Role of Proactive Measures in the Clinical Laboratory Practice

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Objectives

- Review the milestones on risk management and quality control
- Identify the risk and risk management definitions
- Describe the sources of laboratory error
- Describe the implementation a quality control strategy
- Describe the stepwise approach to risk management
- Identify the quality control based on risk management and IQCP
- Perspectives for the future

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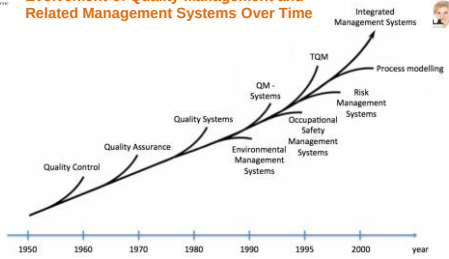
Evolvement of Quality Management and Related Management Systems Over Time



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Milestones - Evolvement of Quality Risk Management Over Time

YEAR	
in the 1970s	United States manufacturers moved beyond statistical quality control in the 1970s to focus on total quality concepts, following the example of Japanese industry.
By the 1990s	quality management systems and risk management had taken hold in the United States as the preferred approach. Risk as used here is the combination of severity of harm and the probability of that harm occurring.
U.S. Department of Health and Human Services. Medicare, Medicaid and CLIA programs: Regulations implementing the Clinical Laboratory Improvement Amendments of 1988 (CLIA). Final rule. Fed Regist 1992; 57:7002-186	While the trend in the medical device manufacturing industry has been away from prescriptive regulation, clinical laboratory regulations in the 1990s prescribed the number of QC tests that must be performed daily regardless of the clinical significance of an erroneous result or the likelihood of occurrence, thus removing an incentive to seek inherently safer IVD medical devices. The revised CLIA regulations retained the prescriptive requirements. (CLIA regulations, 42 CFR Part 493 www.hcfa.gov/medicaid/clia/cliahome.htm)
in 1996	Revamped FDA regulations gave in vitro diagnostic (IVD) and other medical device manufacturers the responsibility to decide the appropriate amount of quality control testing based on risk assessment.

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Milestones - Evolvement of Quality Risk Management Over Time

YEAR	
1998	• Quality System Regulation, US Code of Federal Regulations, 21 CFR Part 820. • Council Directive 98/79/EC of the European Parliament and of the Council of 27 October 1998 on In Vitro Diagnostic Medical Devices," Official Journal of the European Union L331 (December 7, 1998). • Australia, Canada, Japan, and the Global Harmonization Task Force have also embraced or are embracing risk management as part of the quality system. Global Harmonization Task Force, Risk Management as an Integral Part of the Quality Management System, Proposed Draft SG3/N15R6.
2000	ISO 14971:2000 (2007, 2012) Medical Devices – Application of risk management to medical devices
January 1, 2014	the Center for Medicare and Medicaid Services (CMS) www.cms.gov adopted an alternative Quality Control (QC) procedure that would allow laboratories – after appropriate assessment – the choice to implement a more flexible and customized QC procedure that is better adapted to the needs of their institution
Effective 1/1/16	EQC will no longer be available and laboratories will be required to follow either CLIA or IQCP. Also after 1/1/16, laboratories began to be cited for deficiencies under IQCP.

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	GUIDE
IVD	ISO 14971:2007and 2012 International Organization for Standardization. Medical devices – Application of risk management to medical devices ISO 14971:2007. Geneva: International Organization for Standardization, 2007.
LABORATORY	CLSI Guideline C24 – A3 Clinical and Laboratory Standards Institute. Statistical quality control for quantitative measurements procedures: principles and definitions. Approved guideline - 3rd ed. C24 – A3. Wayne, PA: Clinical and Laboratory Standards Institute, 2006.
	ISO 22367:2008Medical Laboratories – Reduction of error through risk management and continual improvement International Organization for Standardization. ISO 22367:2008. Geneva: International Organization for Standardization, 2008.
	ISO 31000:2009 Risk management -- Principles and guidelines
	ISO/IEC 31010:2009 Risk management – Risk assessment techniques
	ISO Guide 73:2009 Risk management — Vocabulary
	CLSI Guideline EP18 - A2 Clinical and Laboratory Standards Institute (CLSI). Risk Management Techniques to identify and control laboratory error sources: Approved guideline - second edition. CLSI Document EP18 – A2 (ISBN 1-56238-712-X). Clinical and Laboratory Standards Institute. 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087 -1898 USA, 2009.
	CLSI Guideline EP23 – A Clinical and Laboratory Standards Institute. Laboratory quality control based on risk management. Approved guideline - 1st edition. EP23 – A. Wayne, PA: Clinical and Laboratory Standards Institute, 2011.
	ISO/TR 31004:2013 Risk management -- Guidance for the implementation of ISO 31000
	ISO/IEC Guide 51:2014 Safety aspects — Guidelines for their inclusion in standards
	ICH Guideline Q9 on quality risk management 2015 European Medicines Agency/CHMP/ICH/24235/2006 Committee for Human Medicinal Products London, UK
	IQCP 2015 - 2016 Individual Quality Control Plan ISO 15189 + ISO 22367 + CLSI EP23-A CMS-CDC

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Risk Definition

ISO/IEC Guide 51:2014

- combination of the probability of occurrence of harm (3.1) and the severity of that harm
- The probability of occurrence includes the exposure to a hazardous situation (3.4), the occurrence of a hazardous event (3.3) and the possibility to avoid or limit the harm.

ISO 31000:2009

- effect of uncertainty on objectives
- An effect is a deviation from the expected — positive and/or negative.
- Risk is often characterized by reference to potential events (2.17) and consequences (2.18), or a combination of these.
- Risk is often expressed in terms of a combination of the consequences of an event (including changes in circumstances) and the associated likelihood (2.19) of occurrence.
- Uncertainty is the state, even partial, of deficiency of information related to, understanding or knowledge of an event, its consequence, or likelihood.

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Risk Management Definition

ISO 31000:2009: Risk management -- Principles and guidelines

- coordinated activities to direct and control an organization with regard to **risk**

ISO 14971:2007: Medical devices -- Application of risk management to medical devices

- systematic application of management policies, procedures and practices to the tasks of analyzing, evaluating, controlling and monitoring risk

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Risk Management Definition

The stepwise risk management process for medical device manufacturers is described in an international standard, ISO 14971.

Key Elements

- Hazard identification
- Risk analysis
- Risk evaluation
- Risk control
- Risk monitoring

RISK ASSESSMENT

RISK MANAGEMENT

Risk management according to ISO 14971 is a product "life-cycle" process, which means it continues as long as the product is being produced and is still in active use.

www.iso.org/ISO 14971:2012

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Risk management is not a new concept for laboratories to date

1970s - Healthcare
2000 - Patient Safety Programs
2003 - Medical Laboratories

- Evaluate the performance of new instruments.
- Troubleshoot instrument problems.
- Respond to physician and patient complaints.
- Estimate harm to a patient from incorrect results.
- Take actions to correct and prevent errors.

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HAZARD ANALYSIS

ISO 14971: IVD RISK MODEL, depicts a sequence of events that starts with a failure in a manufacturer's quality system that results in a defective device.

Manufacturer	Quality System Failure	Defective IVD Medical Device	Fault
Laboratory	Testing Process Failure	Incorrect Result	Hazard
Physician	Diagnostic Process Failure	Inappropriate Medical Treatment	Hazardous Situation
Patient		Injury or Death	Harm

www.iso.org/ISO 14971:2012

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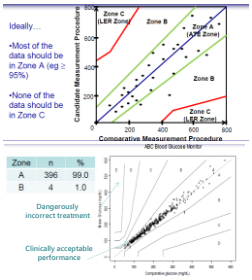
RISK ANALYSIS

Error grid analysis – developed by Clarke et al. (*Diabetes Care 1987*) to classify incorrect glucose results based on the degree of error and the physiological status of the patient.
Parkes et al. developed an error grid based on the consensus of a large number of medical practitioners. (*Diabetes Care 2000*)

An Error grid provides a logical basis for ranking the severity of harm on a scale of 1 (Zone A) to 5 (Zone E)



Nandagopalan S. CLSI

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What could possibly go wrong?

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Achieving a 99% level of quality means accepting 1% an error rate

In France a 1% error rate would mean everyday

- 14 minutes without water or electricity
- 50,000 parcels lost by postal services
- 22 newborns falling from midwives' hands
- 600,000 lunches contaminated by bacteria
- 3 bad landings at Paris Orly airport

Dr Kazunobu Kojima, WHO/HSE/IHR/Lyon Office

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Result: 1% failure

Dr Kazunobu Kojima, WHO/HSE/IHR/Lyon Office

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What are the Sources of Laboratory

?

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Total Testing Process

Phases of the TTP	Definition	Examples of Activities in Phase	Estimated contribution to TTP errors
Pre-Pre Analytical	Activities associated with initial selection of the test	Inappropriate test request, order entry, patient/specimen misidentification, inappropriate sample collection, inappropriate container, handling, storage or transportation.	46–68%
Pre-Analytical	Pre-test laboratory activities	Errors in sorting, pipetting, labeling, centrifugation	3–5%
Analytical	Testing-associated activities	Equipment malfunction, sample mix-ups, assay interference, undetected failure in quality control	7–13%
Post-Analytical	Post-test laboratory activities	Erroneous validation of analytical data, excessive turn-around-time, improper data entry or manual transcription error, failure/delay in reporting critical values	13–20%
Post-Post Analytical	Activities associated with interpretation of test results by the clinician	Delayed/missed reaction to laboratory reporting, incorrect interpretation, inappropriate/inadequate follow-up plan, failure to order appropriate consultation	25–46%

HIGHEST

COLA White Paper: Integrating Laboratories into the PCMH Model of Health Care Delivery. Accessed April 20, 2016

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IFCC WG List of Highest Priority TTP Errors

Process Phase	Quality Indicator
Pre-pre analytical	Patient misidentification errors
	Test Transcription errors
	Incorrect sample type
	Incorrect fill level
	Unsuitable samples for transportation and storage
	Contaminated samples
	Hemolyzed samples
	Clotted samples
Analytical	Test with inappropriate internal QC
	Test performance error discovered with un-acceptable External Quality Assessment or Proficiency Control
	Unacceptable performance in an External Quality Assessment or Proficiency Testing
Post Analytical	Manual transcription data errors
Post-Post Analytical	Inappropriate TAT for STAT tests
	Incorrect laboratory reports
	Failure to notify of critical values

COLA White Paper: Integrating Laboratories into the PCMH Model of Health Care Delivery. Accessed April 20, 2016

Sources of Post-analytical Error

- Transcription error
- Time to deliver the result to the clinician
- Error in transmitting the result over the phone (eg., was it BMP or BNP?)
- Failure to heed errors signaled by the instrument or the LIS/HIS/middleware

The pre-analytical, analytical, and post-analytical factors that are most likely to occur in a hospital setting are not the same as those that might typically occur during blood glucose testing in an outpatient setting. Plebani reported a series of hospital lab errors divided into pre-analytical, analytical, and post-analytical categories. The causes and distributions of that hospital's errors are as follows:

Table 1. Phases in Diagnostic Processing Leading to Missed Diagnoses

Phase	Example of Errors	Percentage of Missed Diagnoses
Preanalytical	• Failure to order appropriate diagnostic or laboratory tests • Adequate diagnostic or laboratory tests ordered but not performed	55
Analytical	• Diagnostic or laboratory test performed incorrectly	8
Postanalytical	• Incorrect interpretation of diagnostic or laboratory tests • Responsible provider did not receive diagnostic or laboratory test results	37

Adapted from Ref. 15.

Diabetes Spectrum Volume 27, Number 3, 2014

Klonoff DC. Diabetes Spectrum 27(3), 2014.
Pfützner A. et al. J Diabetes Sci Technol 7:1275-81, 2013.

The FDA has categorized the most common blood glucose monitor errors in terms of their potential sources (eg., errors caused by monitor design, production, or use). Six error source categories and examples of each are :

Table 2. Potential Sources of Error in Blood Glucose Monitors Based on FDA Experience

Category	Sources of Error or Failure
Operator	Failure to follow procedure correctly, including: • Sample contamination • Incorrect specimen collection (e.g., poor lancet technique and incorrect volume) • Application of an insufficient amount of blood to the strip or incorrect application of blood to the strip • Use of a sample from an alternate site not validated by the manufacturer • Application of blood specimen to the strip more than once (e.g., if the user believes not enough was added the first time) • Incorrect insertion of strip into meter • Inaccurate timing • Use of contaminated, outdated, or damaged strips or reagents, including calibrators or quality control materials • Failure to understand or respond to meter output • Errors in meter maintenance or cleaning • Errors in calibration or failure to calibrate or otherwise adjust the meter or check performance with quality control materials as directed by labeling • Incorrect saving or use of stored data • Improper storage or handling of the meter, calibrators, quality control materials, or test strips or improper maintenance of the meter • Inadvertent changes of parameter (such as units of measurement) • Failure to contact physician when necessary (OTC) • Incorrect incorporation of results into overall treatment plan (prescription POC) • Use of strips not validated for use on the monitor

Klonoff DC. Diabetes Spectrum 27(3), 2014.

Error sources categorised by FDA:

Reagent	• Expired strips or reagents • Damaged or contaminated strip • Failure of strips, calibrators, or quality control materials to perform adequately • Incorrect manufacturing; product fails to conform with specifications • Incorrect dimensions of reagent strip • Interference with chemical reaction on strip (e.g., reducing substances) • Inadequate design of container for strips or other reagents; failure to prevent deterioration; failure of desiccant used to keep strips dry
Environmental	Effects on the device, including: • Temperature • Humidity • Altitude, hyperbaric conditions • Electromagnetic radiation • Visible light, sunlight Effects on humans, including: • Lighting, glare off meter surfaces • Distractions, visual and auditory • Stressful conditions • Limited manual dexterity
Software	• Confusing or obscure user prompts and feedback • Incorrect mathematical algorithm • Undetected or unrecognized signal errors • Timing failure • Incorrect storage of test results in memory, including matching result with correct patient or time of test • Other software failures

Klonoff DC. Diabetes Spectrum 27(3), 2014.

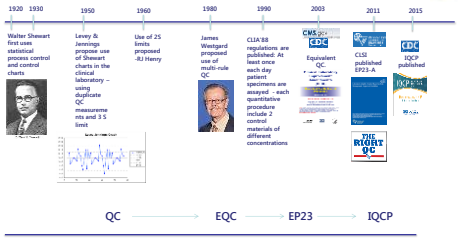
Error sources categorised by FDA:

Category	Sources of Error or Failure
Hardware	• Electronic failure • Physical trauma or vibration • Damage to the device from incorrect strip dimensional tolerances (third-party manufacturer) • Electrostatic discharge • Electromagnetic/radiofrequency interference • Battery reliability, lifetime, and replacement • Component(s) failure • Incorrectly manufactured
System	• Physical trauma or vibration • Incorrect calibration/adjustment (between lots of strips) • Calibration failure, interference, instability, or use beyond the recommended period of stability • Labeling not geared to intended user • Meter or operation complexity not geared to intended user • Inadequate training
Clinical	• Interference from endogenous substances • Severe conditions (e.g., dehydration, hypoxia, hyperglycemic hyperosmolar state, hypotension, ketoacidosis, or shock) • Interference from other sugars (e.g., maltose intravenous solutions)

Klonoff DC. Diabetes Spectrum 27(3), 2014.

Do we need a New Approach to Quality Control with Managing the Risks?

Milestones – Evolvement of Quality Control Over Time



Adapted from Person N. Siemens Healthcare Diagnostics Inc. 2013

Today's Quality Control Process

- Advantages
  - QC monitors the end product (result) of the entire test system.
  - QC has target values: if assay recovers the target, then everything is assumed stable (eg., instrument, reagent, operator, sample).
- Disadvantages
  - When a problem is detected, one must go back and reanalyze patients since the last "good" QC.
  - If results are released, then results may need to be corrected.
  - For Point of Care devices, does traditional QC work for every test?
- Need to get to fully automated analyzers that eliminate errors up front
  - Until that time, need a robust QC plan (QCP)

Types of Quality Control

- "On-Board" or Analyzer QC – built-in device controls or system checks
- Internal QC – laboratory-analyzed surrogate sample controls
- External QC – blind proficiency survey
- Other types of QC – control processes either engineered by a manufacturer or enacted by a laboratory to ensure result reliability

Quality Control Limitations

- No single QC procedure can cover all devices, because the devices may differ.
- QC practices developed over the years have provided laboratories with some degree of assurance that results are valid.
- Newer devices have built-in electronic controls, and "on-board" chemical and biological controls.
- QC information from the manufacturer increases the user's understanding of device's overall quality assurance requirements.

ISO. Clinical laboratory medicine – In vitro diagnostic medical devices – Validation of user quality control procedures by the manufacturer. ISO 15198. Geneva, Switzerland: International Organization for Standardization; 2004.

In October 2011, CLSI published EP 23 and introduced Laboratory Quality Control Based on Risk Assessment

James H.Nichols Ph.D., DABCC, FACB, Chair of the CLSI EP23 Group

- EP23 explains the strengths and weaknesses of the different QC processes, and helps the laboratory determine the right combination of tools: THE RIGHT QC
- Each laboratory's quality control plan is unique based on the device, the laboratory setting, and the risk to patients from inappropriate decisions based on incorrect or delayed test results.
- CLSI EP23 provides a template for laboratories to map their testing processes, identify weaknesses or hazards in the process map, define a control process that can detect failures and/or prevent reporting erroneous results, summarize the control processes in a quality control plan, implement and benchmark the effectiveness of their quality control plan, and modify a quality control plan as part of continual improvement.

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The Quality Control Toolbox

- QC is not only about testing external QC samples, it is all the tools we can use to **monitor test system performance**.
- EP23 recognizes that a variety of QC tools exist and that **no single QC tool is perfect.**
- Analysis of QC samples is certainly a well established tool available to us.
- Key to effective use of QC samples is determining **how often** they need to be tested.

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QC Tools

- Intralaboratory QC
- Interlaboratory QC
- Integrated (built-in) QC
- Measuring system function checks
- Electronic system checks
- Calibration checks
- Repeat testing of patient samples
- Monitoring aggregated patient results
- Implausible values
- Delta checks
- Correlation of multiple analytes in same sample

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Improvement of QC Practices

Curtis Parvin

One – size – fits - all QC vs Right QC

The concept was introduced in November 4, 2011.

- **Every QC tool has its strengths and weaknesses (there is no perfect QC tool).**
- **QC frequency closely connected to managing risk of reporting inaccurate results**
- **Implement a combination of tools in order to properly control a test.**

- Parvin CA. Assessing the Impact of the Frequency of Quality Control Testing on the Quality of Reported Patient Results. *Clin Chem* 2008;54:
- Parvin CA, Robbins S. Evaluation of the Performance of Randomized versus Fixed Time Schedules for Quality Control Procedures. *Clin Chem* 2007;53:575-580
- Parvin CA, Gronowski AM. The effect of analytical run length on quality-control (QC) performance and the QC planning process. *Clin Chem* 1997;43:2149-54
- Parvin CA, et al. Designing a quality control strategy: In the modern laboratory three questions must be answered. ADVANCE for Administrators of the Laboratory 2011;(5):53-54.

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The QC strategy using QC samples should include:

- The <u>frequency</u> of QC sample test events
- The <u>type and number</u> of QC samples tested per test event
- The <u>statistical QC limits</u> used to evaluate the results
- The <u>frequency</u> of periodic review for detecting shifts and trends
- The actions taken when <u>results exceed acceptable limits</u>

CLSI EP-23, Section 5.1.1

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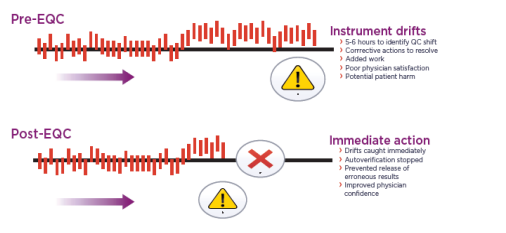
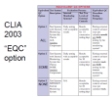


MLO-ONLINE.COM | APRIL 2017

It's official: EQC is out and QC Plans are in!

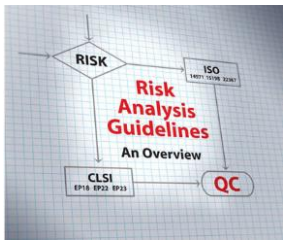
James O. Westgard, Sten A. Westgard
December 2011



http://www.westgardqc.com/official-risk-qc.htm

Quality Control in the age of Risk Management, An Issue of Clinics in Laboratory Medicine
by
James O. Westgard (Editor)

Year: 2013
Issue: Vol 33 | No. 1 | March 2013 | Pages 1-206

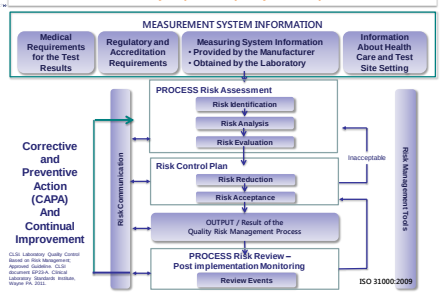


http://james.westgard.com/the_westgard_rules/2012/11/index.html

"The secret of all victory lies in the organization of the non-obvious."

- **Marcus Aurelius**
Roma Emperor and Philosopher

Overview of a typical risk management Process to develop and continually improve a quality control plan

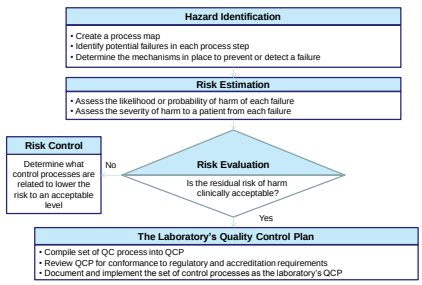


Why Quality Risk Management is important for laboratories?

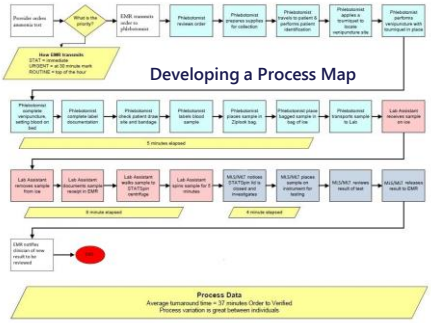
- Risk management may be best proactive approach to design an optimal overall Quality Control Plan for the laboratory.
- We analyze many samples from which we derive information.
- The information impacts upon decision making and health of others.
- Poor information can lead to poor outcomes.
- Our samples have some variables that we can control, and others that are difficult to control, and others that we can not either foresee or control.
- Regardless of contributing events, the laboratory is usually viewed as the source of the problem.

Noble MA. Risk Management in the Medical Laboratory: Reducing Risk through Application of Standards

Using Risk Management to Develop a Quality Control Plan



Developing a Process Map



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Where is the Risk in the Process?

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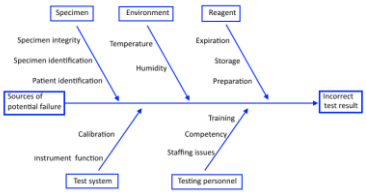
Identify the Risks – Where is the risk in the process?



Malone B. A New Approach To Quality Control. *How Can Risk Management Help Labs?* Clinical Laboratory News, November 2011; (37)11:1-4.

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Risk Management Tools

Examples of common risk management tools

Risk management tool	Description, attributes	Potential applications
Tools		
Diagram analysis • Flowcharts • Check sheets • Process mapping • Cause/effect diagrams	• Simple techniques that are commonly used to gather and organize data, structure risk management processes and facilitate decision-making	• Compilation of observations, trends or other empirical information to support a variety of less complex deviations, complaints, defaults or other circumstances
Risk ranking and filtering	• Method to compare and rank risks • Typically involves evaluation of multiple diverse quantitative and qualitative factors for each risk, and weighting factors and risk score	• Prioritizing operating areas or sites for audit or assessment • Useful for situations when the risks and underlying consequences are diverse and difficult to compare using a single tool
Fault-tree analysis	• Method used to identify all root causes of an assumed failure or problem • Used to evaluate system or subsystem failures one at a time, but can combine multiple causes of failure by identifying causal chains • Relies heavily on full process understanding to identify causal factors	• Investigate product complaints • Evaluate deviations

Risk management tool	Description, attributes	Potential applications
Tools		
Hazard operability analysis (HAZOP)	• Tool assumes that risk events are caused by deviations from the design and operating intentions • Uses a systematic technique to help identify potential deviations from normal use or design intentions	• Access manufacturing processes, suppliers, facilities and equipment • Commonly used to evaluate process safety hazards
Hazard analysis and critical control point (HACCP)	• Identify and implement process controls that consistently and effectively prevent hazard conditions from occurring • Bottom-up approach that considers how to prevent hazards from occurring and/or propagating • Emphasizes strength of preventive controls rather than ability to detect	• Better for preventive applications than reactive • Valuable precursor or complement to process validation • Assessment of the efficacy of critical control points and the ability to consistently execute them for any process
Failure modes effects analysis (FMEA)	• Assumes comprehensive understanding of the process and that CPPs have been defined prior to initiating the assessment. Tool ensures that CPPs will be met. • Assesses potential failure modes for processes, and the probable effect on outcomes and/or product performance • Once failure modes are known, risk reduction actions can be applied to eliminate, reduce or control potential failures	• Evaluate equipment and facilities; analyse a manufacturing process to identify high risk steps and/or critical parameters

WHO guidelines on quality risk management

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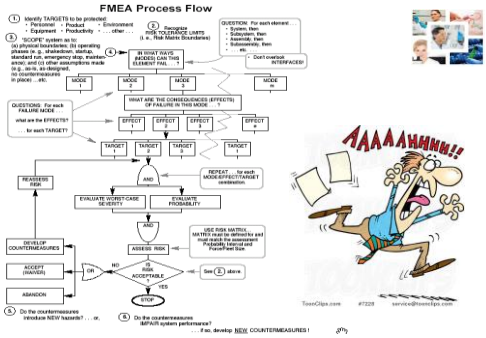
FMEA Process Flow



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An FMEA worksheet is created to record each process failure (hazard), failure cause, effect (harm), severity, existing process controls (to prevent the failure), probability of occurrence (of the failure), detectability (prior to harm), and comments explaining rationale.

#	Component	Potential failure mode	Effect	Failure cause	SEV	Existing controls	OCC	DET	Comments/ Rationale
1	Reagent	Stability not meeting claim (negative drift)	Incorrect results/ misdiagnosis	Reagent deterioration due to improper storage	8	SOP (validated storage conditions), trained personnel, weekly QC	6	2	Manufacturer's instructions
2	Reagent	Large bias shift at lot change	Incorrect results/ misdiagnosis	Reagent lot-lot differences	8	QC acceptance testing, supplier qualification	6	2	
3	Instrument	Increased imprecision at high analyte concentrations	Incorrect results/ misdiagnosis	Lamp aging	6	Preventive maintenance program / SOP (lamp replacement schedule)	2	8	Manufacturer's instructions
4	Instrument	Sporadic "outlier" readings	Incorrect results/ misdiagnosis	Unstable power source in lab	8	Voltage regulator, installation qualification	4	10	Observed with similar instruments
5	Calibrator	Large bias shift after calibration	Incorrect results/ misdiagnosis	Incorrect calibrator value assigned by manufacturer	8	Certificate of traceability, post-calibration QC, proficiency testing	6	2	
6	Calibrator	Large bias shift after calibration	Incorrect results/ misdiagnosis	Calibrator reconstitution error	8	Qualified personnel, SOP, training, post-calibration QC, proficiency testing	4	2	
7	Sample	Sporadic "outlier" results	Incorrect results/ misdiagnosis	Drug interference (known interferent)	8	Specimen requisition form; hospital pharmacy drug alert system	4	10	Observed in method verification study
8	Sample	Unsuitable sample (hemolyzed)	No result/delayed treatment	Improper specimen preparation	4	SOP (sample preparation), training/ personnel qualification	6	4	Requires re-draw

Powers DM. LABMEDICINE 36(10): 2005

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Targeted Failure Mode (Hazard)	Measuring System Feature or Recommended Action	Known Limitations of Feature or Recommended Action	Frequency (1 – 5 scale)	Severity (1 – 5 scale)	Detectability (1 – 5 scale)	Criticality (Frequency X severity X detectability)	Control Process Effective?	The QCP Action Required to Address Known Limitations	Residual Risk Acceptable? (Yes/No)
Measure or attach the test system could fail or error could occur.	*Are there manufacturer control processes, checks or recommended actions to reduce or detect failure?*	*What are the known limitations to the control processes or recommended actions?*	*What is the frequency of failure?*	*How severe is impact of failure on patient?*	*Does the control process detect or prevent the failure? Low = 5 control can detect failure High = 3 control ineffective*	*A measure of laboratory risk and priority for laboratory to address failure mode Low = 10 Med = 20 - 24 High = 29*	*The laboratory's assessment of residual risk with all manufacturer, external, and other control processes implemented*	*The action required to address residual risk to include as an element of the QCP*	*The laboratory's assessment of clinical acceptability of residual risk*
Lipemia	No internal, manufacturer, or other control process available	Manufacturer verbally states that there is no interference from lipemia. Measurement system is not optical. Not stated in operator's manual or test cartridge package insert	5 Lipemic samples occur more than one a week	1 Measurement system not affected by lipemia	1 Measurement system not affected by lipemia	5 Low risk and priority	If laboratory agrees with manufacturer no further action If laboratory remained in doubt information, can conduct own lipemia study	No action required Conduct lipemia study	Yes Yes after lipemia study
Reagent degradation during shipping	No internal or manufacturer control process available	Use external QC to detect cartridge deterioration during shipping	4 Non shipments arrive every 2 months	5 Compromised reagent can impact patient, wrong PCOR results can lead to coumadin overdosing or underdosing	1 External QC will detect compromised reagent before patient testing	20 Medium risk and priority for laboratory to address	External QC will detect compromised reagent before patient testing. Laboratory should ensure QC viability and appropriate ranges set before use	Evaluate each shipment of reagent before use for patient testing	Yes

RISK EVALUATION - Risk acceptability chart

Probability	Severity of Harm: Catastrophic	Critical	Serious	Minor	Negligible
Frequent	Unacceptible Risk	Unacceptible Risk	Unacceptible Risk	Unacceptible Risk	Unacceptible Risk
Probable	Unacceptible Risk	Unacceptible Risk	Unacceptible Risk	Unacceptible Risk	Acceptible Risk
Occasional	Unacceptible Risk	Unacceptible Risk	Acceptible Risk	Acceptible Risk	Acceptible Risk
Remote	Unacceptible Risk	Unacceptible Risk	Acceptible Risk	Acceptible Risk	Acceptible Risk
Inconceivable	Acceptible Risk	Acceptible Risk	Acceptible Risk	Acceptible Risk	Acceptible Risk

Frequent = once/week
Probable = once/month
Occasional = once/year
Remote = once every few years
Inconceivable = once in the life of the measuring system

Negligible = inconvenience or temporary discomfort
Minor = temporary injury or impairment not requiring professional medical intervention
Serious = injury or impairment requiring professional medical intervention
Critical = permanent impairment or life-threatening injury
Catastrophic = results in patient death

ISO 14971

RISK EVALUATION - Risk Matrix, 3 scales can be set up

SCORE	SEVERITY OF HARM (SEV)	PROBABILITY OF OCCURRENCE (OCC)		DETECTABILITY PRIOR TO HARM (DET)
10	Catastrophic – Patient Death	Frequent	≥ 1/1,000	Almost impossible to detect
8	Critical – Permanent impairment or life-threatening injury	Probable	< 1/1,000 and ≥ 1/10,000	Low probability of detection
6	Serious – injury or impairment requiring medical intervention	Occasional	< 1/10,000 and ≥ 1/100,000	Medium probability of detection
4	Minor – temporary injury or impairment not requiring medical intervention	Remote	< 1/100,000 and ≥ 1/1,000,000	High probability of detection
2	Negligible – inconvenience or temporary discomfort	Improbable/ theoretical	< 1/1,000,000	Almost certain to be detected

The risks need to be evaluated against criteria approved by the lab director. Values 6 and above must be addressed.
Detectability scale has an inverse relationship to the probability of detection.

RISK EVALUATION
Frequency (also called "Probability") 1 – 5 scale

Common Terms	Score	Example (ISO 14971)	PROBABILITY OF OCCURRENCE
Frequent	5	≥ 1/1,000	More than 1x/week
Probable	4	< 1/1,000 and ≥1/10,000	Once every few months
Occasional	3	< 1/10,000 and ≥1/100,000	Once a year
Remote	2	< 1/100,000 and ≥1/1,000,000	Once every few years
Improbable	1	< 1/1,000,000 and ≥10,000,000	Unlikely to ever happen

RISK EVALUATION
Severity (Scale 1 – 5)

Common Terms	Score	Possible Description (ISO 14971)
Catastrophic	5	Results in patient death
Critical	4	Results in permanent injury of life-threatening injury
Serious	3	Results in injury or impairment requiring professional medical intervention
Minor	2	Results in temporary injury or impairment not requiring professional medical intervention
Negligible	1	Inconvenience or temporary discomfort

RISK EVALUATION
Detectability (Scale 1 – 5)

Common Terms	Score	Example
Low	5	Control is ineffective
	4	Control less likely to detect the failure
	3	Control may or may not detect the failure
	2	Control almost always detects the failure
High	1	Control can detect the failure

Criticality

Multiply Frequency x Severity x Detectability
Example: Probable (4) x Catastrophic (5) x
High likelihood to detect failure (1) = 20

Criticality	Result
Low	<10
Mid	10 – 20
High	>20

Higher criticality numbers must have quality control actions in place.

RISK EVALUATION

SEVERITY ≥ 6 (or ≥3)	Require an Essential Control Point
OCCURRENCE ≥ 6 (or ≥3)	Require an Essential Control Point which must be an effective method of detection
DETECTABILITY ≥ 6 (or ≥3)	Require an Essential Control which must be a process control that prevents failures
OCCURRENCE ≥ 6 and DETECTABILITY ≥ 6	The process activity lacks adequate controls and corrective action must be initiated, either to reduce the failure rate or to increase the ability to detect a failure or both.

Powers DM. LABMEDICINE 36(10): 2005

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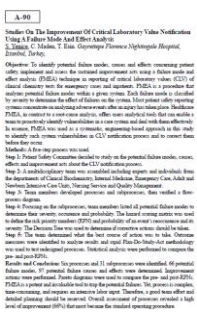
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Studies On The Improvement Of Critical Laboratory Value Notification Using A Failure Mode And Effect Analysis

S. Yenice, C. Maden, T. Esin. *Gaziantepe Florence Nightingale Hospital, Istanbul, Turkey.*

Objective: To identify potential failure modes, causes and effects concerning patient caller, implement and review the sustained improvement cycle using a failure mode and effect analysis (FMEA) technique in reporting of critical laboratory values (CLV) of clinical chemistry tests for emergency cases and inpatients. FMEA is a procedure that analyzes potential failure modes within a given system. Each failure mode is classified by severity to determine the effect of failures on the system. Most patient safety reporting systems concentrate on analyzing adverse events after an injury has taken place. Healthcare FMEA, in contrast to a root-cause analysis, offers team analytical tools that can enable a team to proactively identify vulnerabilities in a care system and deal with them effectively. In essence, FMEA was used as a systematic, engineering-based approach in this study to identify each system vulnerabilities in CLV notification process and to correct them before they occur.

Methods: A five-step process was used.

Step 1: Patient Safety Committee decided to study on the potential failure modes, causes, effects and improvement acts about the CLV notification process.

Step 2: A multidisciplinary team was assembled including experts and individuals from the department of Clinical Biochemistry, Internal Medicine, Emergency Care, Adult and Newborn Intensive Care Units, Nursing Service and Quality Management.

Step 3: Team members developed processes and subprocesses, then verified a flow-process diagram.

Step 4: Focusing on the subprocesses, team members listed all potential failure modes to determine their severity, occurrence and probability. The hazard scoring matrix was used to define the risk priority numbers (RPN) and probability of an event's occurrence and its severity. The Decision Tree was used to determine if corrective actions should be taken.

Step 5: The team determined what the best course of action was to take. Outcome measures were identified to analyze results and rapid Plan-Do-Study-Act methodology was used to test redesigned processes. Statistical analysis was performed to compare the pre- and post-RPNs.

Results and Conclusion: Six processes and 31 subprocesses were identified. 66 potential failure modes, 97 potential failure causes and effects were determined. Improvement actions were performed. Pareto diagrams were used to compare the pre- and post-RPNs. FMEA is a potent and invaluable tool to trap the potential failures. Yet, process is complex, time-consuming, and requires an extensive labor input. Therefore, a good team effort and detailed planning should be reserved. Overall, assessment of processes revealed a high level of improvement (68%) that must become the standard operating procedure.

Yenice S, Maden C, Esin T.

Studies on The Improvement Of Critical Laboratory Value Notification Using A Failure Mode And Effect Analysis.

CLINICAL CHEMISTRY 2010; Vol. 56, No. 6, Supplement: A30.

Identified:
6 major processes
31 subprocesses
66 failure modes
97 potential failure causes

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Acta Medica Marisiensis 2015;61(4):372-377 DOI: 10.1515/amma-2015-0086

UPDATE

Risk Management in Clinical Laboratory: from Theory to Practice

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Clinical laboratory tests ensure approximately 70% of the medical decisions, so that the time until the release of the results and its accuracy are critical for the diagnosis and the efficiency of the treatment [1]. Risk management involves both the anticipation of what could happen erroneous and the assessment of errors' frequency as well as the consequences or the severity of the effects caused by it, and finally to decide what can be done in order to reduce the risk to an acceptable clinical level. For this reason, organizations should not see the risk management as a compliance issue, but as an integral part of the decision-making process. EP23-A is a guideline of CLSI that introduces the risk management principles in the clinical laboratory and encourages the laboratories to develop plans of risk management which are addressed to the risks of each laboratory. EP18-A2 proposes 2 techniques for identifying and controlling the errors in the laboratory: FMEA (Failure Mode and Effects Analysis) and FRACAS (Failure Reporting, Analysis and Corrective Action System). The European Committee of Experts and Management of Safety and Quality in Health Care proposed to use the quality indicators to identify the critical stages of each process, thus being possible to assess continuously the medical processes with the aim of identifying the errors when they occur. This review summarizes the principles of the risk management in the clinical laboratory, thus it can achieve its aims to report valid, accurate and reliable test results

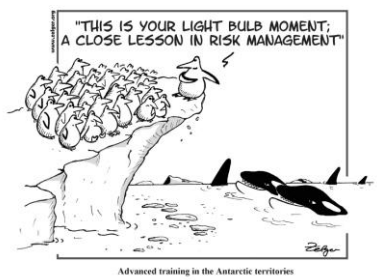
Keywords: pre-analytical error, risk management, quality indicator, FMEA

Received: 11 June 2015 / Accepted:11 August 2015

Audience Response

Does your laboratory currently have a risk assessment plan?

1. Yes
2. No



Advanced training in the Antarctic territories

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The "Individualized Quality Control Plan" (IQCP) is the Clinical Laboratory Improvement Amendments (CLIA) Quality Control (QC) policy became effective as an alternative QC option for all laboratory tests on January 1, 2016.

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What is IQCP?

IQCP is the new QC option for non-waived test devices in US. CMS states that an IQCP is specific for a testing device and testing situation. The intent is to eliminate failures and detect nonconformities before reporting incorrect results.

What is the basis for IQCP?

CMS structured IQCP on the risk management concepts presented in the CLSI EP23-A guideline.

When is IQCP useful?

Manufacturer's instructions for QC are absent or less stringent than CLIA.

Individualized Quality Control Plan (IQCP): A New Quality Control (QC) Option Available at: http://www.cms.gov/Medicare/Provider-Enrollment-and-Certification/SurveyCertificationGenInfo/Downloads/Survey-and-Cert-Letter-13-54.pdf

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Eligible for IQCP

- Syphilis serology
- General Immunology
- Routine Chemistry
- Urinalysis
- Endocrinology
- Toxicology
- Hematology
- Immunochemistry
- Clinical cytogenetics

Radiobioassay
Histocompatibility
Microbiology
- Bacteriology
- Mycobacteriology
- Mycology
- Parasitology
- Virology

Not Eligible for IQCP

- Pathology
- Histopathology
- Oral Pathology
- Cytology

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Joint Commission and CAP developed their own requirements for IQCP. COLA has adopted as it stands.

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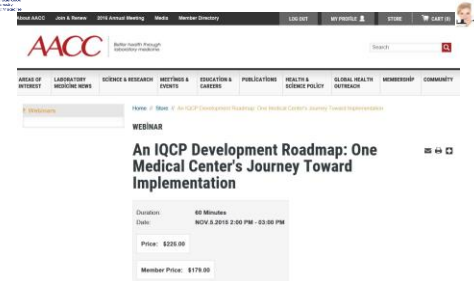

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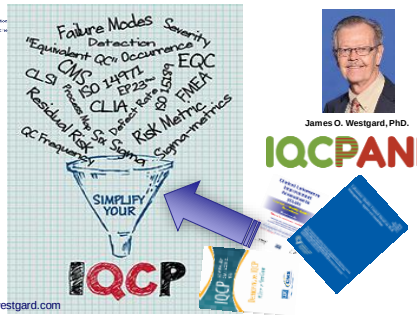

James O. Westgard, PhD.

IQCPANIC?

http://www.westgard.com

Developing an IQCP

IQCP = RA + QCP + QA

Thus, the laboratory will need to consider the corresponding risks in each of these phases and applicable regulatory requirements and include three parts.

IQCP considers the entire testing process: pre-analytic, analytic, and post-analytic

Risk identification
Risk Evaluation
Risk Mitigations

1 RISK ASSESSMENT What can go wrong?

2 QUALITY CONTROL PLAN How do we prevent or detect?

3 QUALITY ASSESSMENT Is it working?

Specimen
Test System
Reagent
Environment
Testing Performed

IQCP Development Process

- Gather Information – IQCP is based on facts
- Medical, regulatory, testing device and situation
- Risk Assessment – know processes; identify potential risks

Preanalytical	Analytical	Postanalytical
Right Patient *Right* Specimen *Right* Sample Handling	*Right* (accurate) Result	*Right* Patient Record

Must assess – samples, operators, test environment, testing systems, reagents

Review policies; remove/handle all significant risks

1 IQCP ACT: Data Gathering

Rapid TAT
Reasonable accuracy & precision
ACT is typically imprecise
O2 saturation imprecision tolerable

ACT (coag) - 2 levels QC each day of testing

Blood Gas – 3 levels QC every 24 hours, with 1 level each 8 hours

ACT: iSTAT, Hemochron

Blood Gas: iSTAT, others

Cardiac Cath lab with testing performed by RN (non-CLS)

Valerie Ng. IQCP Plan

1 IQCP ACT: Risk Assessment

Whole blood – unable to assess specimen integrity

1 Samples
2 Operator
4 Laboratory Environment
Identify Potential Hazards
Incorrect Test Result
3 Reagents
5 Measuring System

Valerie Ng. IQCP Plan

1 IQCP ACT: Risk Assessment

Severity of harm

Probability	Negligible	Minor	Serious	Critical	Catastrophic
Frequent	not ok	not ok	not ok	not ok	not ok
Probable	ok	not ok	not ok	not ok	not ok
Occasional	ok	ok	ok	not ok	not ok
Remote	ok	ok	ok	ok	not ok
Inconceivable	ok	ok	ok	ok	ok

ISO 14971

Frequent = once/week
Probable = once/month
Occasional = once/year
Remote = once every few years
Inconceivable = once in the life of the measuring system

Negligible = inconvenience or temporary discomfort
Minor = temporary injury or impairment not requiring professional medical intervention
Serious = injury or impairment requiring professional medical intervention
Critical = permanent impairment or life-threatening injury
Catastrophic = results in patient death

Valerie Ng. IQCP Plan

The Quality Control Plan

- Construct the QCP.
- A QCP is necessary for result quality, and each QCP is unique.
- Include each of the identified QCP actions in the QCP.
- A QCP is the industry standard. It depends upon the extent to which the device's features achieve their intended purpose in union with the laboratory's expectation for ensuring quality results.
- Monitor QCP for Effectiveness - Once implemented, the QCP is monitored for effectiveness and modified as needed to maintain risk at a clinically acceptable level.

Clinical and Laboratory Standards Institute (CLSI). Risk Management Techniques to identify and and control laboratory error sources: Approved guideline - second edition. CLSI Document EP18 – A2 (ISBN 1-56238-712-X). Clinical and Laboratory Standards Institute . 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA, 2009.

EP-23 Example: Checklist

Appendix E. Quick Guide Checklist for Establishing a Quality Control Plan Based on Risk Management

Recent advances in technology have significantly enhanced the accuracy and reliability of certain measuring systems. In recognition of these advances, regulatory and accreditation bodies may provide opportunities for laboratories to establish QCP based on risk assessments. Appropriate site-specific QCP can be established through a systematic analysis and evaluation of factors that can adversely affect the quality of test results, and by using an assortment of QC tools to mitigate patient risk. The particular combination of measuring system, laboratory, or test site environment and clinical application should be considered when establishing a QCP. Some of the factors considered by the laboratory are listed in this checklist that may provide a useful overview of a laboratory's complete QCP. Additional guidance can be found in CLSI document EP18.[1]

Measuring System: Activated Clotting Time (POCT)

A. Information Gathering. *(Section 6, Appendix A, and EP22, Sections 1 and 2)*	Yes
1. Regulatory and accreditation requirements permit site-specific QC Pts.	☑
2. The quality of laboratory examinations depends on a partnership between IVD manufacturers and the laboratory.	
a. The manufacturer provides adequate instructions for using their methodology with their packaged measuring system.	☑
b. Manufacturer's risk mitigation information includes information regarding the scope and effectiveness of recommended QC procedures in terms of potential measuring system failures and the hazards associated with such failures.	☐ no
c. The manufacturer's risk mitigation information includes recommendations on how to best detect and mitigate residual risks, and describes how the mitigation affects the quality of patient test results.	☐ no

Valerie Ng. IQCP Plan

EP-23 Example: Checklist

1. Hazard identification. *(Section 7)*	
a. The laboratory uses the manufacturer, laboratory, and regulatory information to identify potential weaknesses in the examination process that present risk to patients.	☑
b. The laboratory critically assesses the information to determine if it is appropriate for the conditions that exist in the laboratory or test setting.	☑
Hazard Identification is documented in the following laboratory records: Fishbone analysis	
2. Laboratory identified sources of errors that could lead to patient harm. The laboratory reviews the process flow chart and identifies hazards and measuring system control processes to determine if the risk is clinically acceptable.	☑
Risk assessment is documented in the following laboratory records: ACT hazard analysis	
3. The laboratory's QCP. The laboratory documents all risk mitigation procedures as the QCP. The QCP:	☑
a. Meets regulatory/accreditation requirements.	☑
b. Meets manufacturer's recommendations.	☑
c. Incorporates appropriate QC processes identified to mitigate risk of harm to a patient.	
Risk mitigation is documented in the following laboratory records: P&P QC and ACT validation cover sheet	

Valerie Ng. IQCP Plan

EP-23 Example: Checklist

C. Postimplementation Monitoring. *(Section 8)*	
1. Evaluation of the effectiveness of the laboratory QCP. The laboratory develops a plan for reviewing and evaluating key QC indicators on a periodic basis as well as mechanisms to investigate and evaluate all customer complaints received. A protocol is established to ensure appropriate communication and implementation of any manufacturer updates or recalls.	☑
QCP review is documented in the following laboratory records: Monitor proficiency testing results & patient outcomes	
2. Troubleshooting/determining Cause of unacceptable performance. When unacceptable levels of performance are identified, the cause is determined and the risk of harm to patients is assessed.	☑
Unacceptable levels of performance are documented in the following laboratory records: Unacceptable PT documented with PT summary report, Adverse patient outcome documented as internal investigation.	
3. Corrective action – CQI. The laboratory's implemented QCP is modified as needed to prevent a recurrence of identified problems.	☐
Modifications to the QCP are documented in the following laboratory records:	n/a (yet)

Valerie Ng. IQCP Plan

3

Quality Assessment

Describes the review process for ongoing monitoring of the effectiveness of the IQCP

- QC review/data
- Proficiency testing results
- Patient results review
- Specimen rejection logs
- Turn-around time reports
- Records of preventive measures, corrective actions and follow-up
- Personnel competency records
- Complaints
- Inspection observations
- Investigation of any process failure and follow up activity (modifications as necessary)

Quexit? TExit? or IQCPexit?

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Quexit?

We're in the era where a Quality Exit – QuExit – is being proposed. Some labs may not realize the consequences of such a significant change.

IQCPexit?

It appears that IQCP is simply a very time-consuming paperwork exercise that allows laboratories to maintain the same QC that they were doing back in the EQC era. it's mostly been a "waste of time", an exercise of paperwork to justify current practices, with very little change occurring in QC practices.

TExit?

The campaign to eliminate **Total Error**, despite what has been nearly half a century of widespread utility, continues at the hands of a few aggrieved metrologists.

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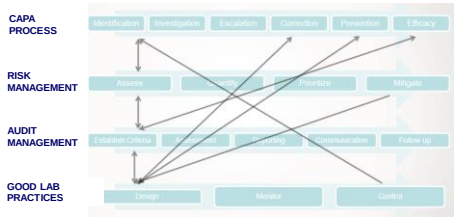
Interconnecting Quality Processes: Closed Loop Quality Management



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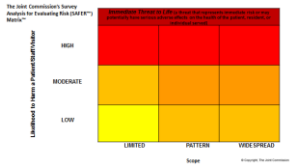
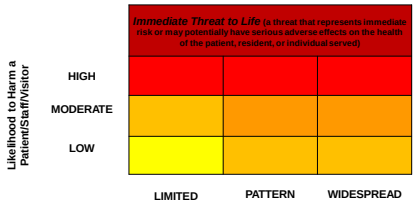
New strategy on the block!



https://www.jointcommission.org/topics/safer_matrix_resources.aspx

The Joint Commission's Survey Analysis for Evaluating Risk (SAFER™) Matrix™

- JC's new (as of 2017) scoring methodology
- Better identifies and communicates risk levels associated with cited deficiencies
- Help organizations prioritize and focus on corrective actions



https://www.jointcommission.org/topics/safer_matrix_resources.aspx

Perspectives for the future: Pros and Cons

- What does Quality Control Plan based on Risk Management mean for laboratories in specific terms? Process maps, fishbone diagrams, in depth - risk analysis, and statistical QC protocols and the cost management?

  It is a big challenge for the labs particularly in the case of developing countries. But identifying risks and controls for all phases of laboratory testing is still a progress and acceptable. IQCP may be way ahead, since the specific guidance, training, workload and extra costs are required.

- The vast majority of errors involving the clinical laboratory occur in the pre- and post-analytical phases of testing, including many steps and processes which are "pre-pre" and "post-post" problems that take place outside the confines of the lab .
  Beyond these steps, the largest challenge for clinical labs are the remaining problems in analytical testing.
  But the need to take on the that with an effective QCP is clear.

Perspectives for the future: Pros and Cons

- Labs have a choice now. They can do a risk assessment evaluation to better determine how their tests are performing and how much QC they should run.
- New regulations of an IQCP may outweigh the cost savings of the small labs with fewer instruments, so they still run daily minimum QC. Labs with many instruments, may find the potential cost savings opportunity is greater than the cost of implementing an IQCP.
- The Quality Risk Management plan defines the control mechanisms for detecting and preventing errors combined with the elements of Closed Loop Quality Management which provides the methodology for periodic quality assessment to ensure QCP effectiveness.

THANK YOU

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