工欲善其事
必先利其器

醫檢品質管制工具的發展與演變

彭永祥

Make Good Use of Quality Laboratory Management Tools : Development and Evolution

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1

Main Theme 主題

工欲善其事
必先利其器

做好QC
✓ 善其事

如何做好
✓ 利其器

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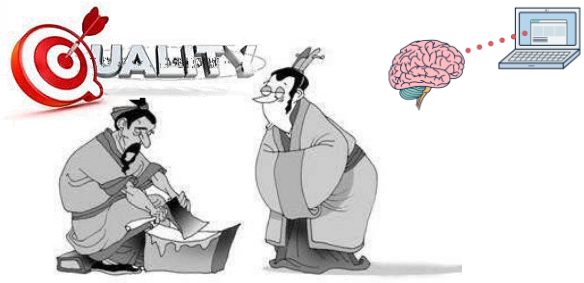
工欲利其器
必先善其事



3

What is (the purpose of) QC?

Why you have to do QC everv day (run)?

善其事

For what purposes?

目的何在?

4

每個實驗室對
品質控制
的程式/解釋可能不盡相同

Internal Quality Control or Invalid Quality Control?

The procedure/interpretation of QC may not be the same for every laboratory

IQC

5

Helps to Meet Accreditation *Requirements*

Quality Control vs Quality Compliance

6

Common Problems

普遍存在的問題
Error is the Enemy

- Bias (Systematic) 偏倚 ← EQA/PT
- Imprecision (Random) 不精密度 ← IQC
- Matrix (Interference) 分析干擾
- Mistakes (To Err is Human)

Standardization & Performance Verification

State-of-the-art Technology/Methodology

7

Quality System Essentials

QSEs

品質體系基礎 QSEs

What are those Requirements?

"In a system you have your core processes and procedures, *preanalytic, analytic, postanalytic*. But you also have processes and procedures that support those core components, as well as procedures for monitoring core processes, including quality indicators, quality control and proficiency testing results, self-inspections, external inspections, accrediting inspections."

"在一個系統中，你有你的核心流程和程式，分析前，分析中，分析後。但你也有流程和支援這些核心元件的程式，以及監測核心過程（包括品質）的程式指標，品質控制和能力測試結果，自檢，外部檢查，認證檢查"

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草案尚未批准

DRAFT INTERNATIONAL STANDARD
ISO/DIS 15189

NEW

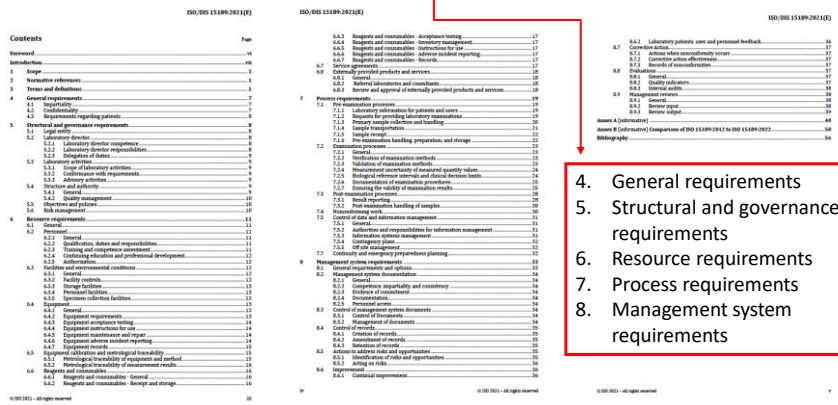
ISO/TC 212 Secretariat: ANSI

Voting begins on: 2021-10-19 Voting terminates on: 2022-01-11

Medical laboratories — Requirements for quality and competence

Laboratoires de biologie médicale — Exigences concernant la qualité et la compétence

ICS: 11.100.01; 03.120.10



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4. General requirements
5. Structural and governance requirements
6. Resource requirements
7. Process requirements
8. Management system requirements

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CAP TODAY

in 2021 Issues, ARTICLES, November 2021

Latest checklist takes quality management to next level

Valerie Neff Newitt

Program vs System

November 2021—In the latest edition of the laboratory general checklist, released in September, the requirements of the CAP Accreditation Programs have been edited to be more aligned with CAP 15189 (ISO 15189) accreditation requirements.

A CAP ISO 15189 Synergy Project Team, with members drawn from the CAP's Checklists, CAP 15189, and Quality Practices committees, has been working to build a philosophical and practical synergy between the CAP's Accreditation Programs and the ISO 15189 standard. Checklist changes made with this coordination in mind will ease the learning curve for laboratories that wish to seek CAP 15189 accreditation after earning accreditation through the CAP Laboratory Accreditation Program.

In the new checklist edition, the term "quality management program" has been replaced with "quality management system," and the requirements will make clear that finding and documenting quality gaps must be followed by effective corrective actions.

The decision to use the term "system" instead of "program" is not just a semantic juggle aimed at an adoption of ISO language, say those on the project team. Rather, it indicates the team's collective thinking at the core of these checklist revisions.

"Our thought process was that a 'system' designation helps all of us think in terms of bringing together a host of quality efforts in an interacting system of various components," explains Joe C. Rutledge, MD, a member of the ISO 15189 Synergy Project Team and CAP 15189 Committee. "We don't want checklist requirements that are just 'things to get done and out of the way.' If you move away from just checking off the boxes, you can build a better, more functional, and more effective system."

Checklists Committee chair Harris S. Goodman, MD, a member of the ISO 15189 Synergy Project Team and the CAP Commission on Laboratory Accreditation, says a quality management system is "more encompassing."

Dr. Goodman

In the new checklist edition, the term "quality management program" has been replaced with "quality management system," and the requirements will make clear that finding and documenting quality gaps must be followed by effective corrective actions. 必須隨後有效 糾正措施

"In a system you have your core processes and procedures—preanalytic, analytic, postanalytic. But you also have processes and procedures that support those core components, as well as procedures for monitoring core processes, including quality indicators, quality control and proficiency testing results, self-inspections, external inspections, accrediting inspections."

A quality management system must also include procedures for improving processes, says Dr. Goodman, chief of the Department of Pathology, Alameda Health System Highland Hospital, Oakland, Calif. "That includes a big one we tackled in 2019—investigation of nonconforming events. Now in 2021 we also must have an evaluation of the effectiveness of corrective actions. After all, if a corrective action doesn't work, you haven't accomplished anything. Phrases like 'we will continue to monitor' when a target is missed will not be enough. This is a significant change in mindset and in the requirements."

ISO 15189 project team member James H. Nichols, PhD, D(ABCC), says use of the term "system" strengthens the connection with ISO 15189 and that "system" is more frequently used across an international pathology population that has become familiar with ISO language.

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7.2.7 Ensuring the validity of examination results

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7.2.7.1 General

The laboratory shall have a procedure for monitoring the validity of results. The resulting data shall be recorded in such a way that trends are detectable and, where practicable, statistical techniques shall be applied to review the results.

NEW

7.2.7.2 Internal quality control (IQC)

a) The laboratory shall have an IQC procedure for monitoring the ongoing validity of examination results, according to defined criteria, that verifies the attainment of the intended quality and ensures consistent validity pertinent to clinical decision making.

ISO 15189

— The intended clinical application of the examination should be considered, as the performance specifications for the same measurand may differ in different clinical settings.

— The procedure should also allow for the detection of lot-to-lot reagent and/or calibrator variation of the examination method. To enable this, the use of third-party IQC material should be considered, either as an alternative to, or in addition to, control material supplied by the reagent or instrument manufacturer.

NOTE Monitoring of interpretations and opinions can be achieved through regular peer review of examination results.

b) The laboratory shall select IQC material that is fit for its intended purpose. Considerations when selecting IQC material shall include:

— its stability;

— that the matrix is as close as possible to that of patient samples;

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Trend 趨勢

— that the IQC material reacts to the examination method in a manner as close as possible to patient samples;

— that the IQC material provides a clinically relevant challenge to the examination method, has concentrations levels at or near clinical decision points and covers the relevant range of the examination method;

c) If appropriate IQC material is not available, the laboratory shall consider the use of other methods for internal quality control.

NEW

Examples of such other methods may include:

— trend analysis of patient samples, (e.g. with moving average of patient samples, or percentage of samples with results below or above certain values or associated with a diagnosis);

Trend Analysis

ISO 15189

— comparison of results for patient samples on a specified schedule to results for patient samples examined by an alternative procedure validated to have its calibration metrologically traceable to the same or higher order references as specified in ISO 17511:2020;

草案尚未批准

— retesting of retained patient samples.

a) IQC shall be performed at a frequency that is based on the stability and robustness of the examination method and the risk of harm to the patient from an erroneous result.

b) The resulting data shall be recorded in such a way that trends and shifts are detectable and, where applicable, statistical techniques shall be applied to review the results.

Trends & Shifts

c) IQC data shall be reviewed, at regular intervals and in a timeframe, which allows a meaningful indication of current performance.

d) IQC data shall be evaluated against pre-defined acceptance criteria. Where IQC fails the pre-determined criteria, corrective action shall be undertaken to rectify the failure.

Pre-defined Criteria

e) The laboratory shall have a procedure to prevent the release of patient results in the event of IQC failure.

— When IQC criteria are not fulfilled and indicate results are likely to contain clinically significant errors, the results shall be rejected and relevant patient samples re-examined after the error has been corrected (see 7.4).

— The laboratory shall also evaluate the results from patient samples that were examined after the last successful IQC event.

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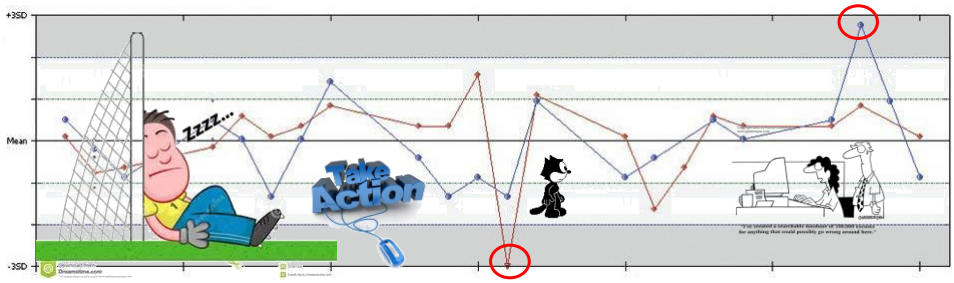
Trends, Drifts and Shifts

Trend
趨勢

- 5.6.2.3 Quality Control Data (ISO 15189:2012)
  - *Quality control data shall be reviewed at regular intervals to detect trends in examination performance that may indicate problems in the examination system. When such trends are noted, preventive actions shall be taken and recorded.*



NOTE Statistical and non-statistical techniques for process control should be used wherever possible to continuously monitor examination system performance.

注：宜儘量採用統計學和非統計學程序控制技術連續監測檢驗系統的性能

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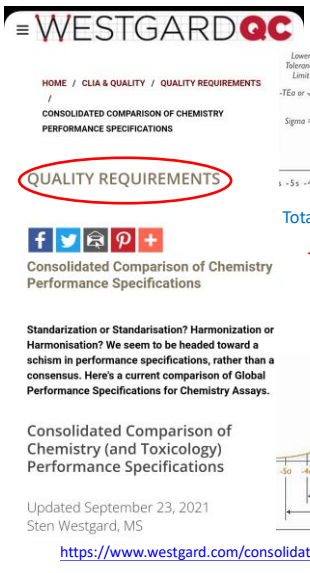
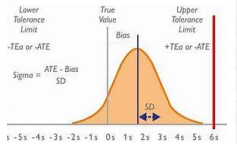
Quality Requirements

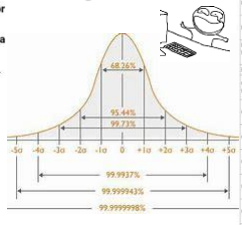
(Pre-define Acceptable Criteria)

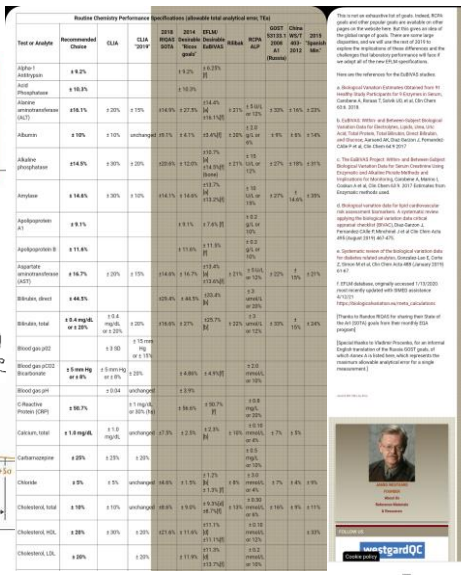




Total Allowable Errors, TEa

The bigger the TEa the higher the Sigma value





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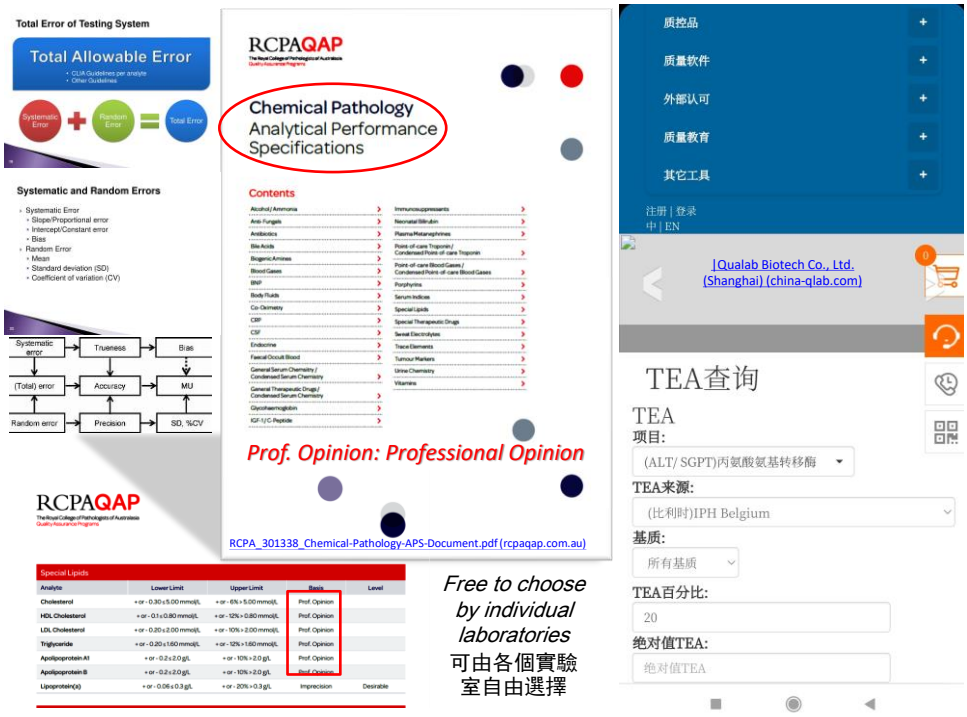

Free to choose by individual laboratories
可由各個實驗室自由選擇

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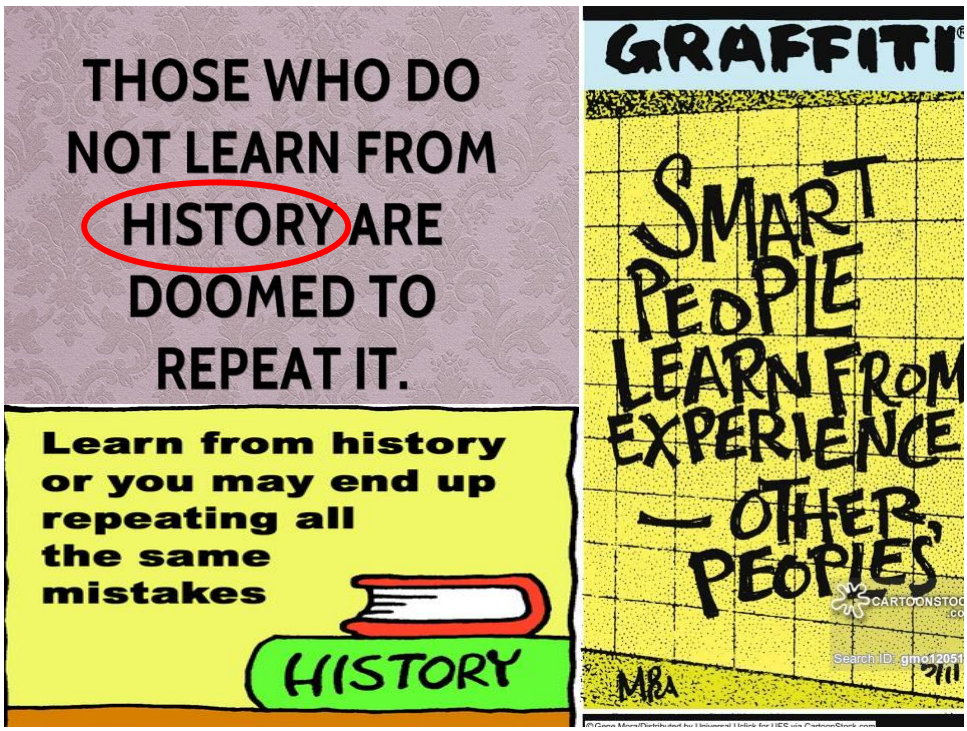

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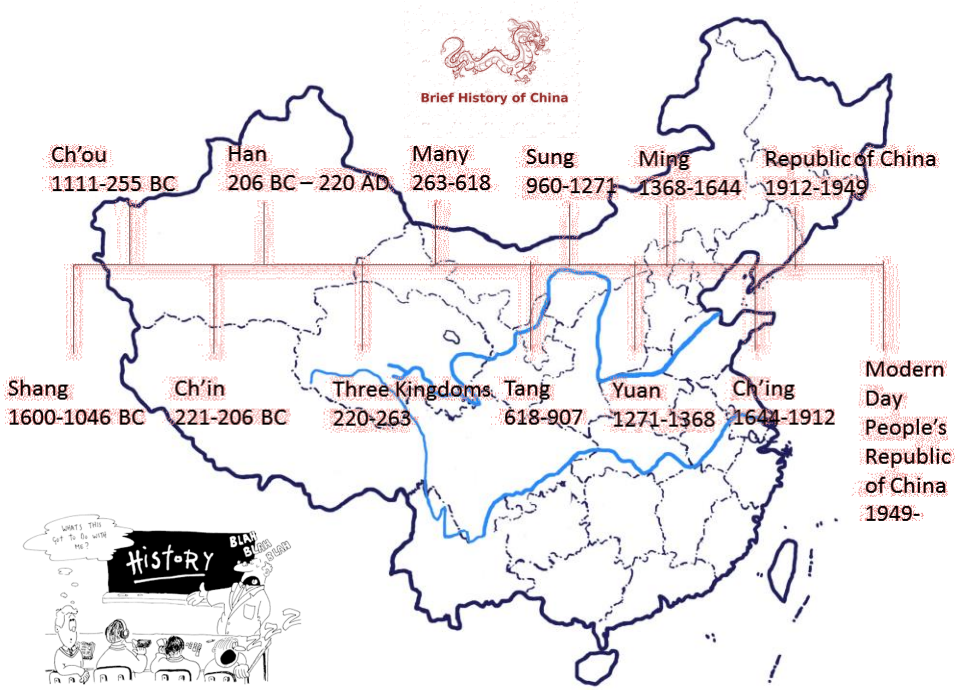

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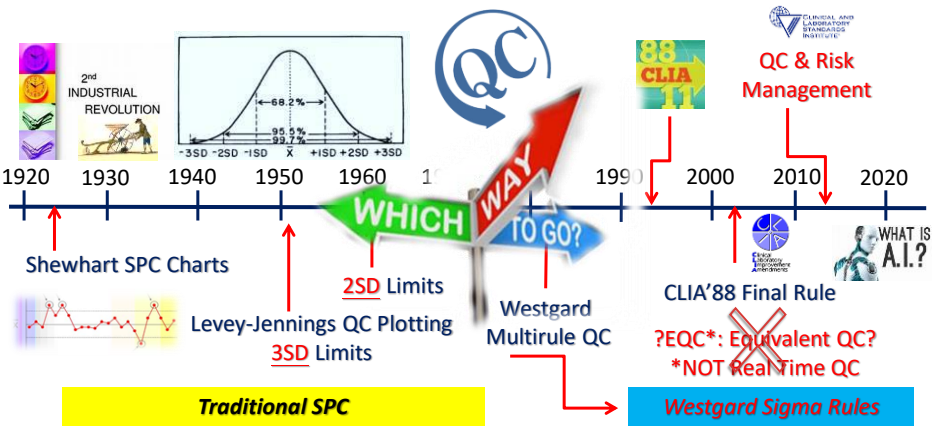
Development and Evolution of Traditional QC (SPC) in Clinical Laboratories

醫學實驗室質控的歷史演變與發展趨勢



The Center for Medicare and Medicaid Services (CMS) has adopted a new Quality Control (QC) option under the Clinical Laboratory Improvement Amendments (CLIA) called the Individualized Quality Control Plan (IQCP) from January 2, 2016.

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Fail to Plan = Plan to Fail

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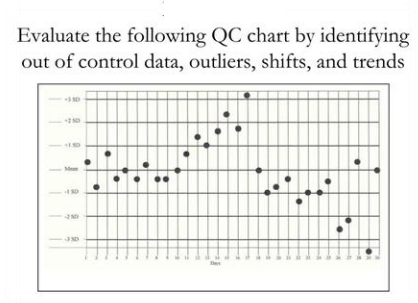
品質控制工具

- 為了要品質控制(QC)與品質改善(CQI)能有效的進行，必須對檢驗的各個階段制程有基本的認識制定全過程(Total Testing Process)品質保證措施
- 在品質計畫中的一個很重要的部分，就是分析過程中品質控制圖表(QC Chart)的製作



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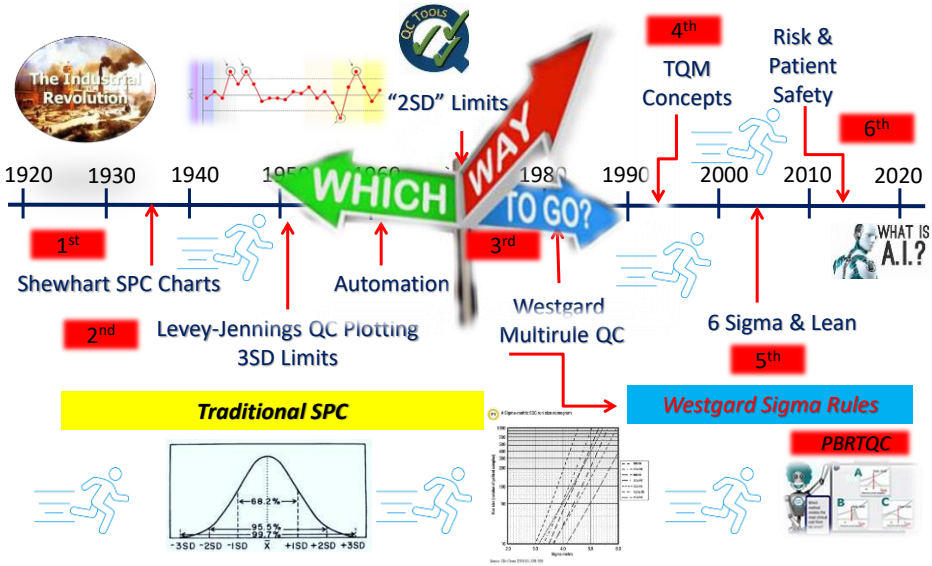
Development and Evolution of QC Tools in Clinical Laboratories

醫學實驗室質量管理工具的歷史演變與發展趨勢



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QC Management Tools

- *1940* In the beginning there was Shewhart
- *1950* Levey and Jennings 1st Generation QC
- *1960* Then there was automation
- *1976* 2nd generation QC "2SD rule"
- *1980* 3rd generation QC Westgard multirule
- *1990* TQM and 4th Generation QC
- *2000* Six Sigma and 5th Generation QC
- *2010* Risk-based 6th Generation QC
- *2022* QC for the Future, what's next?

https://www.westgard.com/history-and-future-of-qc.htm

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SPC Tools

- Power Function Graphs
  - *Clin Chem 1979;25:863-9.*
- Critical-Error Graphs
  - *Clin Chem 1990;36:230-3.*
- QC Selection Grids
  - *Clin Lab Sci 1990;3:271-8.*
- OPSpecs Chart
  - *Clin Chem 1992;38:1226-33.*
- QC Validator
  - *Clin Chem 1997;43:400-3.*
- EZ Rules 3 computer programs
  - *Westgard JO. Assuring the Right Quality Right. Chapter 11. How to use the EZRules 3 computer program. Madison WI: Westgard QC, Inc., 2007.*

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SPC主要是通過各種控制圖和質控規則來達到進行品質分析、品質控制和品質改進的目的

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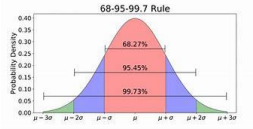
實驗室常用質控規則介紹

- Levey-Jennings質控圖是最普及、最簡單、最常用的方法
  - 優點：方便易行，其質控規則僅為單獨的1_{2s}或1_{3s}，即僅以一個規則(X±2s或X±3s作為質控限)來判斷分析批在控或失控。
  - 局限性：僅涉及一種質控規則而未同時涉及多個質控規則。相對簡單粗糙，往往不能滿足更高的質控要求
  - 如使用具有X±2s質控限的Levey-Jennings質控圖，當每批使用2個質控物時，其假失控概率往往是不可接受的



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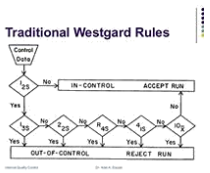
Westgard多規則的局限性

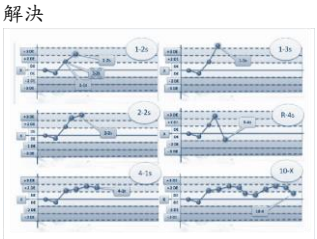
1.違背了特定質控規則可指出誤差的類型
隨機誤差或系統誤差

- 誤差類型很重要，因為它可對誤差出現的可能原因或其來源提供線索
  - 違背2_{2s}，4_{1s}或10_{X}規則說明存在系統誤差;
  - 當系統誤差很大時，也可觀測到違背1_{3s}規則;
  - 違背1_{3s}或R_{4s}規則提示為隨機誤差
- 隨機誤差很大時，則可能違背任何規則
- 發生隨機誤差時，提示了幾種可能的原因：
  - 試劑或測定條件不穩定
  - 計時、移液、或個人技術的變異的。



2.違背的規則並不是發生誤差類型的絕對指征，但它提示調查問題的最初方向

- 當違背涉及同一批兩個不同濃度的質控物時，通常不可能是質控物本身的問題而更可能是校準物、儀器校準、試劑空白等因素的問題，後者將在同一方向影響所有的測定值
- 誤差的可能來源，依賴於特定的測定方法及使用的試劑和儀器的性質。分析人員應借助于廠家的檢修故障指南、儀器和試劑變化的記錄、實驗記錄並根據本人所積累的經驗來使問題儘快得到正確的解決



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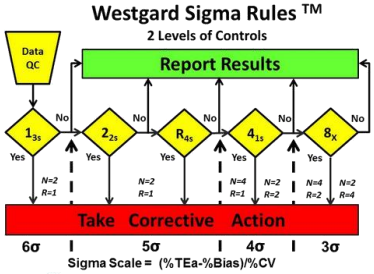
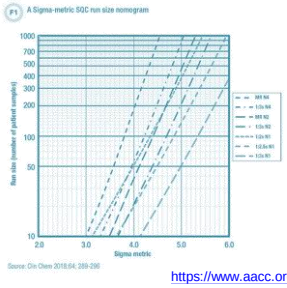
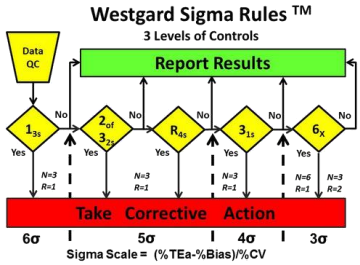
Sigma-Metric SQC

http://www.westgard.com/westgard-sigma-rules.htm





To look for faster and simpler tools that will help laboratories select the right SQC for their own applications.



https://www.aacc.org/publications/cln/articles/2019/june/challenging-the-status-quo-on-quality-control

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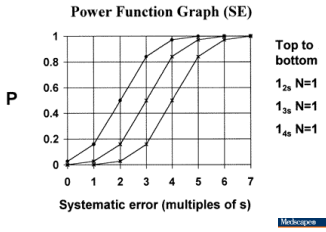
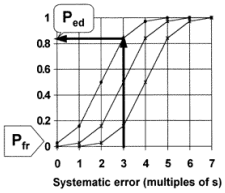
Power Function Graph
功效函數圖
P_{ed} vs P_{fr}

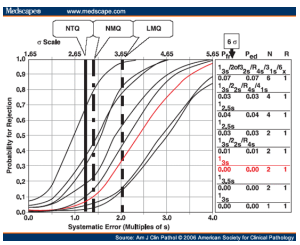


Top to bottom
1_{2s} N=1
1_{3s} N=1
1_{4s} N=1

How do you determine P_{ed} and P_{fr}?

- Read probability for error detection (P_{ed}) at point on power curve corresponding to critical-sized error
- Read probability for false rejection (P_{fr}) from y-intercept





https://www.westgard.com/lesson4.htm

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QUALAB 质量源于理念 Ideas Behind Quality

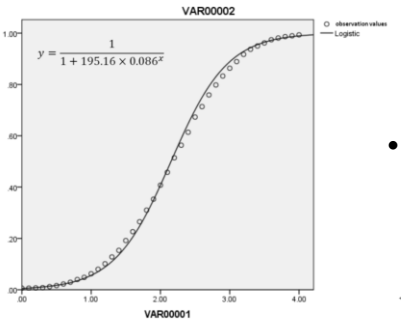
基於實際室內質控策略的討論以及能效曲線的制定

目的：1，推導出更符合實際且誤差檢出率較高的室內質控策略模型2，繪製更加科學且連續功效函數圖的通用方法。

方法：類比不同的質控判斷模型對P_{ed}進行比較，用電腦類比資料的方法以及SPSS統計軟體擬合分別得到P_{ed}觀測值、理論值以及擬合值，通過比較分析最終得到繪製功效函數的通用方法。

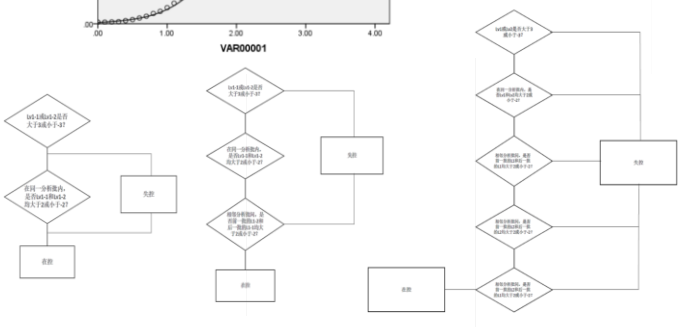
結果：1）相對單水準質控僅批內觸發模型，在其他影響因素（批長度、質控頻率、質控規則組合）固定的情況下，使用多水準質控能夠顯著提高誤差檢出率。2）當引入分析批概念後，使用可以跨批判定的質控規則（2-2s，4-1s等）組合且批內、跨批同時觸發時，相對原模型，在影響因素（質控水準數、批長度、質控頻率、質控規則組合）不變的情況下，能顯著提高該質控規則組合的誤差檢出率。3）用電腦類比資料的方法使用P_{ed}擬合值可以更有效且更精確的獲得P_{ed}，繪製更為科學且連續的功效函數圖。

結論：有效的利用TEa、Sigma水準等量化參數對每個質控專案設計個性化的質控策略很可能成為今後管理工作中的新突破。



關鍵點：

- 雙水準質控，每批次檢測1次質控，分析批內和跨批觸發的質控判斷模型可以獲得最高的誤差檢出率
- 用電腦類比資料的方法使用P_{ed}擬合值可以獲得更有效且更精確的P_{ed}



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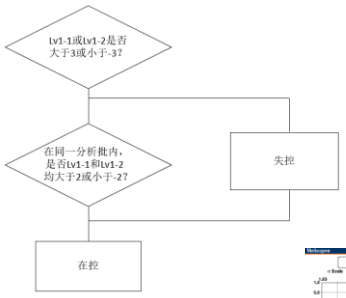

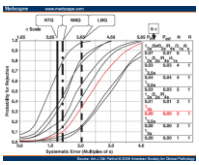

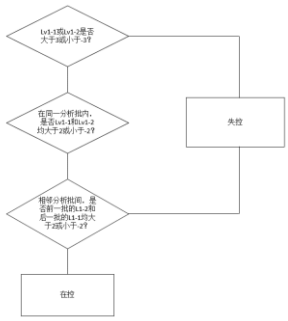

能效曲線（Power Function Curve）已提出多年，以往文獻報導的能效曲線制定都以電腦類比資料的方式，SD以0.1為單位增長取P_{ed}觀測值，如今在P_{ed}觀測值、理論值以及擬合值的比較下，發現P_{ed}擬合值和理論值的相關性極佳，可以使用P_{ed}擬合值來代替P_{ed}觀測值，從而獲得更為科學且連續的功效函數圖。基於功效函數圖的質控規則選擇是風險管理的基礎。

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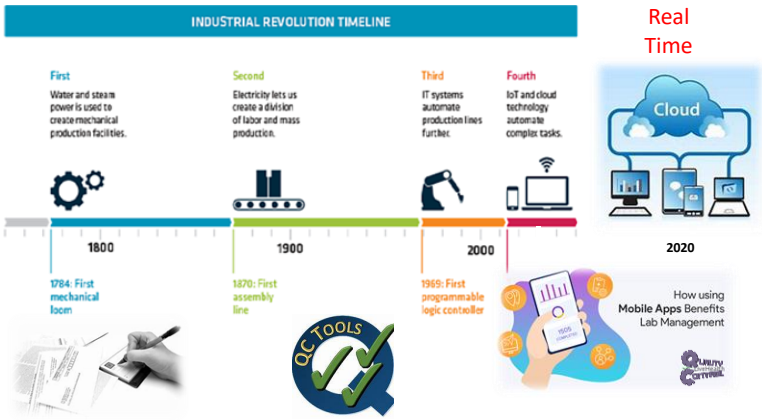
The Fourth Revolution Timeline



The laboratory is also one of the professions in the "*industrial world*"

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PBRTQC可以在一定程度上彌補IQC的不足，因此PBRTQC成為近期質控領域的研究熱點

Need for PBRTQC

"Real Time" Quality

vs

"Too-Late-Time" Quality

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平均值概念

移動平均品質控制 (MAQC)

Moving Average for Continuous Quality Control: Time to Move to Implementation in Daily Practice?

Letters to the Editor

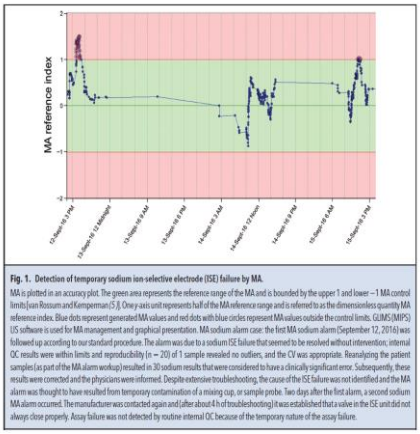

Fig. 1. Detection of temporary sodium ion-selective electrode (ISE) failure by MA.
MA is plotted in an accuracy plot. The green area represents the reference range of the MA and is bounded by the upper 1 and lower −1 MA control limits [van Rossum and Kemperman (5)]. One y-axis unit represents half of the MA reference range and is referred to as the dimensionless quantity MA reference index. Blue dots represent generated MA values and red dots with blue circles represent MA values outside the control limits. GLIMS (MIPS) US software is used for MA management and graphical presentation. MA sodium alarm case: the first MA sodium alarm (September 12, 2016) was followed up according to our standard procedure. The alarm was due to a sodium ISE failure that seemed to be resolved without intervention; internal QC results were within limits and reproducibility (n = 20) of 1 sample revealed no outliers, and the CV was appropriate. Reanalyzing the patient samples (as part of the MA alarm workup) resulted in 30 sodium results that were considered to have a clinically significant error. Subsequently, these results were corrected and the physicians were informed. Despite extensive troubleshooting, the cause of the ISE failure was not identified and the MA alarm was thought to have resulted from temporary contamination of a mixing cup, or sample probe. Two days after the first alarm, a second sodium MA alarm occurred. The manufacturer was contacted again and [after about 4 h of troubleshooting] it was established that a valve in the ISE unit did not always close properly. Assay failure was not detected by routine internal QC because of the temporary nature of the assay failure.

Clinical Chemistry 2017, 63:1042-1043

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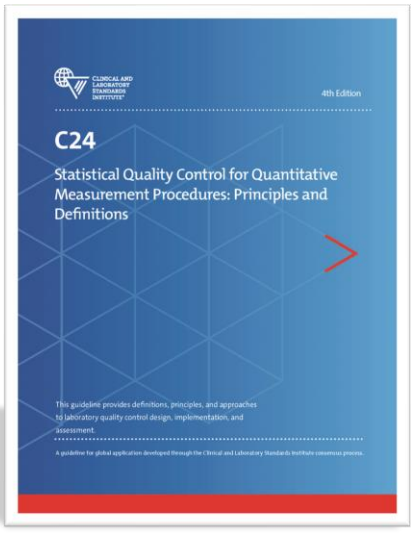
基於病人樣本即時實驗室品質控制（PBRTQC）

- 2016年臨床與實驗室標準化委員會（CLSI）更新了室內質控標準，提出需要基於風險評估確定室內質控的頻率、質控品濃度水準與失控判斷規則。而若要將失控造成的風險控制在更低水準，則需要額外增加人力和物力成本。PBRTQC則可在不額外增加人力和物力成本的情況下即時監測檢測系統的穩定性和判斷有無“失控”情況。



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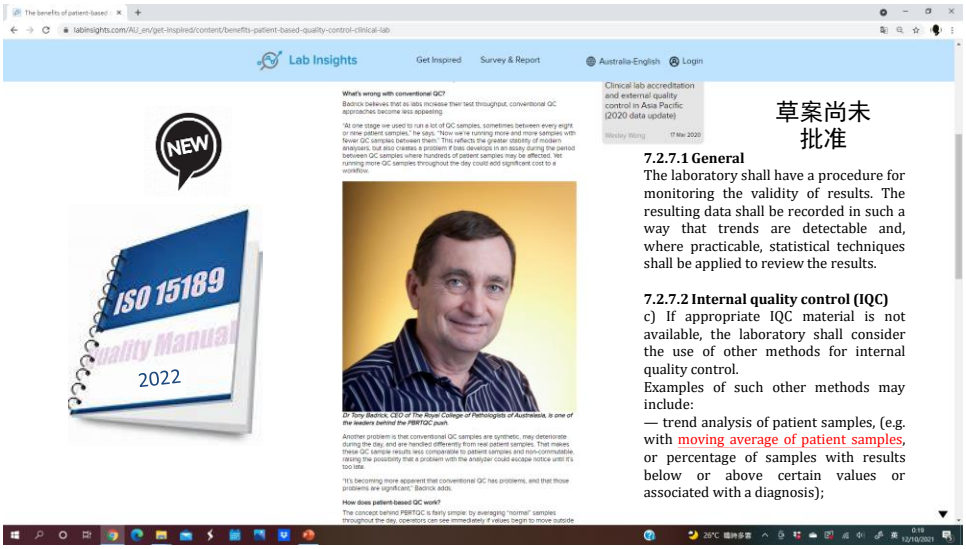
The Benefits of Patient-Based Quality Control in the Clinical Lab



https://www.labinsights.com/AU_en/get-inspired/content/benefits-patient-based-quality-control-clinical-lab

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基於患者的即時品質控制 (PBRTQC) 的益處局限性和爭議以及實踐背後的證據

- 近年來，人們對“舊”平均值概念重新產生興趣，現在通常稱為移動平均品質控制 (MA QC) 或基於患者的即時品質控制 (PBRTQC)。然而，本次審查旨在解決有關 PBRTQC 的一些爭議，同時也指出了 PBRTQC 的當前狀態。
- 該評論提供了某些新描述的優化和驗證方法的背景。它還表明如何設計包含 PBRTQC 的 QC 計畫以提高效率和/或（成本）效率。
- 此外，它還討論了有關獲取 PBRTQC 設置的複雜性、iQC 的替換和軟體功能要求的爭議。
- 最後，它提供了 PBRTQC 附加值和實用性的證據。展望最近的發展，優化和驗證實驗室特定 PBRTQC 程式的類比方法的可用性和可用性使醫學實驗室能夠在日常實踐中實施 PBRTQC。
- 此外，這些方法使得通過兩項前瞻性“臨床”研究和其他調查證明 PBRTQC 的實用性和附加價值成為可能。儘管內部 QC 仍將是任何 QC 計畫的重要組成部分，但應用 PBRTQC 現在可以顯著提高其性能和（成本）效率。這些方法可以通過兩項前瞻性“臨床”研究和其他調查來證明 PBRTQC 的實用性和附加值。
- 儘管內部 QC 仍將是任何 QC 計畫的重要組成部分，但應用 PBRTQC 現在可以顯著提高其性能和（成本）效率。這些方法可以通過兩項前瞻性“臨床”研究和其他調查來證明 PBRTQC 的實用性和附加值。儘管內部 QC 仍將是任何 QC 計畫的重要組成部分，但應用 PBRTQC 現在可以顯著提高其性能和（成本）效率。

https://www.x-mol.com/paper/1390922102527905793

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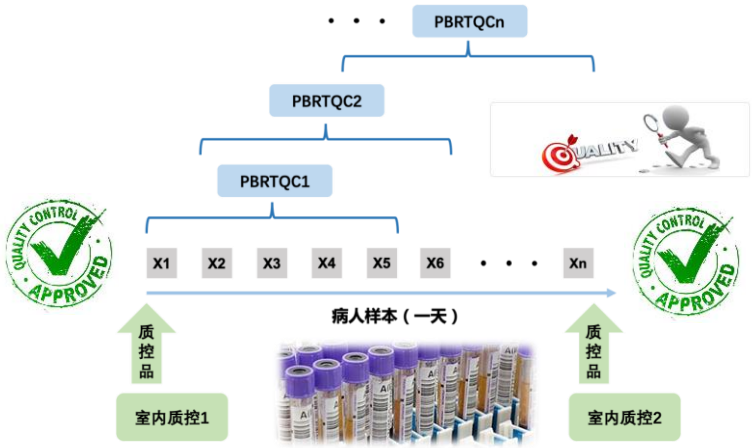
PBRTQC和室內質控對比



圖中顯示了PBRTQC和室內質控的特點，PBRTQC可以在每個病人樣本結果生成後進行計算，可即時監控檢測系統。室內質控根據質控計畫，在不同時間點對檢測系統進行監控。

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ISO 15189:2022 Requirements 7.2.7.2 (c) Examples

草案尚未批准


Clinical Biochemistry

Internal quality control: Moving average algorithms outperform Westgard rules

- Patient-based real-time quality control (PBRTQC) is a laboratory tool for monitoring the performance of the testing process. It includes well-established procedures like Bull's algorithm, average of nomals, moving median, moving average (MA) and exponentially (weighted) MAs. Following the setup and optimization processes, a key step prior to the routine implementation of PBRTQC is the verification and documentation of the performance of the PBRTQC as part of the laboratory quality system.

Internal quality control: Moving average algorithms outperform Westgard rules - ScienceDirect

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Clinica Chimica Acta 495 (2019) 625–629

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journal homepage: www.elsevier.com/locate/cca

Review

Recommendations for laboratory informatics specifications needed for the application of patient-based real time quality control

Tze Ping Loh[a], Mark A. Cervinski[b,h], Alex Katayev[c], Andreas Bietenbeck[d], Huub van Rossum[e,f], Tony Badrick[g,*], on behalf of the International Federation of Clinical Chemistry and Laboratory Medicine Committee on Analytical Quality

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Keywords:
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Moving averages
Middleware
Data mining

ABSTRACT

Patient based real time Quality Control (PBRTQC) algorithms provide many advantages over conventional QC approaches including lower cost, absence of commutability problems, continuous real-time monitoring of performance, and sensitivity to pre-analytical error. However, PBRTQC is not as simple to implement as conventional QC because of the requirement to access patient data as well as setting up appropriate rules, action protocols, and choosing best statistical algorithms. These requirements need capable and flexible laboratory informatics (middleware). In this document, the necessary features of software packages needed to support PBRTQC are discussed as well as recommendations for optimal integration of this technique into laboratory practice.

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Clinical Chemistry 67:10 (2021)
1342–1350

Laboratory Management

Regression-Adjusted Real-Time Quality Control

Xincen Duan,[a,†] Beili Wang,[a,†] Jing Zhu,[a] Chunyan Zhang,[a] Wenhai Jiang,[a] Jiaye Zhou,[a] Wenqi Shao,[a] Yin Zhao,[a] Qian Yu,[a] Luo Lei,[a] Kecek Leung Yiu,[a] Kim Thiam Chia,[a] Baishen Pan,[a,*] and Wei Guo[a,*]

BACKGROUND: Patient-based real-time quality control (PBRTQC) has gained increasing attention in the field of clinical laboratory management in recent years. Despite the many upsides that PBRTQC brings to the laboratory management system, it has been questioned for its performance and practical applicability for some analytes. This study introduces an extended method, regression-adjusted real-time quality control (RARTQC), to improve the performance of real-time quality control protocols.

METHODS: In contrast to the PBRTQC, RARTQC has an additional regression adjustment step before using a common statistical process control algorithm, such as the moving average, to decide whether an analytical error exists. We used all patient test results of 4 analytes in 2019 from Zhongshan Hospital, Fudan University, to compare the performance of the 2 frameworks. Three types of analytical error were added in the study to compare the performance of PBRTQC and RARTQC protocols: constant, random, and proportional errors. The false alarm rate and error detection charts were used to assess the protocols.

RESULTS: The study showed that RARTQC outperformed PBRTQC. RARTQC, compared with the PBRTQC, improved the trimmed average number of patients affected before detection (ANPed) at total allowable error by about 50% for both constant and proportional errors.

CONCLUSIONS: The regression step in the RARTQC framework removes autocorrelation in the test results, allows researchers to add additional variables, and improves data transformation. RARTQC is a powerful framework for real-time quality control research.

Introduction

Patient-based real-time quality control (PBRTQC) has gained increasing attention in recent years. Many reports have addressed the advantage of implementing PBRTQC as a secondary tool for internal quality control (IQC) to minimize the risk of quality incidence. PBRTQC can monitor analytical processes continuously, is not affected by the choice of control, and incurs only development or software costs [1–4].

However, many issues regarding the performance of PBRTQC have not yet been satisfactorily addressed. Recent studies by our team and that of Bietenbeck [5, 6] have pointed out the ineffectiveness of PBRTQC protocols on analytes with high robust normalized spread or highly skewed and disperse distribution, such as alanine aminotransferase (ALT). We also reported a potential loss of performance of optimized PBRTQC if naturally occurring or nonclinically significant trends or seasonality exist for an analyte. Such autocorrelation could cause the false alarm rate (FAR) to be unpredictable and the curves in error detection chart to be asymmetric for the testing set or future data [5]. In addition, most efforts to develop PBRTQC protocols have focused on univariate statistical process control (SPC) algorithms. Ng et al. [7] first developed subpopulation protocols for hospitalized and ambulatory patients to add additional clinical information. Their study showed that using subpopulation protocols, such as hospitalized patient protocols in the morning, can improve their performance, most notably the average number of patients affected before detection (ANPed). However, using the subpopulational protocol is a cumbersome approach to add multivariate information to PBRTQC protocols. When we have more than 2 grouping variables, this approach becomes inefficient to implement in the real world.

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回歸調整的即時品質控制

近年來，基於患者的即時品質控制（PBRTQC）在臨床實驗室管理領域受到越來越多的關注。儘管 PBRTQC 為實驗室管理系統帶來了許多好處，但它的性能和對某些分析物的實際適用性一直受到質疑。本研究引入了一種擴展方法，即回歸調整即時品質控制(RARTQC)，以提高即時品質控制協定的性能。

Clinical Chemistry 67:10
Laboratory Management
1342–1350 (2021)

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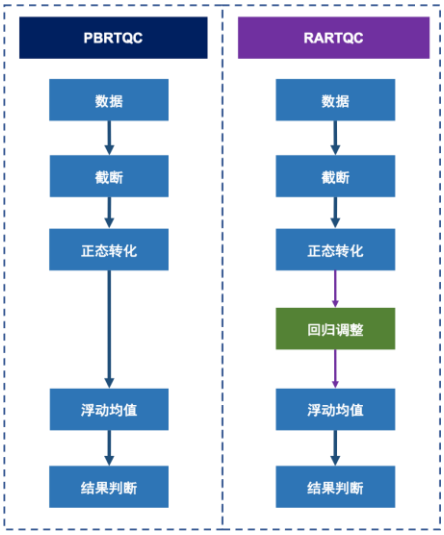
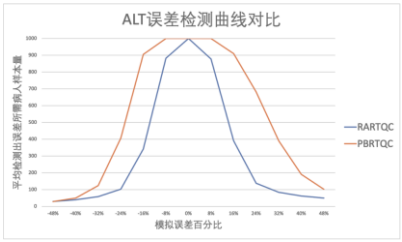
RARTQC和PBRTQC的結構對比



RARTQC可通過回歸分析納入影響檢測結果的不同因素，如患者的年齡、性別、診斷資訊等，計算回歸殘差以調整這些因素對檢測結果的影響，使得輸入常規浮動均值的資料分佈更加集中和對稱，大幅提高浮動均值演算法檢出誤差的性能



使用誤差檢測曲線表示模型的性能，橫坐標是誤差水準，縱坐標是誤差出現後平均檢測出誤差所需的患者樣本量（ANPed），相同誤差水準時，ANPed越低的模型，越能更快發現誤差，因此曲線越低說明該模型誤差檢出的敏感度越高

https://new.qq.com/omn/20211023/20211023A08D7P00.html

复旦大学附属中山医院检验科郭玮、潘柏申、王蓓丽教授团队开发的回归调整实时质控系统 RARTQC（Regression-adjusted real-time quality-control）发表于国际检验医学期刊《Clinical Chemistry》（DOI：10.1093/clinchem/hvab115）

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A major challenge associated with the implementation of Moving Average QC is getting your laboratory specific optimized settings. Most laboratories have software available that support MA calculations such as analyzer software, middleware or laboratory information systems. To program MA calculations several settings have to be selected that include: assay result inclusion criteria (truncation limits), calculation algorithm (mean, median, EWMA, XbarB) and a variable (mean of 5, 10, 25, 50, etc.).

Until today there was no simple method available for laboratories that supports selection of all of these variables based on the MA systematic error detection properties. To make it even more challenging; optimized MA QC is rather laboratory specific.

MA Generator is the first available tool that allows medical laboratories to get their own laboratory specific MA settings to obtain optimal error detection!

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IFCC Paper

Tze Ping Loh*, Andreas Bietenbeck, Mark A. Cervinski, Huub H. van Rossum, Alex Katayev and Tony Badrick, on behalf of the International Federation of Clinical Chemistry and Laboratory Medicine Committee on Analytical Quality

Recommendation for performance verification of patient-based real-time quality control

https://doi.org/10.1515/cclm-2019-1024
Received October 4, 2019; accepted January 13, 2020

Abstract: Patient-based real-time quality control (PBRTQC) is a laboratory tool for monitoring the performance of the testing process. It includes well-established procedures like Bull's algorithm, average of normals, moving median, moving average (MA) and exponentially (weighted) MAs. Following the setup and optimization processes, a key step prior to the routine implementation of PBRTQC is the verification and documentation of the performance of the PBRTQC as part of the laboratory quality system. This verification process should provide a realistic representation of the performance of the PBRTQC in the environment it is being implemented in, to allow proper risk assessment by laboratory practitioners. This document focuses on the recommendation on performance verification of PBRTQC prior to implementation.

Keywords: evaluation; moving average; moving median; patient-based quality control; patient-based real-time quality control; verification.

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Huub H. van Rossum: The Netherlands Cancer Institute, Amsterdam, the Netherlands; and Hunarios, Amsterdam, the Netherlands
Alex Katayev: Laboratory Corporation of America Holdings, Elon, NC, USA
Tony Badrick: RCPA Quality Assurance Programs, St Leonards, Sydney, Australia

Background

Patient-based real-time quality control (PBRTQC) is a laboratory tool for monitoring the performance of the testing process. It includes well-established procedures like Bull's algorithm, average of normals, moving median, moving average (MA) and exponentially (weighted) MAs [1–7]. More recently, novel techniques such as the moving standard deviation, moving delta, moving sum of outliers and moving percentiles have been described [8–10]. These techniques have gained increasing attention owing to maturing statistical methodology, improved information technology capabilities and increasing awareness of the limitations of internal quality control systems [9, 11–16]. Indeed, Bull's algorithm (a form of average of normals) is routinely used in clinical hematology laboratories.

Recent successful implementations and proof of value of PBRTQC in complex laboratories have further given confidence in this technique [17–19]. The cost savings and potential ability to withhold results until the verification of performance of the testing system are further advantages that fit well in the austere and risk-aware climate in laboratory medicine practice.

The International Federation of Clinical Chemistry and Laboratory Medicine PBRTQC Working Group has recently produced separate documents that provide guidance on the informatics considerations [20] and implementation of PBRTQC [21]. These documents serve to facilitate the adoption of PBRTQC in routine laboratories, and readers are strongly encouraged to read them to familiarize themselves with key concepts before this document. A key step prior to the routine implementation of PBRTQC is the verification and documentation of the performance of the PBRTQC as part of the laboratory quality system. This verification process should provide a realistic representation of the performance of the PBRTQC in the environment it is being implemented in, to allow proper risk assessment by the laboratory practitioners. This document focuses on the recommendation on performance verification of PBRTQC prior to implementation.

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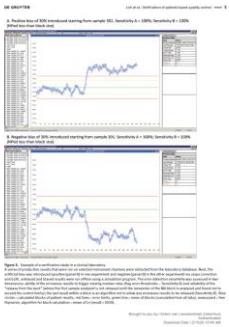
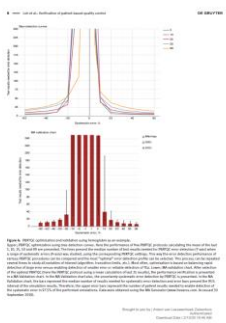
PBRTQC系統的開發與驗證





- PBRTQC系統的核心包括演算法和各種參數，如計算樣本數、分組、截斷值等超參數和模型參數控制限等
- 開發流程主要包括提取歷史檢測資料進行清理、分析、必要時的正態轉換，以及構建“虛擬日”和人工加誤差等
- 首先在類比資料上進行建模，即通過電腦運行確定演算法與各種參數的最優值。隨後在另一個相對的資料集上進行驗證、評估誤差檢出的性能與時效性。最終在真實世界中進行驗證與不斷優化

Clin Chem Lab Med 2020, 58: 1205-1213

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Customer Expectation for a QC Tool (Software)

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Quality Laboratory Management Tools

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QC Software軟體

What is desirable?

- Implement Optimum QC Rules（應用最佳質控規則）
- Identify Analytical Goals（確定分析目標）
  - Agreed clinical targets（公認的臨床目標）
  - RCPA-AACB Analytical Performance Specifications (APS) formerly called Allowable Limits of Performance (ALP)
  - CLIA targets
- Set up a QC program with the aid of QC software which has a high probability of detecting an error (P_{ed}) together with a low false-rejection rate (P_{fr})
- 在質控軟體的說明下設定質控程式，該程式既具有高的誤差檢出率，又具有低的誤拒絕率）.

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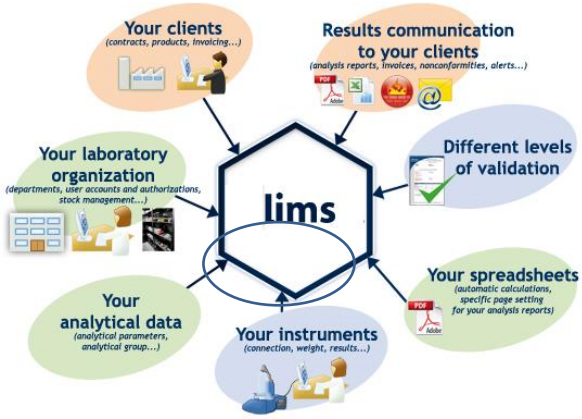
Quality Management Tools
(Not only QC)



品質管制系統可以系統地掌握問題，尋找到實現目的的最佳手段，廣泛應用於品質管制中，如品質管制因果圖的分析、品質保證體系的建立、各種品質管制措施的開展等

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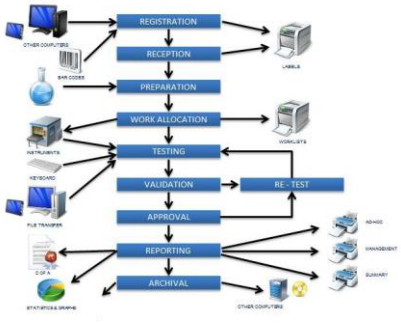
Automate and Centralize Lab QC



What Are Those Key Benefits of Automation and Centralization of Lab QC?

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Accreditation Requirements

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Laboratories look at the extra functionality of the upgrade LIS option and decide that, for the price, they don't get much more functionality than what they already have with their existing LIS. Middleware is inexpensive, from both a financial viewpoint and in terms of time to implement and maintain. Furthermore, the better middleware products are licensed in a manner that allows labs to buy only the functionality they need at the time.

實驗室會查看升級 LIS 選項的額外功能，並決定，就價格而言，他們獲得的功能不會比現有 LIS 已經擁有的功能多得多。從財務角度以及實施和維護時間來看，中介軟體都很便宜。此外，更好的中介軟體產品的許可方式允許實驗室僅購買當時需要的功能。

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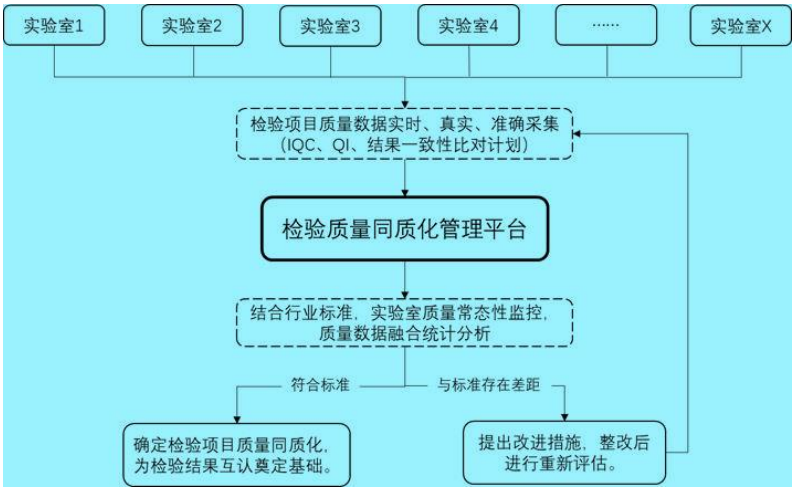
The Ultimate Laboratory Quality Control Software

Cloud Real-Time Application



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Quality Management System
Not just a Program

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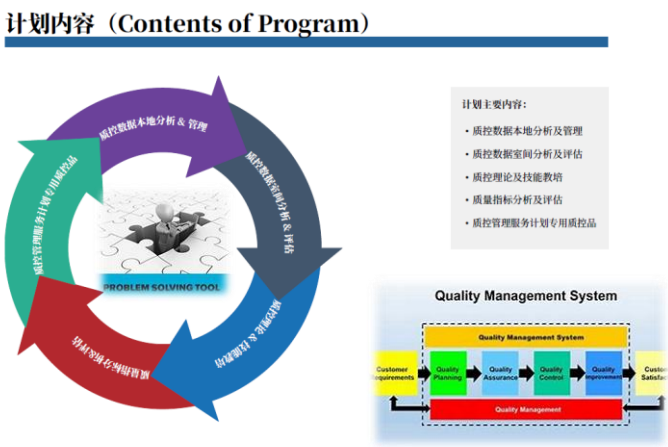
Quality Management System
Not just a Program

04



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Quality Management System
Not just a Program

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Eliminate the Need to Enter Data onto Paper or into a PC Program

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Measurement Uncertainty (MU)

?The Role of QC Software

Monthly Summary Report

5.5.1.4 Measurement uncertainty of measured quantity values
被測量值的測量不確定度 (ISO 15189:2012)

ISO 15189

實驗室應為檢驗過程中用於報告患者樣品被測量值的每個測量程式確定測量不確定度。實驗室應規定每個測量程式的測量不確定度性能要求，並定期評審測量不確定度的評估結果。

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草案尚未批准

7.2.4 Measurement uncertainty of measured quantity values

a) The measurement uncertainty (MU) of measured quantity values shall be evaluated and maintained for its intended use, where relevant.

NOTE ISO/TS 20914:2019 provides detail on these activities together with examples.

b) MU estimations shall be regularly reviewed.

c) For measurements where estimation of MU is not possible or applicable, the rationale for exclusion from MU estimation shall be documented.

d) MU information shall be made available to laboratory users on request.

e) When users have inquiries on MU, the laboratory's response should take into account other sources of uncertainty, such as, but not limited to biological variation.

f) If the qualitative result of an examination relies on a test which produces quantitative output data and is defined as positive or negative, based on a threshold, MU in the output quantity should be estimated using representative positive and negative samples.

g) For examinations with nominal data, MU in intermediate measurement steps or quality control results which produce quantitative data should also be considered for key (high risk) parts of the process.

h) MU should be taken into consideration when performing verification, when relevant.

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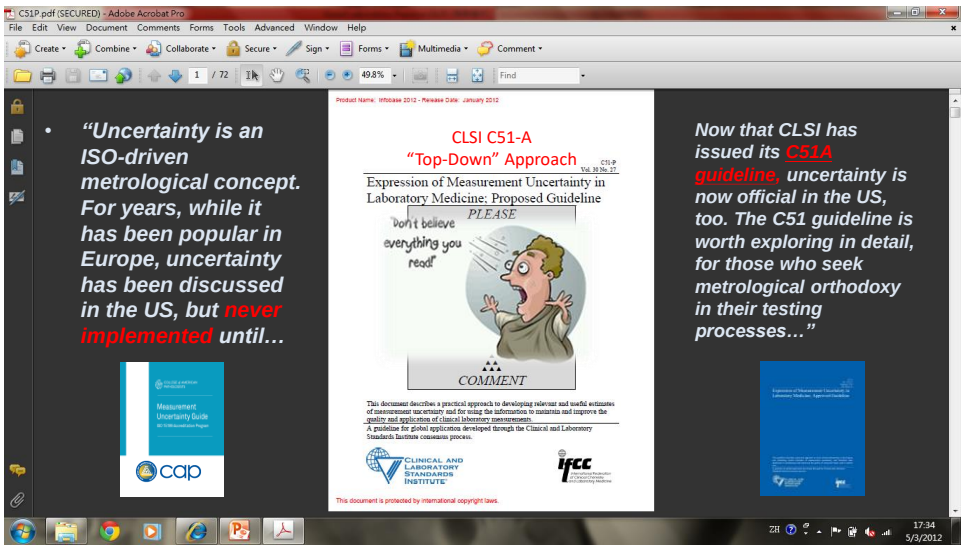
Expression of Measurement Uncertainty in Laboratory Medicine



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Monthly Summary Report

The laboratory must have a system of long-term monitoring of internal quality control results to assess method performance.

SIEMENS DIMENSION RXL - A

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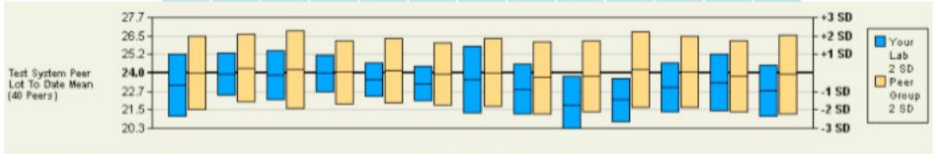

	LTD	Dec 2008	Nov 2008	Oct 2008	Sep 2008	Aug 2008	Jul 2008	Jun 2008	May 2008	Apr 2008	Mar 2008	Feb 2008	Jan 2008
Your Lab Mean	23.2	23.9	23.9	24.0	23.5	23.3	23.5	22.9	21.8	22.2	23.0	23.3	22.8
Your Lab SD	1.0	0.7	0.8	0.6	0.6	0.6	1.1	0.8	1.0	0.7	0.8	0.9	0.8
Your Lab CV %	4.4	2.9	3.4	2.5	2.4	2.5	4.7	3.6	4.5	3.3	3.6	4.0	3.7
Your Lab N	375	31	30	31	31	32	30	31	31	33	31	29	30
Test System Peer Mean	24.0	24.3	24.2	24.0	24.1	23.9	24.0	23.7	23.8	24.2	24.0	23.8	23.9
SDI	-0.7	-0.4	-0.3	-0.1	-0.5	-0.6	-0.4	-0.6	-1.7	-1.6	-0.9	-0.4	-0.8
CVI	0.9	0.6	0.6	0.6	0.5	0.6	1.0	0.7	0.9	0.6	0.7	0.8	0.7
Peers	40	24	30	29	29	30	31	31	34	34	31	26	16

A mid-term SD

A period of 6 months should be practical in many laboratories and matches the CLSI recommendation for establishing control limits

Multiply by a coverage factor of 2

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Calculations (Estimates) of Uncertainty

Standard Expanded Uncertainty

$U = SD \times 2$

Uses only imprecision in the form of a standard deviation (SD) to calculate the uncertainty and then multiplied by 2 for expanded (or 95% Confidence interval) uncertainty.

Consistent with the requirements per RCPA and NABL India

Combined Expanded Uncertainty (+ Interlaboratory Bias)

$U = 2 \times \sqrt{(SD^2 + \left(\frac{Bias}{\sqrt{3}}\right)^2 + SDBias^2)}$

Uses imprecision, bias and SD of the bias (uncertainty of the bias) and then multiplied by 2 for expanded uncertainty.

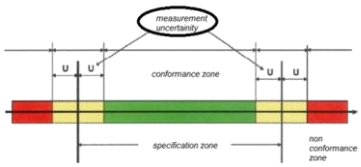
Consistent with the recommendations per SH GTA 14 (France)

Combined Expanded Uncertainty (+ Calibration Uncertainty)

$U = 2 \times \sqrt{(SD^2) + Cal\ U^2}$

Uses imprecision and Calibrator uncertainty (provided by Calibrator manufacturer) and then multiplied by 2 for expanded uncertainty.

Consistent with the recommendations per SH GTA 14 (France)



ISO 15189 **does not recommend a methodology to calculate measurement uncertainty**. However, since ISO is a member of the working groups of the Guide to the uncertainty of measurement (GUM) and the Vocabulary of international metrology (VIM), it is presumed that an "Uncertainty approach" () model is mandatory.

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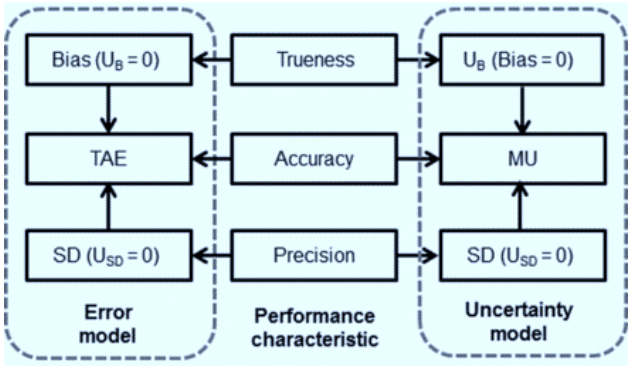
Comparison of Error Model with Uncertainty Model showing measures used for Analytical Characteristics of Trueness, Accuracy, and Precision



Clinical Chemistry, Volume 64, Issue 4, 1 April 2018, Pages 636–638

Clin Chem, Volume 64, Issue 4, 1 April 2018, Pages 636–638, https://doi.org/10.1373/clinchem.2017.284406

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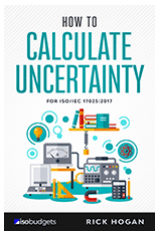
Free Uncertainty Calculator Software

- Below is a list of uncertainty calculator software that you can download and install on your computer so you can begin estimating uncertainty.
- *1. Gum Tree Calculator*
  2. QMSys GUM Standard
  3. Metrodata GmbH GUM Workbench Pro
  4. MUKit – Measurement Uncertainty Kit
  5. NIST Uncertainty Machine
  6. Hewlett-Packard UnCal 3.2
  7. Uncertainty Sidekick
  8. NPL Measurement Uncertainty Software



8 Free Uncertainty Calculator Software You Can Download Now – isobudgets

Mostly for ISO 17025 Accreditation

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What's next?

利其器

Autoverification
(Patient Test Results)
Quality Indicators
(Total Testing Process)

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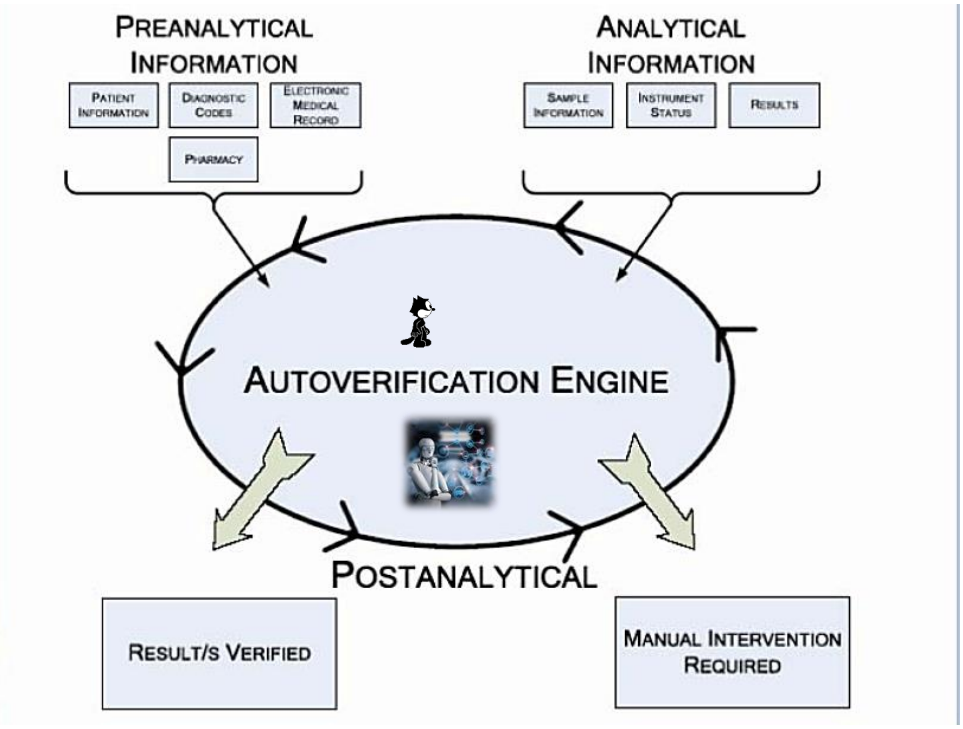

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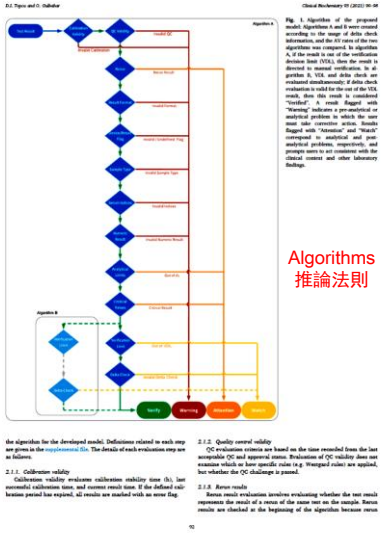

Algorithms
推論法則

Clinical Biochemistry 93: (2021) 90–98

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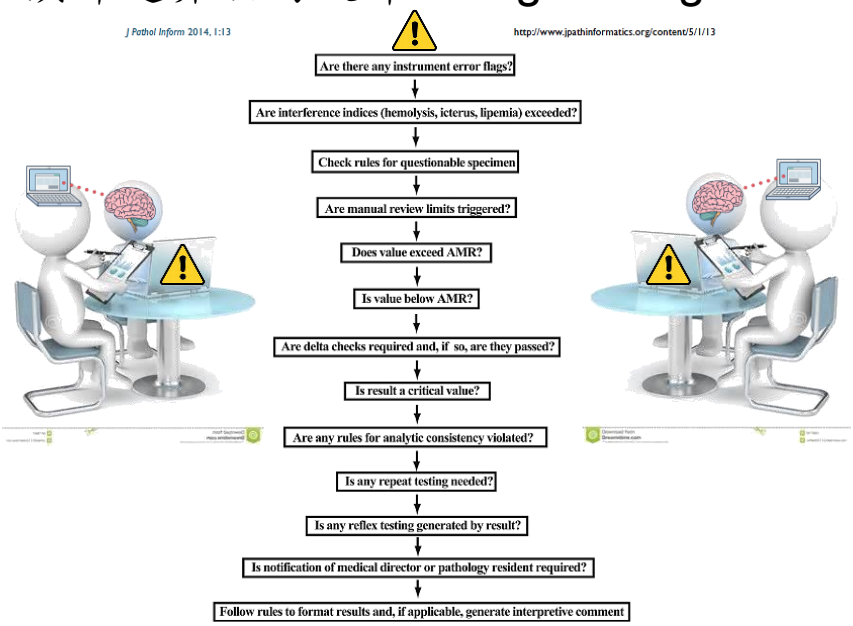
演繹運算法的設計 Design of Algorithms



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Quality Indicators

2021年度室間品質評價服務滿意度調查通知 (nccl.org.cn)

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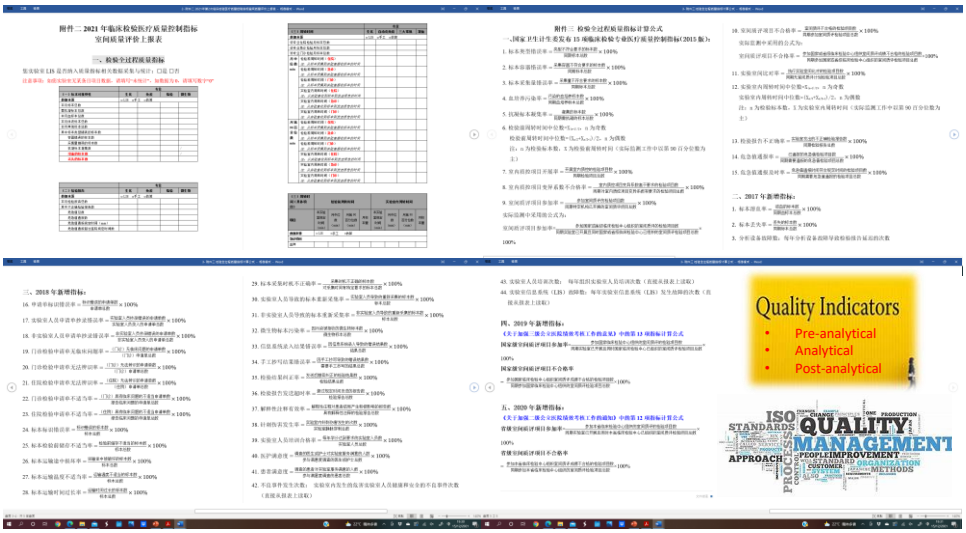
National Center for Clinical Laboratories



2021年度室間品質評價服務滿意度調查通知 (nccl.org.cn)

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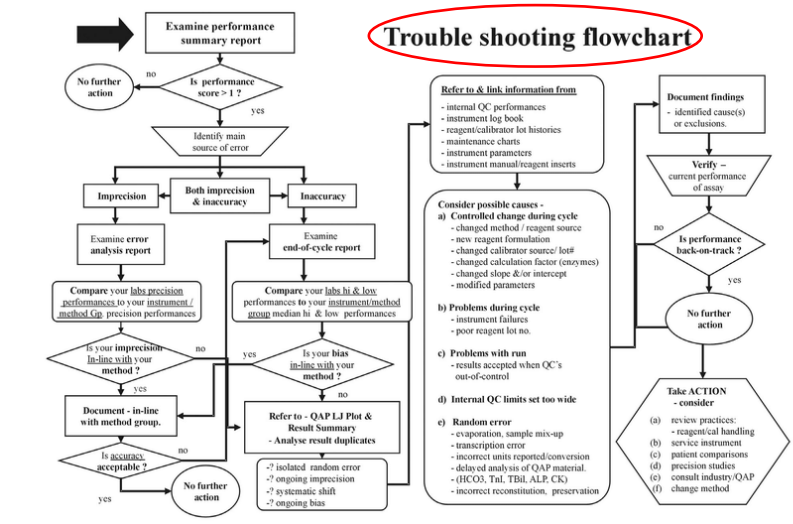
Logical Thinking



Quality Leadership and Quality Control
(Clin Biochem Rev 2003; 24: 81-93)

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人
Human Resources
HR
Global Impact
Q
力
財
FOLLOW ME

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Software as a Service
IDEA IDEA IDEA IDEA
GOOD BETTER BEST
QUALITY MANAGEMENT
Brain Storming

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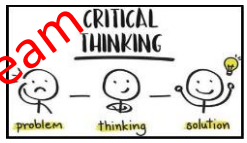
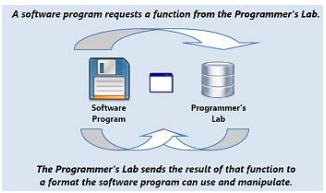


Nobody Is Perfect BUT A Team Can Be



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工欲善其事
必先利其器

Questions…

ProQ@live.hk

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