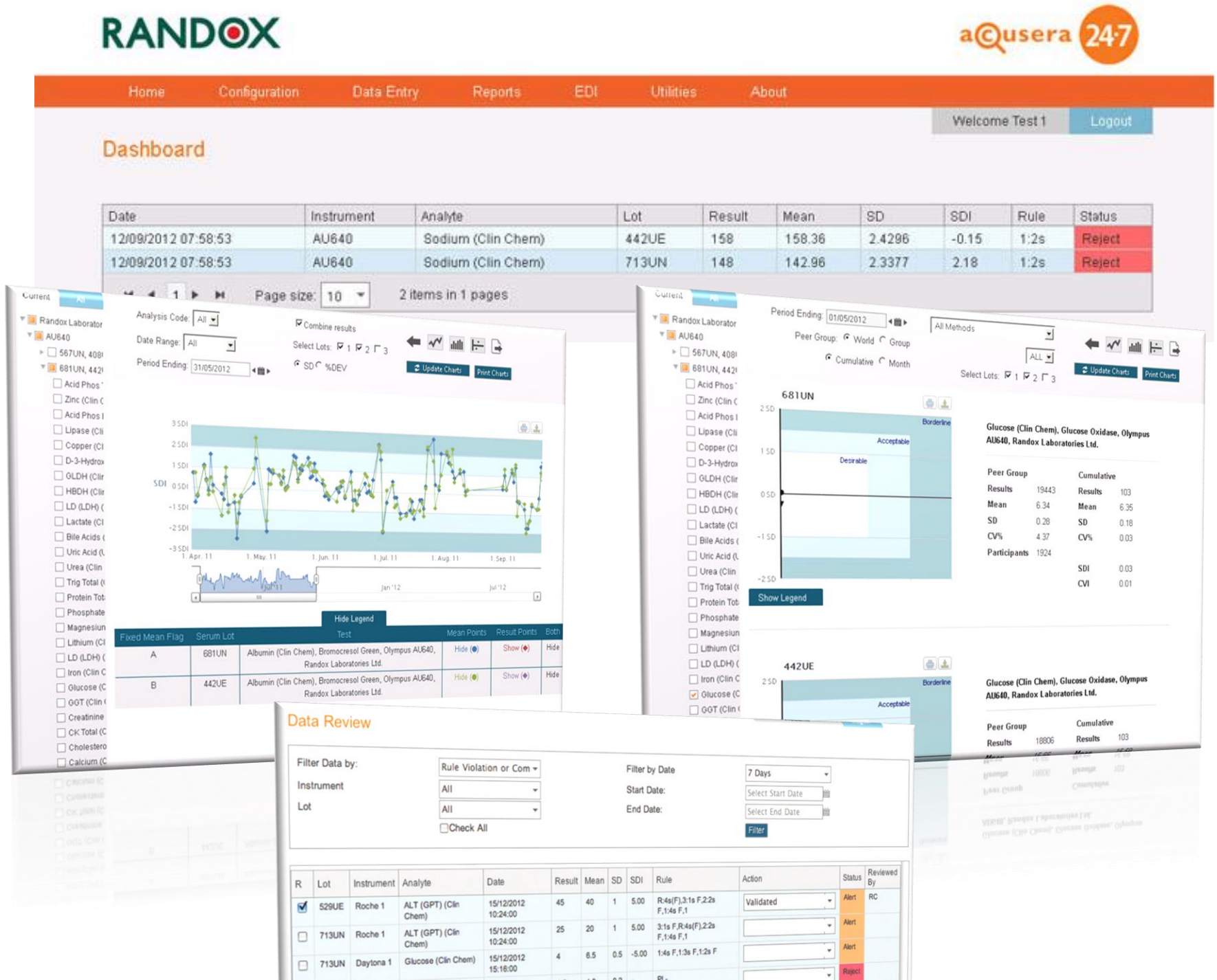
ALP	LABMED			WWR			FİRMA		
	Hedef	Min	Max	Hedef	Min	Max	Hedef	Min	Max
26471	102,0	89,8	114,2	102,9	80,49	125,31	108	66	150
26472	400,8	361,6	440,0	402,4	351,82	452,98	409	252	566



Çoklu cihaz karşılaştırması yapabilir miyim?

Sadece BioRad kontrolleri ile mi çalışılır




RANDOX
aQusera 24·7
Home
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EDI
Utilities
About
Welcome Test 1
Logout
Dashboard
Date
Instrument
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Lot
Result
Mean
SD
SDI
Rule
Status
12/09/2012 07:58:53
AU640
Sodium (Clin Chem)
442UE
158
158.36
2.4296
-0.15
1:2s
Reject
12/09/2012 07:58:53
AU640
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713UN
148
142.96
2.3377
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Page size: 10
2 items in 1 pages
Randox Laborator
AU640
Analysis Code:
Date Range:
Period Ending:
Combine results
Select Lots:
SD
%DEV
Update Charts
Print Charts
SDI
1. Apr. 11
1. May. 11
1. Jun. 11
1. Jul. 11
1. Aug. 11
1. Sep. 11
Jan '12
Jul '12
Hide Legend
Fixed Mean Flag
Serum Lot
Test
Mean Points
Result Points
Both
A
681UN
Albumin (Clin Chem), Bromocresol Green, Olympus AU640, Randox Laboratories Ltd.
B
442UE
Albumin (Clin Chem), Bromocresol Green, Olympus AU640, Randox Laboratories Ltd.
Period Ending:
Peer Group:
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Group
Cumulative
Month
All Methods
681UN
Borderline
Acceptable
Desirable
Show Legend
Glucose (Clin Chem), Glucose Oxidase, Olympus AU640, Randox Laboratories Ltd.
Peer Group
Results 19443
Mean 6.34
SD 0.28
CV% 4.37
Participants 1924
Cumulative
Results 103
Mean 6.35
SD 0.18
CV% 0.03
SDI 0.03
CVI 0.01
442UE
Glucose (Clin Chem), Glucose Oxidase, Olympus AU640, Randox Laboratories Ltd.
Peer Group
Results 18806
Cumulative
Results 103
Data Review
Filter Data by:
Rule Violation or Com
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529UE
Roche 1
ALT (GPT) (Clin Chem)
15/12/2012 10:24:00
45
40
1
5.00
R:4s(F),3:1s F,2:2s F,1:4s F,1
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Roche 1
ALT (GPT) (Clin Chem)
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3:1s F,R:4s(F),2:2s F,1:4s F,1
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Glucose (Clin Chem)
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0.5
-5.00
1:4s F,1:3s F,1:2s F
Alert
Reject

Roche laboratuvarlar arası karşılaştırma

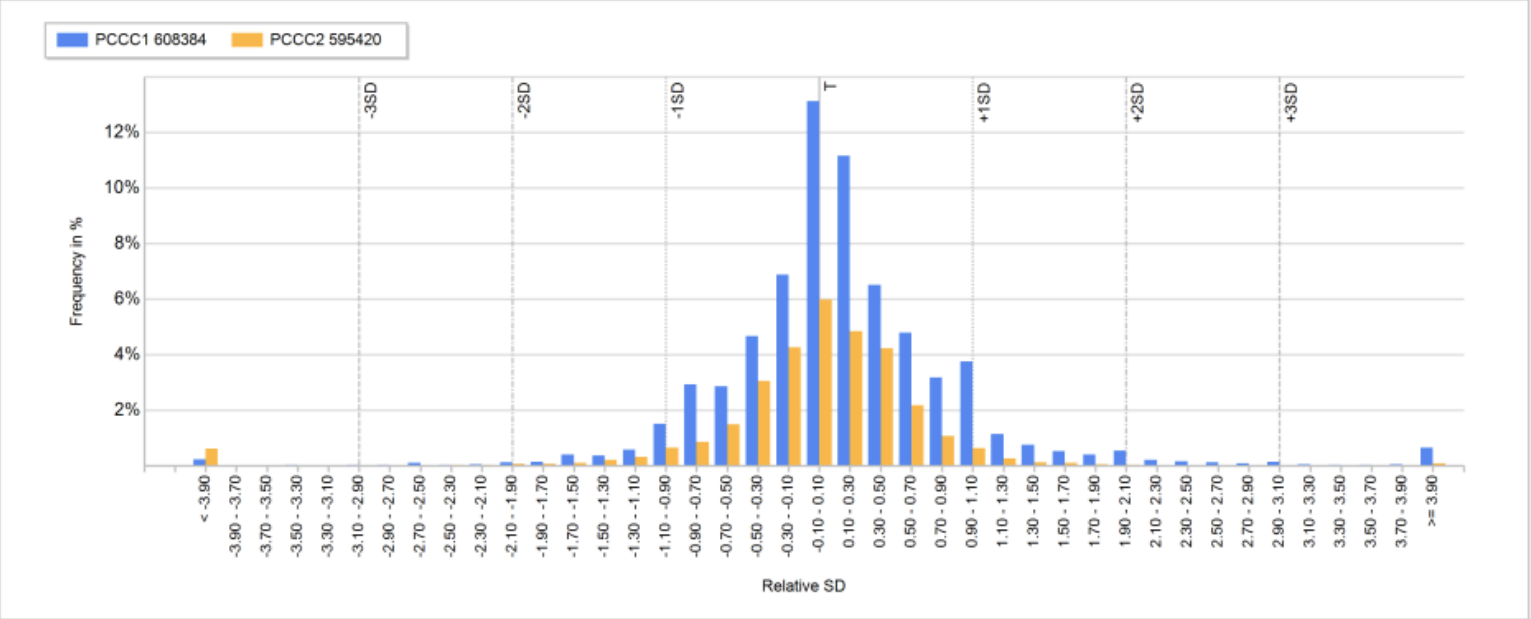
Turkey

cobas® e-LabPerformance Global Recovery

Zubeyda Nur Yilmaz
(zubeyda_nur.yilmaz@contractors.roche.com)

Period: 2023-04-01 - 2025-03-03
Module type: ISE c8000
Axis Scale: Relative SD

Test Name: ISE K (990); Reference: Manufacturer Target Value



Statistics

Test Name	Control Lot	Reagent Lot	Mean (mmol/l)	SD (mmol/l)	CV (%)	Modules Count	Lab Count	No. Results	No. Excluded Results	No. Control Expired Results	No. Reagent Expired Results	Manufacturer Target Value (mmol/l)	Manufacturer Target SD (mmol/l)
ISE K (990)	PCCC2 595420	N/A	7.46	0.11	1.5	288	113	72980	2822	0	0	7.45	0.22
ISE K (990)	PCCC1 608384	N/A	3.69	0.07	1.9	715	346	159496	4964	0	0	3.68	0.11

Technopath laboratuvarlar arası karşılaştırma

IAMQC® PEER - REPORTS

Six Sigma Report

- A detailed sigma table is also provided showing the full data used for the calculations. It can also be used as a comparison across instruments showing the individual sigma score per test on each instrument.

Sigma Detailed :

			Level 1								Level 2								Level 3							
Analyte	Units	Instrument	Mean	SD	%CV	Peer Avg. Mean	% Bias	% TEa	Sigma Calc	Sigma Score	Mean	SD	%CV	Peer Avg. Mean	% Bias	% TEa	Sigma Calc	Sigma Score	Mean	SD	%CV	Peer Avg. Mean	% Bias	% TEa	Sigma Calc	Sigma Score
25-OH Vitamin D	nmol/L	1	38.33	1.42	3.72	38.44	0.29	20.00	5.30	5	55.01	1.63	2.97	56.13	2.01	20.00	6.06	6	94.28	2.93	3.11	96.56	2.36	20.00	5.68	5
Alpha Fetoprotein (AFP)	IU/mL	1	5.11	0.15	2.90	4.97	2.83	20.00	5.92	5	60.73	1.12	1.84	60.65	0.14	20.00	10.81	6	148.20	2.57	1.74	148.46	0.17	20.00	11.42	6
Alpha Fetoprotein (AFP)	IU/mL	2	4.80	0.14	2.95	4.97	3.34	20.00	5.65	5	60.45	1.91	3.16	60.65	0.33	20.00	6.23	6	148.15	3.75	2.53	148.46	0.21	20.00	7.82	6
CA 125	U/mL	1	11.87	0.34	2.85	12.65	6.18	20.00	4.85	4	25.76	0.58	2.25	26.52	2.85	20.00	7.62	6	61.38	2.14	3.49	63.43	3.23	20.00	4.80	4
CA 125	U/mL	2	12.35	0.35	2.86	12.65	2.38	20.00	6.15	6	26.80	0.57	2.11	26.52	1.06	20.00	8.97	6	63.05	1.34	2.13	63.43	0.59	20.00	9.11	6
CA 15-3	U/mL	1	12.15	0.46	3.80	11.88	2.24	20.00	4.67	4	37.14	1.10	2.96	36.50	1.76	20.00	6.16	6	73.99	1.70	2.30	71.86	2.97	20.00	7.39	6
CA 15-3	U/mL	2	11.40	0.14	1.24	11.88	4.07	20.00	12.84	6	35.65	1.48	4.17	36.50	2.33	20.00	4.24	4	71.70	1.98	2.76	71.86	0.22	20.00	7.16	6
Carcinogenic Embryonic Antigen (CEA)	ng/mL	1	2.57	0.14	5.64	2.64	2.87	20.00	3.04	3	20.03	0.35	1.76	20.00	0.10	20.00	11.28	6	39.38	1.46	3.71	39.85	1.19	20.00	5.07	5

TECHNOPATH
CLINICAL DIAGNOSTICS

KK materyali nasıl üretilir?
Neden commutabil değildir?

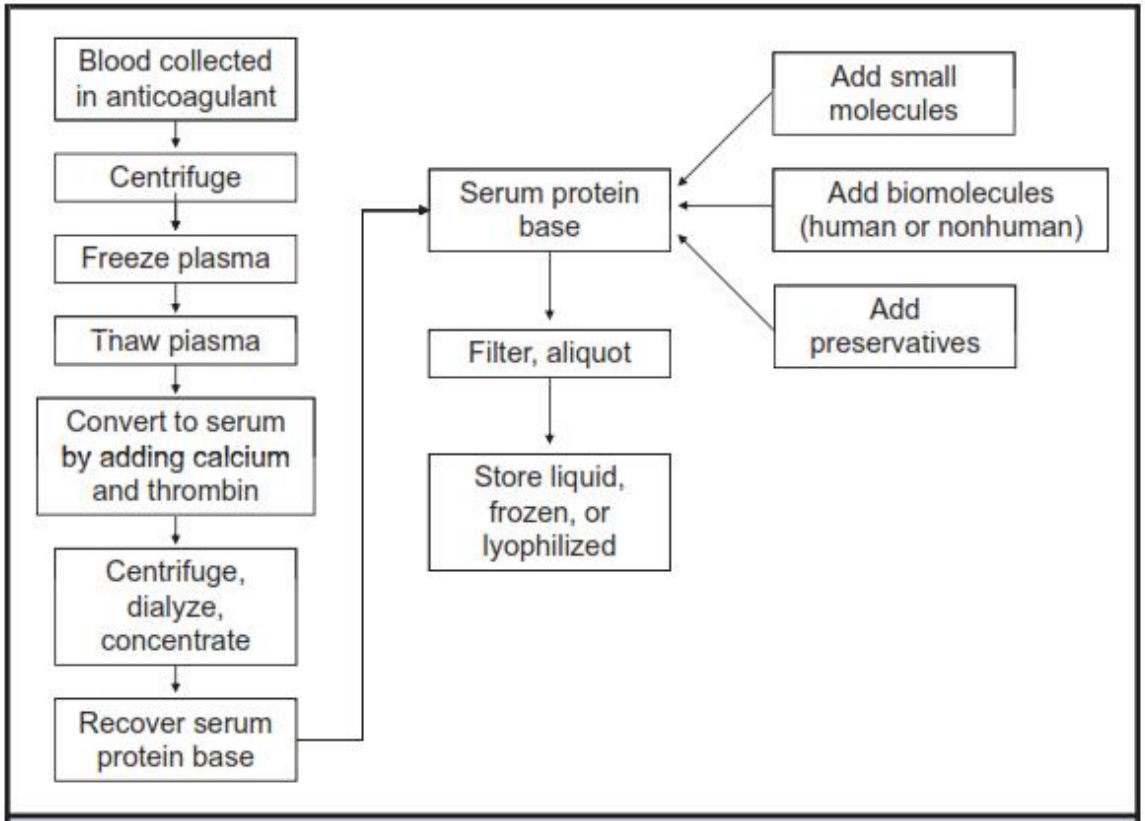


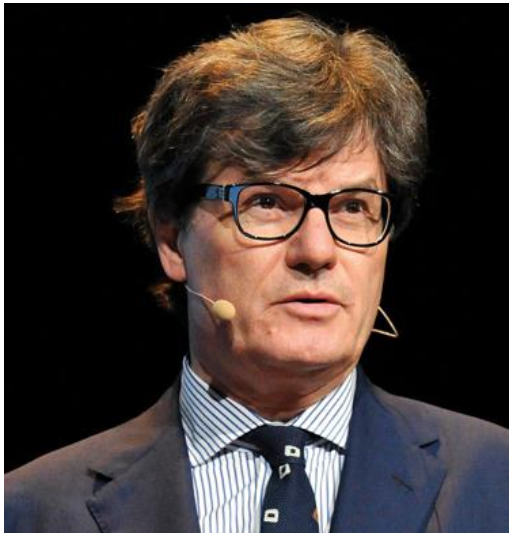
Fig. 2. Representative preparation steps for a serum-based PT/EQA sample to illustrate potential influences on its commutability.

5. Miller WG, Myers GL, Rej R. Why commutability matters. Clin Chem 2006;52:553–4.
6. Vesper HW, Miller WG, Myers GL. Reference materials and commutability. Clin Biochem Rev 2007;28:139–47.
7. CLSI. Characterization and qualification of commutable reference materials for laboratory medicine; approved guideline. CLSI document C53-A. Wayne (PA): CLSI; 2010.
8. International Organization for Standardization. In vitro diagnostic medical devices—measurement of quantities in biological samples—metrological traceability of values assigned to calibrators and control materials. ISO 17511. Geneva: ISO; 2003.
9. Miller WG. Specimen materials, target values and commutability for external quality assessment (proficiency testing) schemes. Clin Chim Acta 2003;327:25–37.

Clinical Chemistry 57:12
1670–1680 (2011)

Kalite kontrol matreryali !

- **Commutability**
- **Stabilite***
- **Materyal farklılıkları**
- **Homojenite**
- **Katılımcı sayısı**
- **Özel testler (idrar vs)**
- **İzlenebilirlik !!!!**



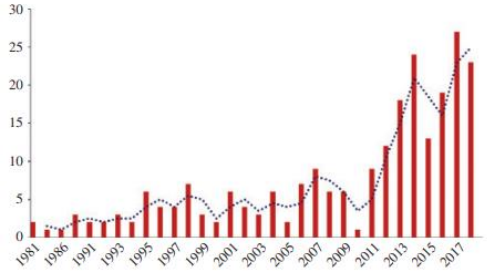
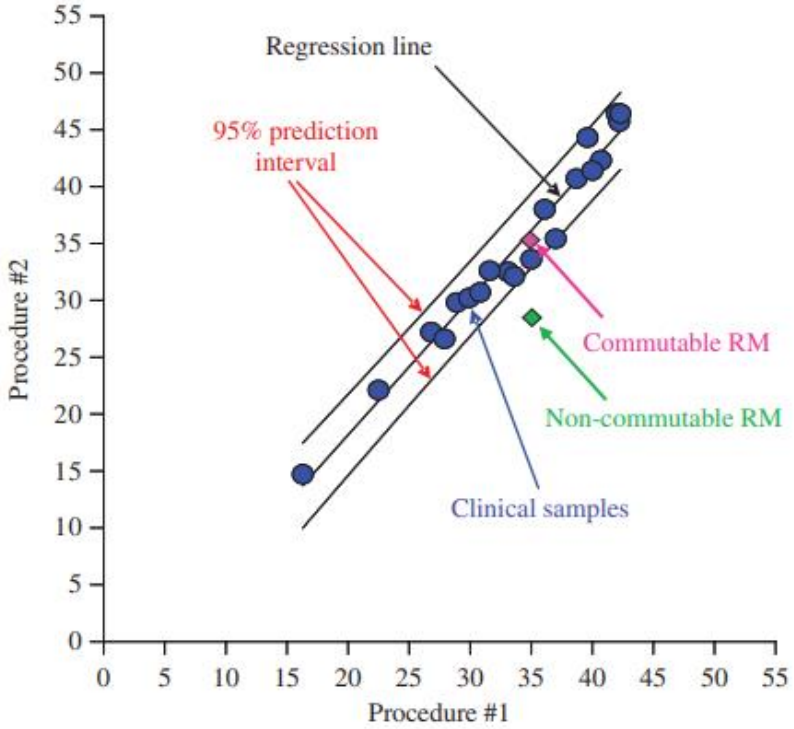
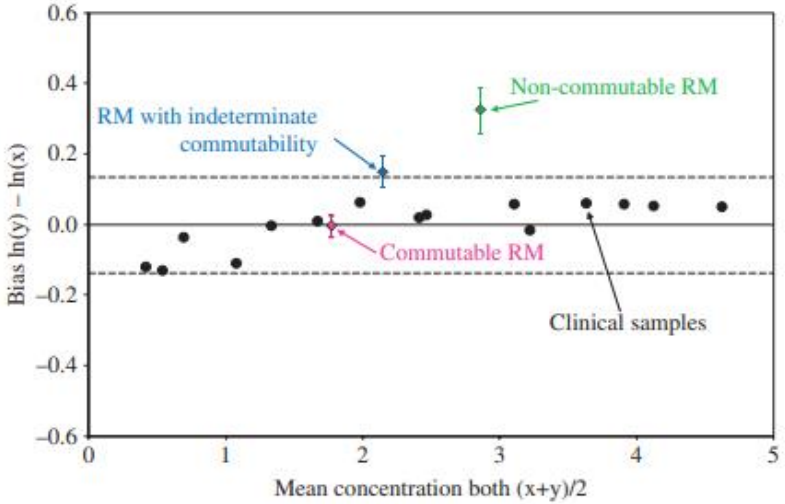


Figure 1: Number of hits retrieved from PubMed using the key word "Commutability" (www.ncbi.nlm.nih.gov/pubmed, Accessed January 2019).

•Clin Chim Acta. 2025 Feb 1:567:12009

CLSI EP14-ED4:2022 Evaluation of Commutability of Processed Samples, 4th Edition





Clin Chem Lab Med 2019; 57(7): 967–973

Uygulayabilir misin?

HAYIR

Commutability

Kontrol materyal matriksinin serum materyali ile uyumluluğudur

- **Stabilizatörler, Liyofilizasyon, İlave edilen analitin farklılığı ….**

Table 1
Examples of method-specific matrix-corrected target values for cholesterol[a]

Reference method value = 4.40 mmol/l				
Method	PT material result (mmol/l)	Calibration bias from FF[b] result (%)	Matrix bias (%)	Matrix-corrected target value[c] (mmol/l)
Hitachi/Roche	4.23	0.3	− 4.2	4.22 ± 0.02
Dimension	3.99	1.2	− 10.5	3.94 ± 0.02
Beckman	4.51	3.1	− 0.5	4.38 ± 0.02
Vitros	4.35	− 2.8	1.8	4.48 ± 0.02

- Miller G, Specimen materials, target values and commutability for external quality assessment (proficiency testing) schemes, Clinica Chimica Acta 327 (2003) 25–37
- Naito HK, Kwak YS, Hartfiel JL, et al. Matrix effects on proficiency testing materials: impact on accuracy of cholesterol measurement in laboratories in the nation's largest hospital system. Arch Pathol Lab Med 1993;117:345 – 51.

Pahalı ise kendimiz yapabilir miyiz ?

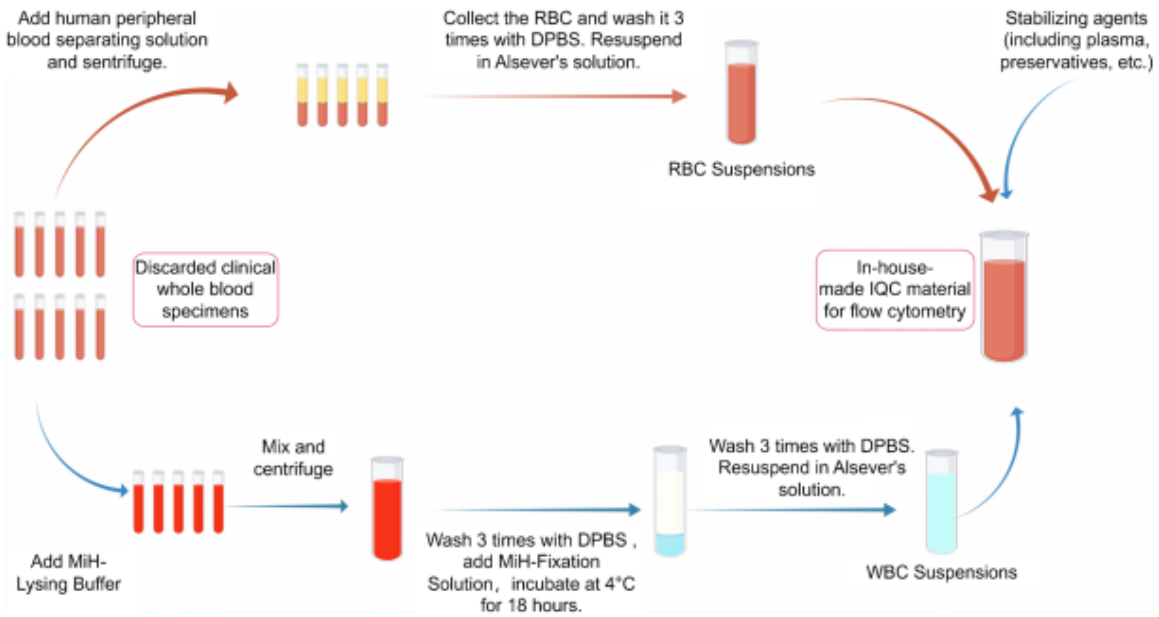


Fig. 1 Schematic illustration of the preparation process for IQC whole blood materials in clinical flow cytometry

Tam kan örneği

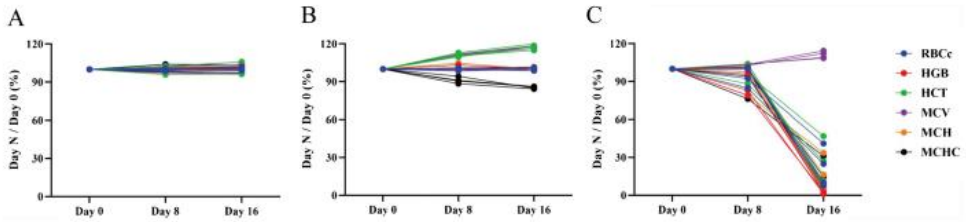


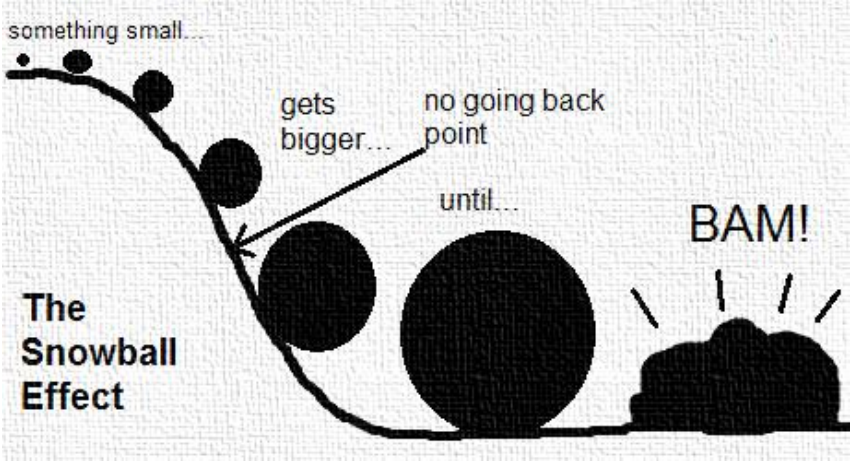
Fig. 3 Stability of cytological parameters in RBC suspensions mixed with different ABO blood groups under specific storage conditions. **A** Stability of mixed RBC suspensions resuspended in Alsever's solution. **B** Stability of mixed RBC suspensions resuspended in DPBS. **C** Stability of non-washed mixed samples. Alsever's solution demonstrated the best stabilizing effect

Chong HM et al. Cost-effective in-house-made whole blood materials for internal quality control in clinical flow cytometry analysis. Anal Bioanal Chem. 2025 Apr;417(10):2121-2132.

Kalite Kontrol materyalleri birbirinden farklıdır !!!

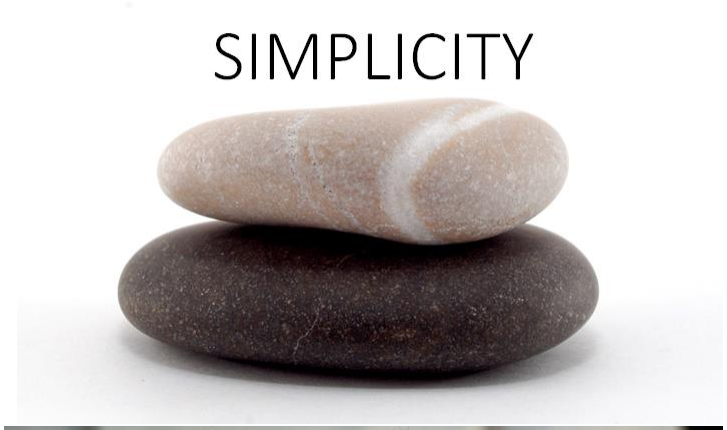
Çözülmesi gereken sorunlarımız

- Hedef değer (Biorad Unity, 7/24 ☺)
- Limitleri (SD)
- Aylık %CV takibi
- Üretici, 3. parti materyal
- Sıklıkları
- Kurallar
- Her analit için aynı , ayrı kural
- Liyofilize, sıvı materyal
- Maliyet
- Problem durumunda çözüm ?
- Uygulama farklılıkları (cihaz, lab vs)
- Cihaz, system ve LIS farklılıkları, sorunları
- İmmunoassay, tam kan, koagülasyon, idrar vs için farklı dizaynlar gereklidir
- > 200 testi ile aynı anda başetmek zorundayız



Literatür ve deneyimlerimizin sonucu

- **“Klasik” sistemin çok karmaşık ve çok pahalı** olduğu yönünde eleştiriler de yapılmaktadır.
- Birçok tıbbi laboratuvarın **bilimsel temellere dayanan bir IKK stratejisini hiç veya kısmen** (?) bazı analitler için uygulamaktadır.
- **Westgard kuralları ve analitik hedeflerin sıkça alıntılandığı**, ancak rutin tıbbi laboratuvar uygulamalarında nispeten ve **nadiren uygulandığı söylenebilir**.
- IKK stratejisi hakkındaki **bilimsel tartışmalar ile laboratuvarlardaki klinik gerçeklik** arasında önemli farklar olduğunu göstermiştir.
- Klasik” İKK stratejisinin önemli bir varsayımı, kullanılan kontrol örneklerinin hasta örnekleriyle aynı şekilde tepki vereceğidir **(commutability).***
- Maliyette önemli bir gider olmasına **ragmen İKK uygunsuzluk oranı çok düşük**. Bu durumun klinik çıktıları konusundada yeterli bilgimiz yok.
- Bazı araştırmacılar, tüm personelin belirlenen protokol ve uygulamaları titizlikle ve kolayca takip edebilmesi için IQC stratejisinin **basit tutulmasını önermektedir**.
- Bunlar göz önüne alındığında h**asta temelli kalite kontrol uyulamalarını (?)** önerenler (?) vardır.



Howanitz, P.J.; Tetrault, G.A.; Steindel, S.J. Clinical laboratory quality control: A costly process now out of control. Clin. Chim. Acta 1997, 260, 163–174

Westgard, S.A. Rhetoric versus reality? Laboratory surveys show actual practice differs considerably from proposed models and mandated calculations. Clin. Lab. Med. 2017, 37, 35–45.

Rosenbaum, M.W.; Flood, J.G.; Melanson, S.E.F.; Baumann, N.A.; Marzinke, M.A.; Rai, A.J.; Hayden, J.; Wu, A.H.B.; Ladror, M.; Lifshitz, M.S.; et al. Quality control practices for chemistry and immunochemistry in a cohort of 21 large academic medical centers. Am. J. Clin. Pathol. 2018, 150, 96–104

Badrick, T.; Loh, T.P. Developing an evidence-based approach to quality control. Clin. Biochem. 2023, 114, 39–42.

Gruber L, Hausch A, Mueller T. Internal Quality Controls in the Medical Laboratory: A Narrative Review of the Basic Principles of an Appropriate Quality Control Plan. Diagnostics (Basel). 2024 Oct 5;14(19):2223.

İlave neler yapıyoruz?

- Teknisyen ve **uzman onayları**
- Onay destek sistemleri
- Delta Check
- Kritik değer bildirimleri
- Retrospektik hasta sonuç incelemeleri
- Gerektiğinde laboratuvarlar arası karşılaştırma ve taze serum çalışması
- Klinisyen geri dönüşleri
- ISO 15189 Akreditasyonu

Laboratuvar uzmanı için “Analyse-it”