EP23 Laboratory QC Based on Risk Management Update

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Surrogate QC

- Stablized sample of similar matrix and analyzed like patient specimens
- Historically, derived from industrial practice of sampling product on a factory line.
- QC has target values, if assay recovers target, then everything is assumed stable (instrument, reagent, operator, sample)
- Benefit – surrogate QC monitors the end product (result) of the entire test system

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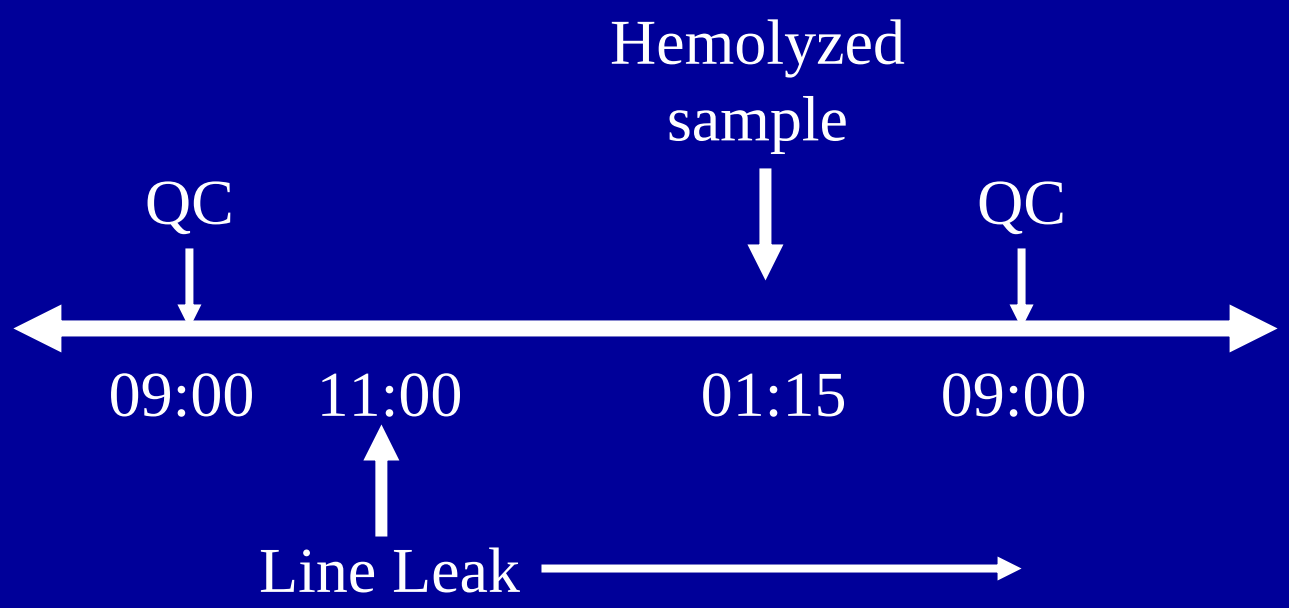
Quality Control



- QC daily at 09:00, two levels
- Line leak occurs at 11:00, dispenses partial reagent causing 25% decrease in values, not detected until next day QC at 09:00. (Systematic Error), must reanalyze all specimens since previous QC at 09:00, the previous day.
- Hemolyzed specimen (Random error) affects one sample

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Surrogate Quality Control

- Advantages
  - Analyzed like patient specimen
  - Can detect systematic errors: drift, imprecision, chemical deterioration (one point in time onward)
- Disadvantages
  - Patients can be reported before problem detected
  - When problem detected must go back and reanalyze patients since last “good” QC
  - Doesn’t detect random errors or work well with unit use devices
- Need to get to fully automated analyzers that eliminate errors upfront, provide assured quality with every sample

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Manufacturer Checks – QC Processes

- Some devices have internal checks which are performed automatically with every specimen:
  - Development of a line (Pregnancy test, Occult blood)
  - Sensor signal (blood gas analyzer, clots)
  - Flow resistance and liquid sensors (clots or bubbles in analyzer pipettes)
- Other checks engineered into device:
  - Temperature indicator in shipping carton
  - Barcoding of reagent expiration dates (prevents use)
  - Lockout features that require successful QC
  - Disposable analyzer cuvettes/pipette tips (carry-over)

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Variety of New Devices and Control Configurations

- Unique device methods/control configurations
  - Immunoassay – hCG, Drug Testing, Occult blood with internal controls
  - Glucose and Coagulation – Electronic monitors
  - Blood Gas
    - Multi-use Cartridges with liquid control/calibrators
    - Individual tests and readers with internal controls on both
  - In-vivo – continuous pH/glucose monitors, indwelling catheters
  - Alternative specimens – breath alcohol
  - Transcutaneous – neonatal bilirubin, pulse oximeters
- Traditional surrogate QC requirements may not apply

Total Quality Assurance

- Holistic or global approach to QA
- Every instrument or device is different
- Hazard analysis and risk mitigation
  - Hazard analysis defines the sources of potential error for an instrument or device, the frequency of those errors and potential consequences from not detecting an error
  - Risk mitigation involves the development of checks or other means for detecting and preventing a potential error.

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Status Report: CLSI EP23 Guideline

Title: *Laboratory Quality Control Based on Risk Management—Proposed Guideline*

- Project authorized: February 2006
- Project re-authorized: June 2008
- Timeline for Subcommittee Vote – Fall 08

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EP23 Subcommittee Members

- James H. Nichols, PhD, DABCC, FACB, Chairholder
- Greg Cooper, CLS, MHA
- Devery Howerton, PhD
- Ellis Jacobs, PhD, DABCC, FACB
- Ronald H. Laessig, PhD
- Ronalda Leneau, MS, MT(ASCP)
- W. Gregory Miller, PhD
- Robert Murray, JD, PhD
- Valerie L. Ng, PhD, MD
- Nils B. Person, PhD, FACB
- Arleen Pinkos, MT(ASCP)
- Marcia L. Zucker, PhD

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Intended Users: CLSI EP23

- Document intended for users of Laboratory and POC systems with alternative control processes.

- All labs (waived and nonwaived) will find the manufacturer's test limitations and risk mitigation information useful.

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Scope: CLSI EP23

- Labs will receive guidance to enable them to develop effective, cost-efficient QC protocols that will ensure appropriate application of local regulatory requirements based on the technologies selected by the lab and reflective of the lab's unique environmental aspects.

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Scope: CLSI EP23

- Labs will receive guidance to develop QC processes and procedures to:
  - Reduce negative impact of test system's limitation, while considering laboratory environmental/operator factors like personnel competency, temperature, storage conditions, clinical use of test results, etc.
  - Monitor immediate and extended test performance.

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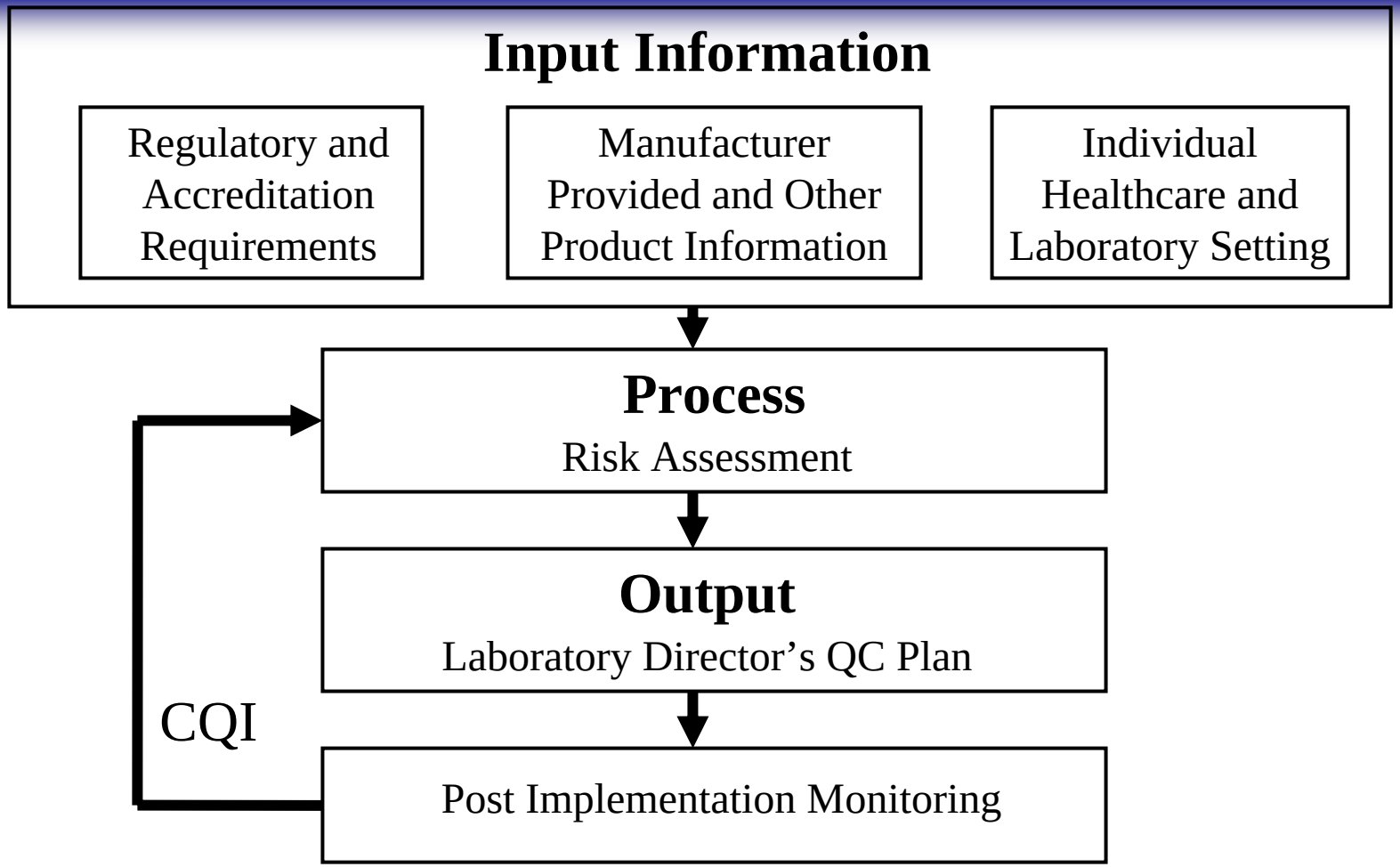
EP23 Laboratory QC Based on Risk Management



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Manufacturer Risk Assessment

Targeted Failure Mode	Device Feature or Recommended Action	How feature or action performs intended function	Known limitations of feature or action	Actions required to address known limitations	Studies to verify intended feature or action achieves intended purpose

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Manufacturer Risk Assessment EP22/EP23 Glucose Example

Targeted Failure Mode	Device Feature or Recommended Action	How feature or action performs intended function	Known limitations of feature or action	Actions required to address known limitations	Studies to verify intended feature or action achieves intended purpose
Incorrect results due to sample carryover	Wash mechanism for probes	Wash mechanism reduces risk of sample carryover	Inadequate washing following high sample can affect next sample	Run surrogate QC periodically and perform routine maintenance -check probe	Sample carryover study

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Laboratory Risk Assessment

- Washing mechanism cleans sample probe after each aliquot.
- Manufacturer recommends periodic surrogate QC to detect dirty probes and routine maintenance to clean and replace probes
- Limitation – process may fail to clear a high sample. Studies <15% bias for samples up to 486 mg/dL. What about DKA, high glu?

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Laboratory Risk Assessment

- Lab director could conduct own carry-over study (using higher glucose samples) or repeat next sample after any glucose >500 mg/dL until sufficient data is collected.
- Residual risk with probe wash and repeating next sample after a high patient
  - Probability of carry-over – remote (that both wash and repeat testing will fail)
  - Severity – serious – unknown effect > 500 mg/dL
  - Residual risk – clinically acceptable
- QC elements (manufacturer probe wash plus laboratory repeat next sample after > 500 mg/dL result) are added to a Lab Risk Assessment and QC Plan

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Laboratory Risk Assessment

- Process is repeated for each risk identified, whether from manufacturer or lab identified.
- For each risk, a mitigation strategy is found that will reduce the residual risk to an acceptable level
- Sum of all QC elements (manufacturer provided and laboratory added) becomes the laboratory's QC plan specific to this device and the laboratory environment.
- This plan is then checked against manufacturer QC and local regulatory requirements

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EP23 Glucose Example

- Carried through EP22 and EP23 – bench-top, multi-analyte, random access analyzer with a number of internal features and checks.
- Manufacturer provides a table containing a dozen risks and mitigation strategies (some internal, others lab recommended actions)
- EP23 works through the example, builds a lab specific QC plan addressing all identified risks.
- QC plan employs surrogate QC, proficiency surveys, added maintenance checks, and operator training elements (checking critical instrument settings, etc.)

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EP23

- Key component of EP23 is follow-up and occurrence management
  - troubleshooting problems after implementing the QC plan,
  - what went wrong,
  - why the QC plan did not catch the problem,
  - modifying the QC plan to mitigate the newly identified risk for the future.

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Document Content: CLSI EP23

- Table of Contents
- Foreword – Shared foreword with EP18, EP22, and EP23
- Section 1 – Scope
- Section 2 – Introduction
- Section 3 – Standard Precautions
- Section 4 – Terminology
  - Definitions – Shared with EP18, EP22, and EP23
  - Abbreviations and Acronyms

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Document Content: CLSI EP23

- Section 5 – Available Quality Control Tools
  - o Surrogate Sample (traditional) QC protocols to Monitor or Mitigate Errors
    - Nonintegrated
    - Integrated (QC built into device)
  - o Alternative QC Processes and Other Laboratory Error Identification and Avoidance Techniques
- Provide strengths and weaknesses of each QC mechanism or process

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Document Content: CLSI EP23

- Section 6 – Information to be gathered – manufacturer recommendations, laboratory specific applications of the test, and local laws and accreditation requirements
- Section 7 – Development of Laboratory-Specific QC Protocols
- Section 8 – Surveillance and Follow-up

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EP23

- Doesn’t replace surrogate QC, but incorporates surrogate QC to address the potential for certain risks
- Utilizes a risk management approach to developing a customized QC plan.
- Provides a scientific basis for justifying QC strategies (useful for lab inspectors)
- QC plan proactively addresses the potential for risk before a wrong result is released as opposed to current QC strategies that react to a QC failure

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Summary

- EP23 still in draft and being revised
- EP23 provides guidance for labs to develop a customized QC plan based on risk management.
- Assist laboratories by describing the multiple factors that must be considered when developing laboratory-specific QC protocols
- Possible future spin-off product of EP23 in nontechnical terms for physician's office market and non-laboratorians

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Thank You

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