Linking QC Performance to Patient Risk

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Bio-Rad Laboratories
Learning Objectives

• Discuss the importance of a “patient risk” approach to QC planning
• Describe the elements of a QC system that impact patient risk
• Identify the ways in which labs can reduce patient risk with QC
• Analyze the relationship between QC performance and patient risk
Laboratory Medicine

• Goal: To improve patient health
• Tools: Laboratory tests
• Mechanism: Support medical decisions
  • Produce accurate results
  • Minimize patient risk
Risk Management Principles

• Risk management guidelines for the laboratory
  – ISO 15189: Medical laboratories – Requirements for quality and competence
  – ISO 14971: Medical devices – Application of risk management to medical devices
  – CLSI EP23: Laboratory quality control based on risk management
Risk Management Principles

• Risk management provides a formal approach to
  – Identify potential failure modes in the lab
  – Rank identified failure modes in terms of their patient risk
  – Establish policies and procedures to prevent or reduce (mitigate) the risks
  – Focus on the highest ranked risks

• Patient risk is defined as the combination of
  – The probability of occurrence of patient harm
  – The severity of patient harm
EP23-A: Probability of Patient Harm

Sequence of Events Creating Risk of Harm for a Patient (Example)

CLSI EP23, Figure 6
Probability of Patient Harm

Sequence of Events Creating Risk of Harm for a Patient (Example)

Probability of patient harm from a failure:
- Frequent
- Probable
- Occasional
- Remote
- Improbable
## Probability of Harm Categories

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<th>ISO 14971 Example</th>
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If lab averages 100 analyte results per day:

\[
\frac{1}{(100 \times 365)} = \frac{1}{36,500}
\]
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- If lab averages 20 analyte results per day
  - \( \frac{1}{20 \times 365} = \frac{1}{7,300} \)
Severity of Harm

• Severity of harm is described in terms of the severity of the consequence to the patient
• Severity of harm depends on
  • Analyte
  • Patient care situation
Severity of Harm Categories

- Both ISO 14971 and CLSI EP23 give the same example severity of harm categories
  - 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 = patient death
# EP23-A Risk Acceptability Matrix

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# ISO 14971 - Risk Acceptability Matrix

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Acceptable in EP23 matrix
### ISO 14971 - Risk Acceptability Matrix

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Probability of Patient Harm

Sequence of Events Creating Risk of Harm for a Patient

1. Initiating cause
2. Testing process failure
3. Incorrect result generated
4. Incorrect result reported
5. Misdiagnosis
6. Hazardous medical action
7. Patient harmed
Probability of Patient Harm

Sequence of Events Creating Risk of Harm for a Patient

- Initiating cause
- Patient harmed

Probability of patient harm from a failure:
- Frequent
- Probable
- Occasional
- Remote
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Probability of Patient Harm

Sequence of Events Creating Risk of Harm for a Patient

We should be able to do better than this!

Initiating cause → Patient harmed

Probability of patient harm from a failure:
- Frequent
- Probable
- Occasional
- Remote
- Improbable
Predicting Probability of Patient Harm

Initiating cause → Testing process failure → Incorrect result generated → Incorrect result reported → Misdiagnosis → Hazardous medical action → Patient harmed
Predicting Probability of Patient Harm

What do we mean by an incorrect result?
The Quality Required of Patient Results

• ISO 15189 Clause 5.6.1: *Laboratory QC should assure that patient results meet the quality required for their intended use*

• The quality of a patient result depends on the difference between the correct value and the value reported.

• If the error in a patient’s result exceeds the allowable total error (TEₐ) the result is considered **erroneous** (incorrect, unacceptable) and creates a hazardous situation for the patient.
CLSI C24, 4th Edition

C24
Statistical Quality Control for Quantitative Measurement Procedures: Principles and Definitions

This guideline provides definitions, principles, and approaches to laboratory quality control design, implementation, and assessment.

A guideline for global application developed through the Clinical and Laboratory Standards Institute consensus process.
Statistical Quality Control for Quantitative Measurement Procedures: Principles and Definitions

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Greg Miller, PhD
Megan E. Sawchuk, MT(ASCP)

Abstract

Clinical and Laboratory Standards Institute guideline C24—Statistical Quality Control for Quantitative Measurement Procedures: Principles and Definitions discusses the principles of statistical QC, with particular attention to the planning of a QC strategy and the application of statistical QC in a medical laboratory. Although these principles are of interest to manufacturers, this guideline is intended for use by medical laboratory personnel in order to provide a QC strategy that uses control materials that are external to a reagent kit, instrument, or measuring system and that are intended to simulate the measurement of a patient specimen.
CLSI C24, 4th Edition: Definitions

**analyte** – constituent of a sample with a measurable property; **NOTE**: In “mass of protein in 24-hour urine,” “protein” is the analyte and “mass” is the property. In “concentration of glucose in plasma,” “glucose” is the analyte and “concentration” is the property. In both cases, the full phrase represents the measurand.

**bias (of measurement)** – estimate of a systematic measurement error; difference between the expectation of a test result or measurement result and a true value; **NOTE 1**: In practice, the accepted reference value is substituted for the true value; **NOTE 2**: Bias represents the quantitative expression of trueness.

**coefficient of variation (CV)** – (positive random variable) standard deviation (SD) divided by the mean; **NOTE 1**: The CV is commonly reported as a percentage; **NOTE 2**: The predecessor term “relative SD” is deprecated by the term CV.

**control limit** – the most extreme value of a quality control material that is still considered to be acceptable.

**erroneous result** – a patient result that fails its quality requirement; **NOTE 1**: The quality requirement is usually expressed in terms of an allowable total error (TEa) requirement. If the measurement error in a patient’s result exceeds the TEa requirement, the result is erroneous; **NOTE 2**: May also be referred to as an incorrect result or an unacceptable result.

**error (of measurement)** – measured quantity value minus a reference quantity value; **NOTE 1**: The concept of “measurement error” can be used both a) when there is a single reference quantity value to...
Predicting Probability of Patient Harm

- Initiating cause
- Testing process failure
- Incorrect result generated
- Incorrect result reported
- Misdiagnosis
- Hazardous medical action
- Patient harmed
Predicting Probability of Patient Harm

The probability of producing erroneous results in the absence of a testing process failure.
Probability of Erroneous Results in the Absence of a Testing Process Failure

- The probability of producing erroneous results in the absence of a testing process failure can be computed based on:
  - a measurement procedure’s bias and imprecision
  - the allowable total error requirement for an analyte.
Probability of Erroneous Results in the Absence of a Testing Process Failure
Probability of Erroneous Results in the Absence of a Testing Process Failure

Measurement Procedure Bias

Measurement Error

$-\text{TE}_a \quad 0 \quad +\text{TE}_a$
Probability of Erroneous Results in the Absence of a Testing Process Failure
Probability of Erroneous Results in the Absence of a Testing Process Failure
Predicting Probability of Patient Harm

The frequency of testing process failures reflects the measurement procedure’s reliability.
Measurement Procedure Reliability

• From a patient risk perspective, measurement procedure reliability is best expressed as the mean # of in-control patient results reported between testing process failures (MPBF)
  • MPBF can be obtained from;
    • An estimate of mean time between test system failures,
    • The average number of patient results for the analyte per day
Predicting Probability of Patient Harm

The likelihood that erroneous results are generated after a testing process failure depends on the magnitude of the out-of-control condition.
Erroneous Results when In-Control

-6σ  -5σ  -4σ  -3σ  -2σ  -1σ  0  1σ  2σ  3σ  4σ  5σ  6σ

-TE_a  Measurement Error  TE_a
Erroneous Results when In-Control

\[ \approx 3 \text{ in } 1,000 \text{ chance of exceeding } TE_a \]
Erroneous Results when Out-of-Control

>15% chance of exceeding $TE_a$
Predicting Probability of Patient Harm

The number of erroneous results reported depends on the effectiveness of the laboratory’s QC strategy.
Number of Erroneous Patient Results

• The number of erroneous patient results due to an out-of-control condition in a measurement procedure depends on
  – The quality specification (allowable total error)
  – The size of the out-of-control condition
  – The frequency of QC testing
  – The power of the QC rule(s) to detect the out-of-control error condition
Erroneous Patient Results: Example 1

2 QC Concentrations: $QC_1 = 60 \text{ mg/dL}$, $QC_2 = 130\text{ mg/dL}$

$TE_a = 10\%$, $CV = 2.5\%$, QC Rule: 1-3s/2-2s/R-4s
Erroneous Patient Results: Example 1

2 QC Concentrations: QC\(_1\) = 60 mg/dL, QC\(_2\) = 130 mg/dL

\[ TE_a = 10\%, \ CV = 2.5\%, \ QC \text{ Rule: 1-3s/2-2s/R-4s} \]
Erroneous Patient Results: Example 1

2 QC Concentrations: QC$_1$ = 60 mg/dL, QC$_2$ = 130 mg/dL

-5% Shift Occurs

Measurement Error in Each Result

TE$_a$ = 10%, CV = 2.5%, QC Rule: 1-3s/2-2s/R-4s
Erroneous Patient Results: Example 1

2 QC Concentrations: \( QC_1 = 60 \text{ mg/dL}, \ QC_2 = 130\text{mg/dL} \)

Error Condition Occurs

\( TE_a = 10\%, \ CV = 2.5\%, \ QC \text{ Rule: 1-3s/2-2s/R-4s} \)
Erroneous Patient Results: Example 1

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Erroneous Patient Results: Example 1

2 QC Concentrations: QC$_1$ = 60 mg/dL, QC$_2$ = 130 mg/dL

QC Rule Rejects

$TE_a$ = 10\%, CV = 2.5\%, QC Rule: 1-3s/2-2s/R-4s
Erroneous Patient Results: Example 1

2 QC Concentrations: $QC_1 = 60 \text{ mg/dL}$, $QC_2 = 130 \text{ mg/dL}$

89 patient results affected by the error condition

$TE_a = 10\%$, $CV = 2.5\%$, QC Rule: 1-3s/2-2s/R-4s

Measurement Error

Time
Erroneous Patient Results: Example 1

2 QC Concentrations: $QC_1 = 60 \text{ mg/dL}, QC_2 = 130\text{ mg/dL}$

$TE_a = 10\%, CV = 2.5\%, QC \text{ Rule: 1-3s/2-2s/R-4s}$

3 of the affected patient results are erroneous
Erroneous Patient Results: Example 1

2 QC Concentrations: \( QC_1 = 60 \text{ mg/dL}, QC_2 = 130 \text{ mg/dL} \)

\[ TE_a = 10\%, \ CV = 2.5\%, \ QC \text{ Rule: 1-3s/2-2s/R-4s} \]

1 erroneous result was after the last accepted QC
Erroneous Patient Results: Example 1

2 QC Concentrations: QC\(_1\) = 60 mg/dL, QC\(_2\) = 130 mg/dL

-5% Shift Occurs

\[\text{TE}_a = 10\%, \text{ CV} = 2.5\%, \text{ QC Rule: 1-3s/2-2s/R-4s}\]

2 erroneous results were prior to the last accepted QC
Erroneous results can be divided into 2 groups:

- Those that are corrected before they are acted on
  - $E(N_{uc})$: Expected number of unacceptable correctable results

- Those that are never corrected
  - Final results that create hazardous situations
  - $E(N_{uf})$: Expected number of unacceptable final results

If erroneous results back to the last accepted QC can be corrected before acted on:

- $E(N_{uc}) = \#$ erroneous results back to last accepted QC
- $E(N_{uf}) = \#$ erroneous results prior to last accepted QC
Erroneous Patient Results: Example 1

Glucose, TEa = ±10.0%, 1:3s/2:2s/R:4s Rule, NB = 50, SE = -5.0%

- NQCE: mean = 2.5
- Naff: mean = 97.9
- Nuf: mean = 1.3
- Nuc: mean = 1.0
Erroneous Patient Results: Example 1

Glucose, TEa = ±10.0%, 1:3s/2:2s/R:4s Rule, NB = 50, SE = -5.0%

Number of QC Events to Detection

NQCE: mean = 2.5

Naff: mean = 97.9

Nuf: mean = 1.3

Nuc: mean = 1.0
Erroneous Patient Results: Example 1

Glucose, TEa = ±10.0%, 1:3s/2:2s/R:4s Rule, NB = 50, SE = -5.0%

Number of Affected Patient Results

NQCE: mean = 2.5
Naff: mean = 97.9
Nuf: mean = 1.3
Nuc: mean = 1.0
Erroneous Patient Results: Example 1

Glucose, TEa = ±10.0%, 1:3s/2:2s/R:4s Rule, NB = 50, SE = -5.0%

- NQCE: mean = 2.5
- Naff: mean = 97.9
- Nuf: mean = 1.3
- Nuc: mean = 1.0

Number of Erroneous Final Results
Erroneous Patient Results: Example 1

Glucose, TEa = ±10.0%, 1:3s/2:2s/R:4s Rule, NB = 50, SE = -5.0%

Number of Erroneous Correctable Results

NQCE: mean = 2.5
Naff: mean = 97.9
Nuf: mean = 1.3
Nuc: mean = 1.0
Erroneous Patient Results: Example 1

Glucose, TEa = ±10.0%, 1:3s/2:2s/R:4s Rule, NB = 50, SE = -5.0%

NQCE: mean = 2.5

Naff: mean = 97.9

Nuf: mean = 1.3

Nuc: mean = 1.0

89 affected results in the example
Erroneous Patient Results: Example 1

Glucose, TEa = ±10.0%, 1:3s/2:2s/R:4s Rule, NB = 50, SE = -5.0%

- NQCE: mean = 2.5
- Naff: mean = 97.9
- Nuf: mean = 1.3
- Nuc: mean = 1.0

$\text{ANP}_{\text{ed}} = \text{the average number of affected results}$
Erroneous Patient Results: Example 1

Glucose, TEa = ±10.0%, 1:3s/2:2s/R:4s Rule, NB = 50, SE = -5.0%

- NQCE: mean = 2.5
- Naff: mean = 97.9
- Nuf: mean = 1.3
- Nuc: mean = 1.0

2 erroneous results prior to last accepted QC in the example
Erroneous Patient Results: Example 1

Glucose, TEa = ±10.0%, 1:3s/2:2s/R:4s Rule, NB = 50, SE = -5.0%

E(N_{uf}) is the average number

NQCE: mean = 2.5

Naff: mean = 97.9

Nuf: mean = 1.3

Nuc: mean = 1.0
Erroneous Patient Results: Example 2

2 QC Concentrations: $QC_1 = 60 \text{ mg/dL}$, $QC_2 = 130\text{ mg/dL}$

$TE_a = 10\%$, $CV = 2.5\%$, QC Rule: 1-3s/2-2s/R-4s
Erroneous Patient Results: Example 2

2 QC Concentrations: QC$_1$ = 60 mg/dL, QC$_2$ = 130 mg/dL

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An Error Condition Occurs

$T_{E_a} = 10\%$, $CV = 2.5\%$, QC Rule: 1-3s/2-2s/R-4s

---

Time
Erroneous Patient Results: Example 2

2 QC Concentrations: $QC_1 = 60 \text{ mg/dL}$, $QC_2 = 130 \text{ mg/dL}$

$TE_a = 10\%$, $CV = 2.5\%$, QC Rule: 1-3s/2-2s/R-4s

QC Rule Rejects
Erroneous Patient Results: Example 2

2 QC Concentrations: \( QC_1 = 60 \text{ mg/dL}, \ QC_2 = 130 \text{ mg/dL} \)

\( TE_a = 10\%, \ CV = 2.5\%, \ QC \text{ Rule: } 1-3s/2-2s/R-4s \)

25 patient results affected by the error condition
Erroneous Patient Results: Example 2

2 QC Concentrations: $QC_1 = 60 \text{ mg/dL}, QC_2 = 130\text{mg/dL}$

$T_{EA} = 10\%, CV = 2.5\%, \text{QC Rule: 1-3s/2-2s/R-4s}$

12 erroneous results since the last accepted QC
Erroneous Patient Results: Example 2

No erroneous results prior to the last accepted QC because error condition detected at 1st QC event

$2 \text{ QC Concentrations: } QC_1 = 60 \text{ mg/dL, } QC_2 = 130 \text{ mg/dL}$

$T_{ea} = 10\%, CV = 2.5\%, QC \text{ Rule: } 1-3s/2-2s/R-4s$
Erroneous Patient Results: Example 2

Glucose, TEa = ±10.0%, 1:3s/2:2s/R:4s Rule, NB = 50, SE = 9.0%

ANPed when SE = 9%

E(Nuf) when SE = 9%

ANPed when SE = 9%

Nuf: mean = 0.2

Nuc: mean = 8.8
Average # of Affected Patient Results

![Graph showing the relationship between ANP_{ed} and SE(%) with a peak at a specific SE value.]
Expected # of Erroneous Patient Results
Prior to Last Accepted QC Event

![Graph showing expected number of erroneous patient results prior to last accepted QC event.](image-url)
The probability that erroneous reported results lead to inappropriate decisions or actions causing patient harm depends on the analyte and how it is used in patient care.
Probability Erroneous Results Lead to Harm

• The probability that erroneous reported results lead to patient harm will depend on;
  • knowledge of how test results are used to make patient care decisions.
  • may be obtained from expert opinion, the literature, or consultation with local physicians.
Predicting Probability of Patient Harm

Initiating cause → Testing process failure → Incorrect result generated → Incorrect result reported → Misdiagnosis → Hazardous medical action → Patient harmed
Predicting Probability of Patient Harm

The probability of producing erroneous results in the absence of a testing process failure.
Predicting Probability of Patient Harm

The frequency of testing process failures reflects the measurement procedure’s reliability.

The probability of producing erroneous results in the absence of a testing process failure.
Predicting Probability of Patient Harm

The number of erroneous results reported depends on the effectiveness of the laboratory’s QC strategy.
Predicting Probability of Patient Harm

The probability that erroneous reported results lead to inappropriate decisions or actions causing patient harm depends on the analyte and how it is used in patient care.

Initiating cause → Testing process failure → Incorrect result generated → Incorrect result reported → Misdiagnosis → Hazardous medical action → Patient harmed

The probability of producing erroneous results in the absence of a testing process failure.

The frequency of testing process failures reflects the measurement procedure’s reliability.

The number of erroneous results reported depends on the effectiveness of the laboratory’s QC strategy.

The probability that erroneous reported results lead to inappropriate decisions or actions causing patient harm depends on the analyte and how it is used in patient care.
Predicting Probability of Patient Harm

1. Initiating cause
2. Testing process failure
3. Incorrect result generated
4. Incorrect result reported
5. Misdiagnosis
6. Hazardous medical action
7. Patient harmed

$P_E(0)$

MPBF

$E(N_{uf}(SE))$

$\text{ANP}_{ed}(SE)$

$P_{h|u}$
Predicting Probability of Patient Harm

\[ P_H(\text{SE}) = \{P_E(0) + \frac{E(N_{uf}(\text{SE}))}{(\text{MPBF} + \text{ANP}_{ed}(\text{SE}))}\} \times P_{h|u} \]

- Initiating cause
- Testing process failure
- Incorrect result generated
- Incorrect result reported
- Misdiagnosis
- Hazardous medical action
- Patient harmed

\[ PE(0) \]
\[ E(N_{uf}(\text{SE})) \]
\[ \text{ANP}_{ed}(\text{SE}) \]
\[ \text{MPBF} \]
\[ P_{h|u} \]
Predicting Probability of Patient Harm

We should be able to do better than this!

Probability of patient harm from a failure:
- Frequent
- Probable
- Occasional
- Remote
- Improbable
Predicting Probability of Patient Harm

\[ P_H(SE) = \{P_E(0) + \frac{E(N_{uf}(SE))}{MPBF + ANP_{ed}(SE)}\} \times P_{h|u} \]

- Initiating cause
- Testing process failure
- Incorrect result generated
- Incorrect result reported
- Misdiagnosis
- Hazardous medical action
- Patient harmed
Predicting Probability of Patient Harm

• Can be computed based on;
  • The in-control probability of producing erroneous results
  • The reliability of the measurement procedure
  • The effectiveness of the QC strategy
  • The likelihood that erroneous reported results cause harm

• Cannot be computed without computer software that performs the required computations
Predicted Probability of Harm Example

- Glucose: CV = 2.5%, TEa = ±10%
- Average # patient results / day = 100
- Mean days between test system failures = 30
  - MPBF = 100 * 30 = 3,000
- QC Strategy:
  - 2 QC levels,
  - QC evaluated once per day,
  - 1:3s QC rule
- Probability of harm given incorrect result = 0.5
Predicted Probability of Harm Example

What’s the predicted probability of harm?

Initiating cause

Patient harmed

Probability of patient harm from a failure:

- Frequent
- Probable
- Occasional
- Remote
- Improbable
Predicting Probability of Patient Harm

\[ P_H(SE) = \left\{ P_E(0) + \frac{E(N_{uf}(SE))}{MPBF + ANP_{ed}(SE)} \right\} \times P_{h|u} \]
Predicted Probability of Harm Example

\[ P_H(SE) = \{P_E(0) + \frac{E(N_{uf}(SE))}{(MPBF + ANP_{ed}(SE))}\} \times P_{h|u} \]
Predicted Probability of Harm Example

\[
P_H(SE) = \left\{ P_E(0) + \frac{E(N_{uf}(SE))}{(MPBF + ANP_{ed}(SE))} \right\} \times P_{h|u}
\]

In-Control Predicted Probability of Harm, \( P_H(0) = \frac{1}{31,574} \)
Predicted Probability of Harm Example

\[ P_H(SE) = \{P_E(0) + E(N_{uf}(SE)) / (MPBF + ANP_{ed}(SE))\} \times P_{h|u} \]

Predicted probability of harm averaged across all SE values, \( P_H = 1/4,284 \)
Predicted and Acceptable Probability of Harm

• Predicted probability of harm depends on;
  • The measurement procedure’s in-control performance and reliability,
  • The lab’s QC strategy,
  • How analyte is used in medical decisions.

• Acceptable probability of harm is derived from;
  • Severity of harm,
  • Risk acceptability matrix.
We define the patient risk management index as:

\[ \text{RMI} = \frac{\text{Predicted PH}}{\text{Acceptable PH}} \]

- RMI ≤ 1 implies acceptable risk.
- RMI values permit easy assessment and comparison of multiple analytes:
  - with different frequencies of test system failure
  - with different probabilities of harm from erroneous results
  - with different severities of patient harm
RMI Example

- Glucose severity of harm = Minor
## ISO 14971 - Risk Acceptability Matrix

<table>
<thead>
<tr>
<th>Probability of Harm</th>
<th>Negligible</th>
<th>Minor</th>
<th>Serious</th>
<th>Critical</th>
<th>Catastrophic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequent</td>
<td>Unacceptable</td>
<td>Unacceptable</td>
<td>Unacceptable</td>
<td>Unacceptable</td>
<td>Unacceptable</td>
</tr>
<tr>
<td>Probable</td>
<td>Unacceptable</td>
<td>Unacceptable</td>
<td>Unacceptable</td>
<td>Unacceptable</td>
<td>Unacceptable</td>
</tr>
<tr>
<td>Occasional</td>
<td>Acceptable</td>
<td><strong>Acceptable</strong></td>
<td>Unacceptable</td>
<td>Unacceptable</td>
<td>Unacceptable</td>
</tr>
<tr>
<td>Remote</td>
<td>Acceptable</td>
<td>Acceptable</td>
<td>Acceptable</td>
<td><strong>Unacceptable</strong></td>
<td>Unacceptable</td>
</tr>
<tr>
<td>Improbable</td>
<td>Acceptable</td>
<td>Acceptable</td>
<td>Acceptable</td>
<td>Acceptable</td>
<td>Acceptable</td>
</tr>
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</tr>
<tr>
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<td>Unacceptable</td>
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<td>Unacceptable</td>
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<tr>
<td>Remote</td>
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<td>Acceptable</td>
<td>Acceptable</td>
<td>Acceptable</td>
<td>Unacceptable</td>
</tr>
<tr>
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<td>Acceptable</td>
<td>Acceptable</td>
<td>Acceptable</td>
<td>Acceptable</td>
<td>Acceptable</td>
</tr>
</tbody>
</table>
RMI Example

- Glucose severity of harm = Minor
- Acceptable $P_H$:
  - Acceptable frequency of harm level: Occasional
<table>
<thead>
<tr>
<th>Category Level</th>
<th>CLSI EP23 Example</th>
<th>ISO 14971 Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequent</td>
<td>Once/week</td>
<td>≥1/1,000</td>
</tr>
<tr>
<td>Probable</td>
<td>Once/month</td>
<td>&lt;1/1,000 and ≥1/10,000</td>
</tr>
<tr>
<td>Occasional</td>
<td>Once/year</td>
<td>&lt;1/10,000 and ≥1/100,000</td>
</tr>
<tr>
<td>Remote</td>
<td>Once/few years</td>
<td>&lt;1/100,000 and ≥1/1,000,000</td>
</tr>
<tr>
<td>Improbable</td>
<td>Once/life of measuring system</td>
<td>&lt;1/1,000,000</td>
</tr>
</tbody>
</table>
RMI Example

- Glucose severity of harm = Minor
- Acceptable $P_H$:
  - Acceptable frequency of harm level: Occasional
  - Using ISO 14971 Risk Acceptability Matrix: $P_H < 1/10,000$

\[
\text{RMI} = \frac{\text{Predicted } P_H}{\text{Acceptable } P_H}
\]
RMI Example

• Glucose severity of harm = Minor

• Acceptable $P_H$:
  • Acceptable frequency of harm level: Occasional
  • Using ISO 14971 Risk Acceptability Matrix: $P_H < 1/10,000$

\[
RMI = \frac{\text{Predicted } P_H}{\text{Acceptable } P_H} = \frac{1/4,284}{1/10,000} = 2.3
\]
Change QC Rule

- Glucose: CV = 2.5%, TEa = ±10%
- Average # patient results / day = 100
- Mean days between test system failures = 30
  - MPBF = 100*30 = 3,000
- Probability of harm given incorrect result = 0.5
- QC Strategy:
  - 2 QC levels,
  - 1:3s QC rule,
  - QC evaluated once per day
Change QC Rule

- Glucose: CV = 2.5%, TEa = ±10%
- Average # patient results / day = 100
- Mean days between test system failures = 30
  - MPBF = 100*30 = 3,000
- Probability of harm given incorrect result = 0.5
- QC Strategy:
  - 2 QC levels,
  - 1:3s/2:2s/R:4s QC rule,
  - QC evaluated once per day
What’s the predicted probability of harm?

Probability of patient harm from a failure:
- Frequent
- Probable
- Occasional
- Remote
- Improbable
1:3s QC Rule

\[ P_H(SE) = \left\{ P_E(0) + \frac{E(N_{uf}(SE))}{(MPBF + ANP_{ed}(SE))} \right\} \times P_{h\mid u} \]

\[ P_H = 1/4,284 \]

\[ P_H(0) = 1/31,574 \]
$P_H(\text{SE}) = \{P_E(0) + \frac{E(N_{uf}(\text{SE}))}{(\text{MPBF} + \text{ANP}_{ed}(\text{SE}))}\} \times P_{h|u}$
$P_H(SE) = \{P_E(0) + \frac{E(N_{uf}(SE))}{MPBF + ANP_{ed}(SE)}\} \times P_{h|u}$

$P_H = \frac{1}{7,203}$

$P_H(0) = \frac{1}{31,574}$

$RMI = \left(\frac{1}{7,203}\right) / \left(\frac{1}{10,000}\right) = 1.4$
Change QC Frequency

- Glucose: CV = 2.5%, TEa = ±10%
- Average # patient results / day = 100
- Mean days between test system failures = 30
  - MPBF = 100*30 = 3,000
- Probability of harm given incorrect result = 0.5
- QC Strategy:
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Change QC Frequency

- Glucose: CV = 2.5%, TEa = ±10%
- Average # patient results / day = 100
- Mean days between test system failures = 30
  - $\text{MPBF} = 100 \times 30 = 3,000$
- Probability of harm given incorrect result = 0.5
- QC Strategy:
  - 2 QC levels,
  - 1:3s/2:2s/R:4s QC rule,
  - QC evaluated twice per day
Change QC Frequency

What’s the predicted probability of harm?

Initiating cause

Probability of patient harm from a failure:

• Frequent
• Probable
• Occasional
• Remote
• Improbable

Patient harmed
QC Evaluated Once Per Day

\[ \text{RMI} = \frac{1/7,203}{1/10,000} = 1.4 \]

\[ P_H = \frac{1}{7,203} \]

\[ P_H(\text{SE}) = \{P_E(0) + E(N_{uf}(\text{SE})) / (\text{MPBF} + \text{ANP}_{ed}(\text{SE}))\} \times P_{h|u} \]
QC Evaluated Twice Per Day

\[ \text{PH} = \frac{1}{11,270} \]

\[ \text{RMI} = \frac{1}{11,270} / \frac{1}{10,000} = 0.9 \]

\[ \text{PH}(\text{SE}) = \left( P_{E}(0) + \frac{\mathbb{E}(N_{uf}(\text{SE}))}{\text{MPBF} + \text{ANP}_{ed}(\text{SE})} \right) \times \text{PH}_{ju} \]
Predicted Probability of Patient Harm

Probability of patient harm from a failure:
- Frequent
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Predicted Probability of Patient Harm

\[ P_H(\text{SE}) = \{P_E(0) + \frac{E(N_{uf}(\text{SE}))}{(MPBF + ANP_{ed}(\text{SE}))}\} \times P_{h|u} \]
Summary

• A lab’s tolerance for reporting erroneous patient results should depend on:
  • the likelihood that erroneous patient results lead to harm,
  • the severity of patient harm.

• The lab’s impact on patient risk depends on:
  • The in-control performance of the lab’s measurement procedures
  • The reliability of the lab’s measurement procedures
  • The lab’s QC strategy

• It’s important to be able to objectively assess the impact of a lab’s QC strategy on patient risk.

• One way to link QC performance to patient risk is to compute RMI and seek QC strategies with RMI < 1.
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