Best Practices in Quality Control: 10 Simple Recommendations

Curtis A. Parvin, Ph.D.

15 July, 2020

Learning Objectives

1. Identify factors in QC error that contribute to increased patient risk.

2. Describe ways in which quality risk management has contributed to an added set of values that the laboratory should be aware of.

3. Recommend 5 QC practices which you can apply in your lab.

Laboratory Medicine

- Goal: To improve patient health

- Tools: Laboratory tests

- Mechanism: Support medical decisions
  - Produce accurate results
  - Minimize patient risk

What is Patient Risk?

- In statistics risk is defined as the probability of an unwanted event.

- In risk management patient risk is defined as the combination of
  - The probability of occurrence of patient harm
  - The severity of patient harm

Probability of Harm Categories

Category Level	CLSI EP23 Example	ISO 14971 Example
Frequent	Once/week	≥1/1,000
Probable	Once/month	<1/1,000 and ≥1/10,000
Occasional	Once/year	<1/10,000 and ≥1/100,000
Remote	Once/few years	<1/100,000 and ≥1/1,000,000
Improbable	Once/life of measuring system	<1/1,000,000

3

Severity of Harm

- Severity of harm is described in terms of the severity of the consequence to the patient

- Severity of harm is considered independently of probability of harm

- Severity of harm depends on
  - Analyte
  - How the analyte is used in the clinical setting

4

Severity of Harm Categories

- CLSI EP23 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
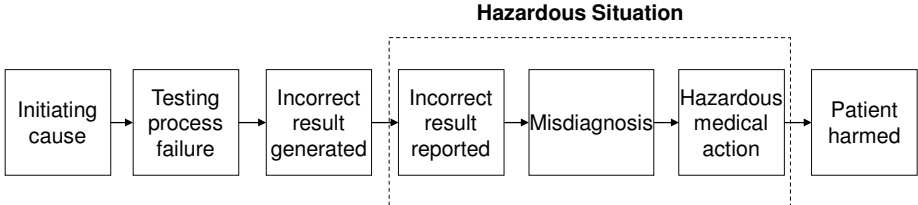 - Catastrophic = patient death

5

Risk Acceptability Matrix

Probability of Harm	Severity of Harm				
	Negligible	Minor	Serious	Critical	Catastrophic
Frequent	Unacceptable	Unacceptable	Unacceptable	Unacceptable	Unacceptable
Probable	Acceptable	Unacceptable	Unacceptable	Unacceptable	Unacceptable
Occasional	Acceptable	Acceptable	Acceptable	Unacceptable	Unacceptable
Remote	Acceptable	Acceptable	Acceptable	Acceptable	Unacceptable
Improbable	Acceptable	Acceptable	Acceptable	Acceptable	Acceptable

CLSI EP23, Table 3
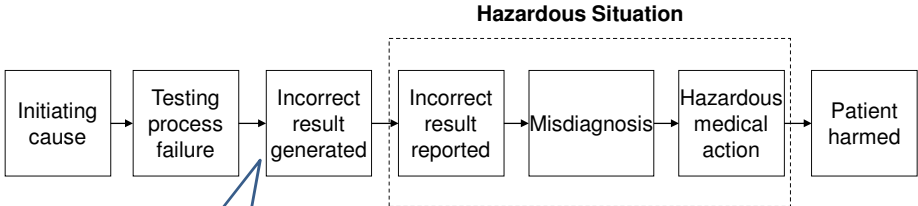
6

4

Probability of Patient Harm

Sequence of Events Creating Risk of Harm for a Patient

Hazardous Situation

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

CLSI EP23, Figure 6

7

Probability of Patient Harm

Sequence of Events Creating Risk of Harm for a Patient

Hazardous Situation

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

What do we mean by an incorrect result?

CLSI EP23, Figure 6

7

CLSI C24, 4th Edition: Definitions

analyte – constituent of a sample with a measurable property[13]; **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.[13]

bias (of measurement) – estimate of a systematic measurement error[12]; difference between the expectation of a test result or measurement result and a true value[14]; **NOTE 1:** In practice, the accepted reference value is substituted for the true value[14]; **NOTE 2:** Bias represents the quantitative expression of trueness.

coefficient of variation (CV) – (positive random variable) standard deviation (SD) divided by the mean[15]; **NOTE 1:** The CV is commonly reported as a percentage[15]; **NOTE 2:** The predecessor term "relative SD" is deprecated by the term CV.[15]

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.
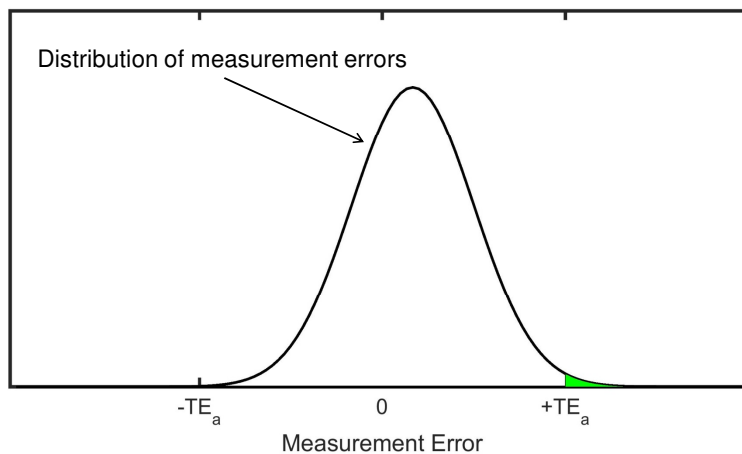
error (of measurement) – measured quantity value minus a reference quantity value[12]; **NOTE 1:** The concept of "measurement error" can be used both a) when there is a single reference quantity value to

3

8

Erroneous Results

Distribution of measurement errors

$-TE_a$ 0 $+TE_a$

Measurement Error

9

6

Erroneous Results

-TE$_a$ 0   +TE$_a$

Measurement Error

Allowable total error limits

9

Erroneous Results

Erroneous

-TE$_a$ 0   +TE$_a$

Measurement Error

9

Probability of Patient Harm

Sequence of Events Creating Risk of Harm for a Patient

Hazardous Situation

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

10

Probability of Patient Harm

Sequence of Events Creating Risk of Harm for a Patient

Hazardous Situation

Initiating cause → Testing process failure → Incorrect result generated → Incorrect result reported → Misdiagnosis → Hazardous medical action → Patient harmed
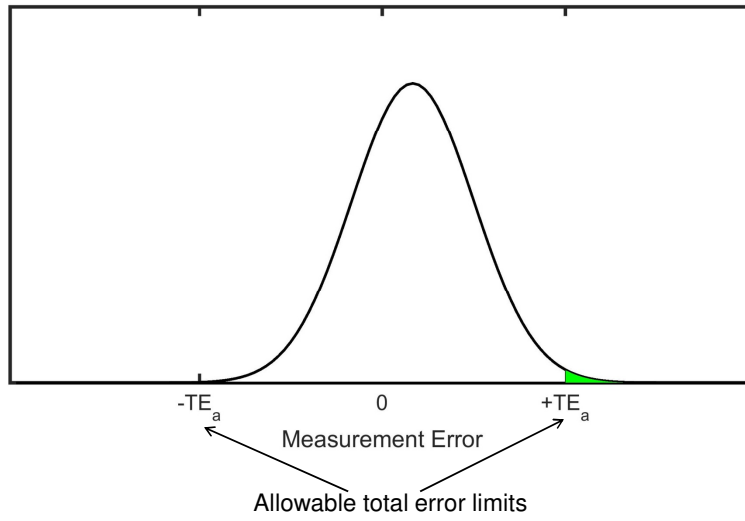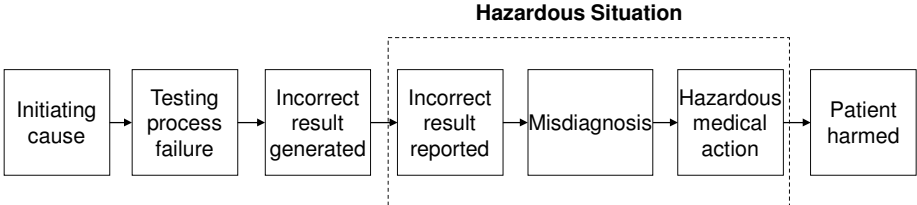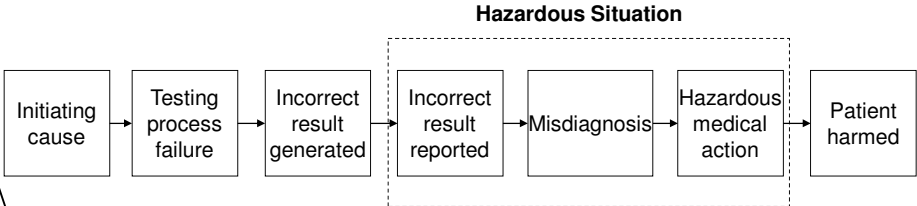
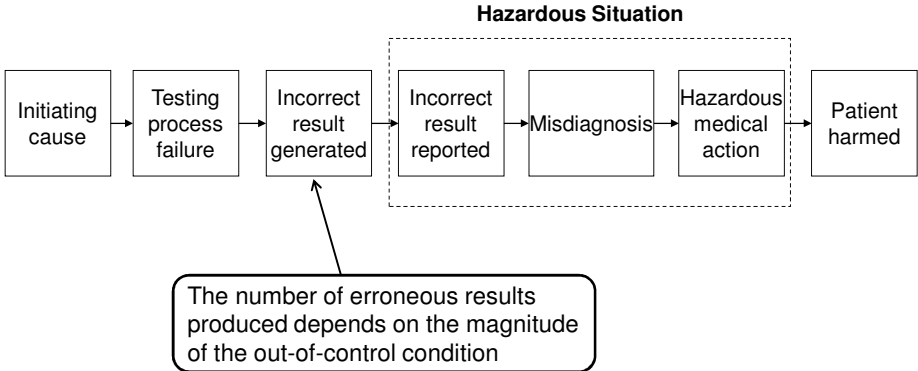The in-control probability of producing erroneous results reflects the sigma value for the measurement procedure

10

8

Probability of Patient Harm
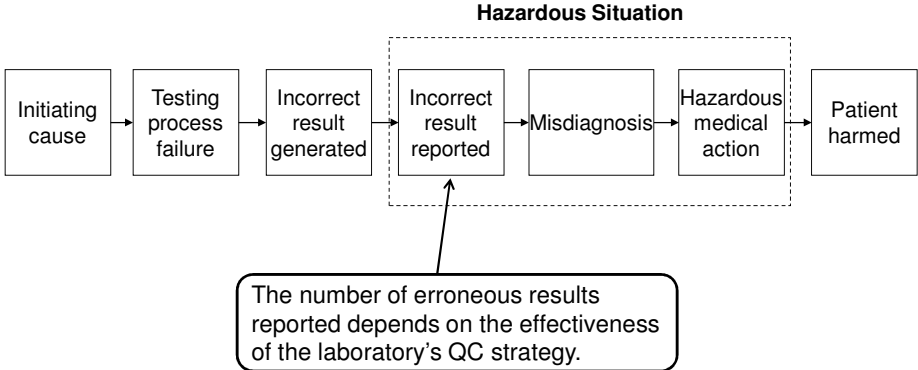
Sequence of Events Creating Risk of Harm for a Patient

Hazardous Situation

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

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

10

Probability of Patient Harm

Sequence of Events Creating Risk of Harm for a Patient

Hazardous Situation

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

The number of erroneous results produced depends on the magnitude of the out-of-control condition

10

9

Probability of Patient Harm

Sequence of Events Creating Risk of Harm for a Patient

Hazardous Situation

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

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

10

Probability of Patient Harm

Sequence of Events Creating Risk of Harm for a Patient

Hazardous Situation

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

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.

10

Probability of Patient Harm

Sequence of Events Creating Risk of Harm for a Patient

Hazardous Situation

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

10

Probability of Patient Harm

Sequence of Events Creating Risk of Harm for a Patient

Hazardous Situation

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

This is where laboratory QC plays a role

10

Probability of Patient Harm

Sequence of Events Creating Risk of Harm for a Patient

Hazardous Situation

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

But our QC practices must also consider the implications here

10

---

10 QC Recommendations to Help Minimize Patient Risk

- Widely applicable.

- Implementation is straightforward.

- No advanced math required to understand or implement.

- Should help reduce patient risk.

11

12

Recommendation #1

Always end patient testing with a QC evaluation.
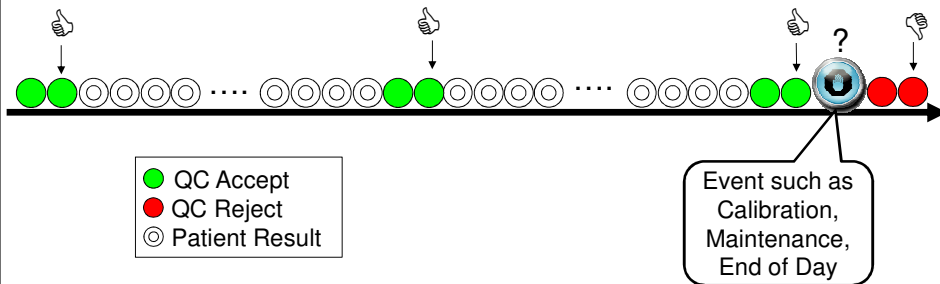
12

Recommendation #1
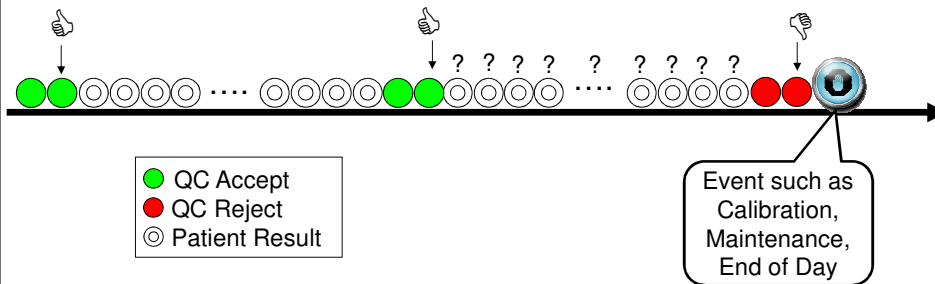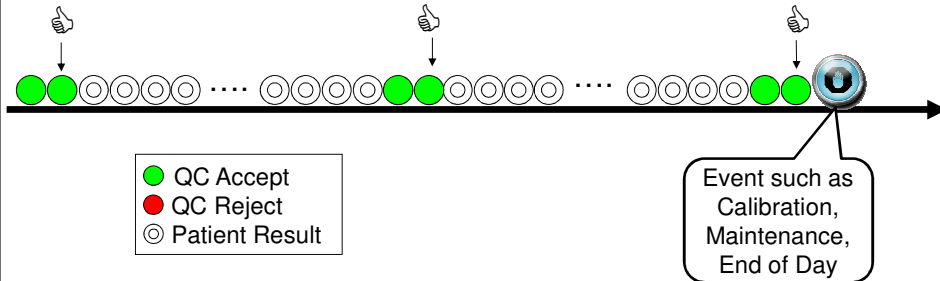
Continuous Testing

? ? ? ?   ?   ? ? ? ?

- 🟢 QC Accept
- 🔴 QC Reject
- ◎ Patient Result

Event such as Calibration, Maintenance, End of Day

13

Recommendation #1

Continuous Testing

QC Accept
QC Reject
Patient Result

Event such as Calibration, Maintenance, End of Day

13

Recommendation #1

Continuous Testing

QC Accept
QC Reject
Patient Result

Event such as
Calibration,
Maintenance,
End of Day
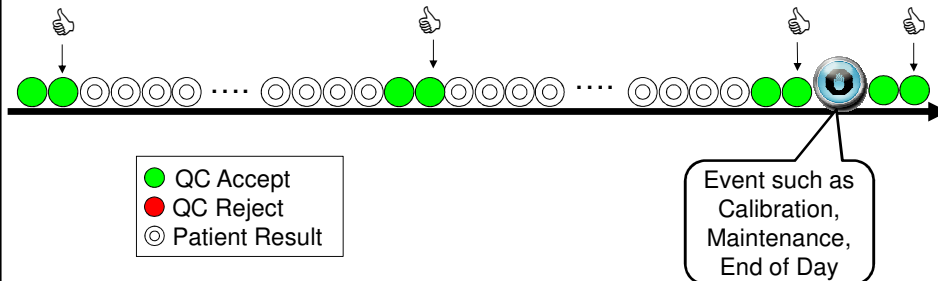
13

Recommendation #2

Try to make the time between QC
evaluations no longer than the
time needed to correct results
before they're acted on.

14

Recommendation #2

- ISO 15189 states that when QC detects an out-of-control condition laboratories should inspect and correct adversely affected patient results already released.

|correct before acted on|
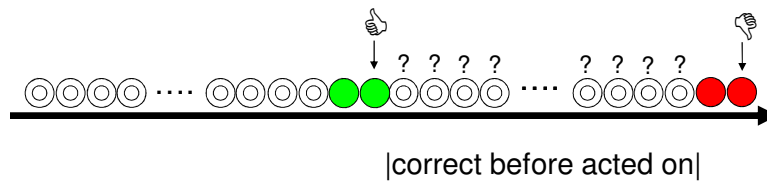
- Correction time requirement depends on how the analyte is used in patient care.

Recommendation #3

Know the number of patient results between QC evaluations.

Recommendation #3

- Patient risk related to *recovering* from an out-of-control condition depends on time (Suggestion #2).
- Patient risk related to *detecting* an out-of-control condition depends on the number of results between QC evaluations.
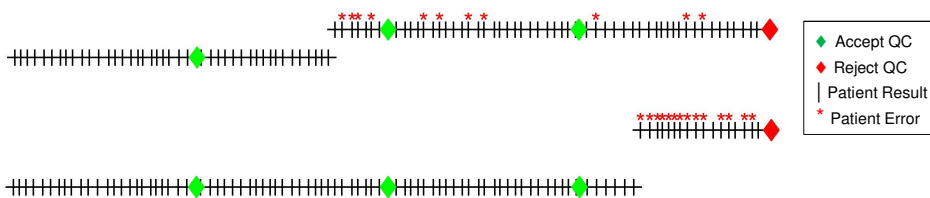

♦ Accept QC
♦ Reject QC
| Patient Result
* Patient Error
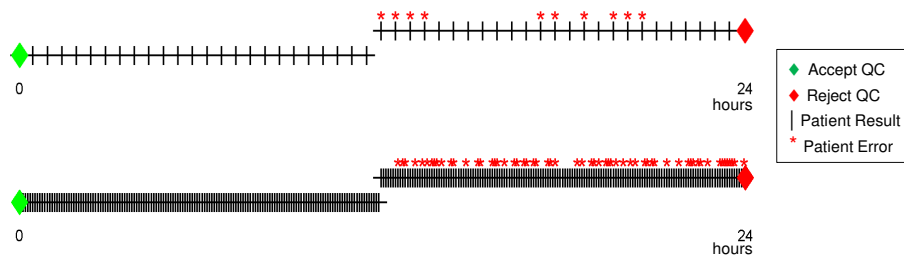
17

Recommendation #4

Estimate the magnitude of an out-of-control condition before correcting it.

18

Recommendation #4

- When QC detects an out-of-control condition
  - First estimate the magnitude of the failure
    - The QC results that triggered the QC rejection provide little information about the magnitude of the failure
  - Then identify the cause and correct the failure
  - Then recover from the failure
    - estimated magnitude of the failure helps guide recovery

◆	Accept QC
◆	Reject QC
	Patient Result
*	Patient Error

19

Recommendation #5

# If you're using a 1:2s QC rule and you get a rule failure, repeat it - but just once!

20

18

Recommendation #5

- Repeat 1:2s QC Rule with 2 levels of QC
  - Measure the 2 QCs
  - If both are within ±2s then accept
  - If both are outside ±2s then reject
  - Otherwise repeat both QCs
  - If both repeated values are within ±2s then accept
  - Otherwise reject

- This is NOT "repeat, repeat, repeat, got lucky"!
  - It's a QC rule with the possibility of running a second set of QCs depending on the results obtained in the first set.

21

Recommendation #5
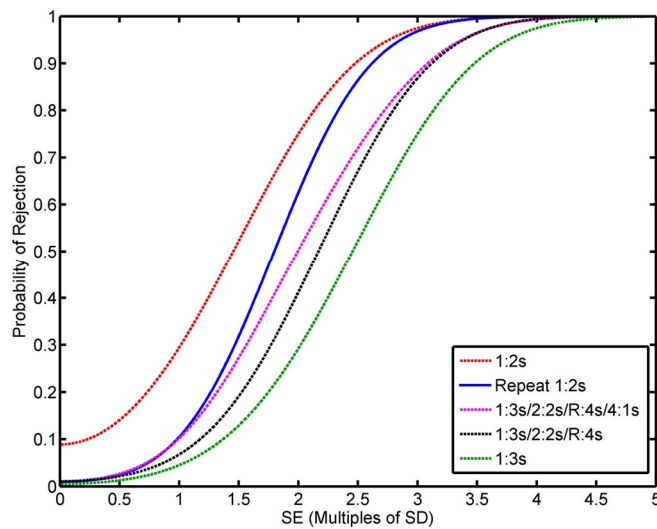
Clinical Chemistry 58:5 (2012)

22

Recommendation #6

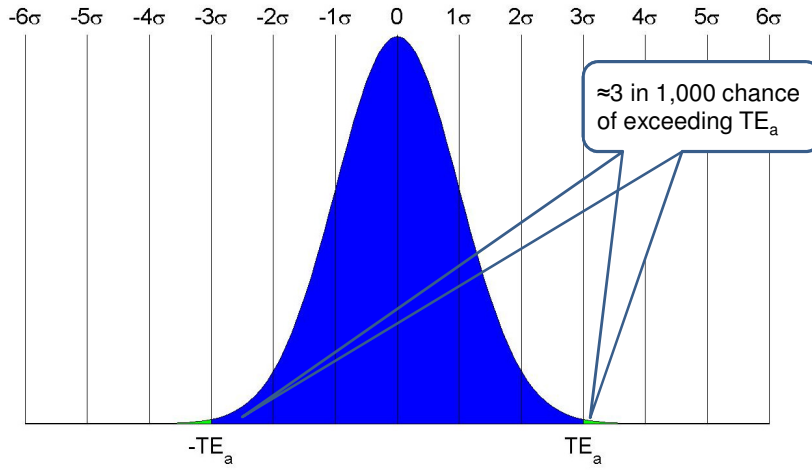# Divide analytes into high and low sigma metric groups.

23

Recommendation #6

- Sigma Metric = $(TE_a - |Bias|) / SD$

- The sigma metric is the number of process SD's that fit within the allowable total error specification.

- High sigma metric processes are easy to QC

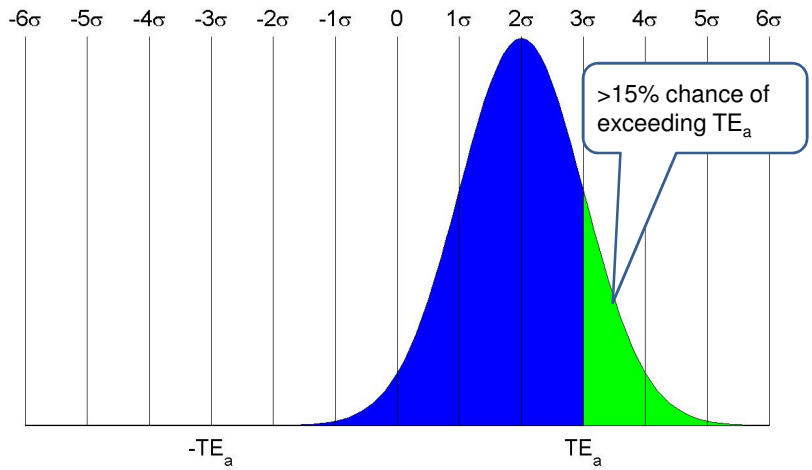- Low sigma metric processes are hard to QC

24

Recommendation #6

A 6 sigma process

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

≈2 in a billion chance of exceeding TE$_a$

-TE$_a$

TE$_a$

27

Recommendation #6

A 6 sigma process

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

<1 in 10,000 chance of exceeding TE$_a$

-TE$_a$

TE$_a$

28

22
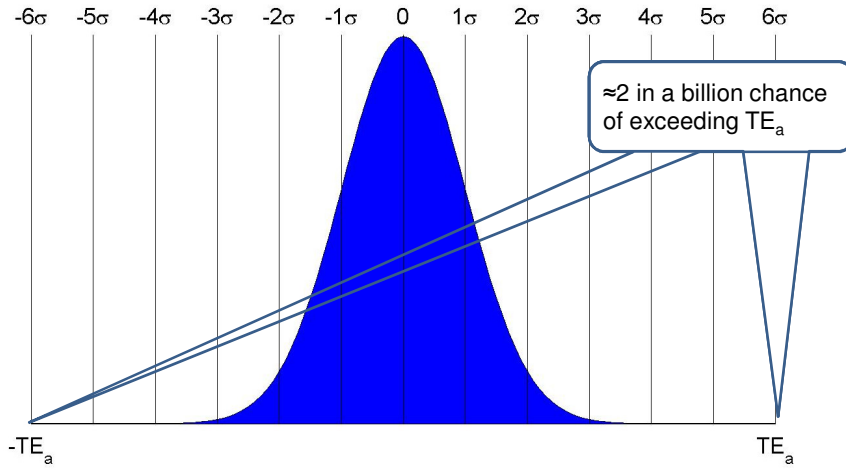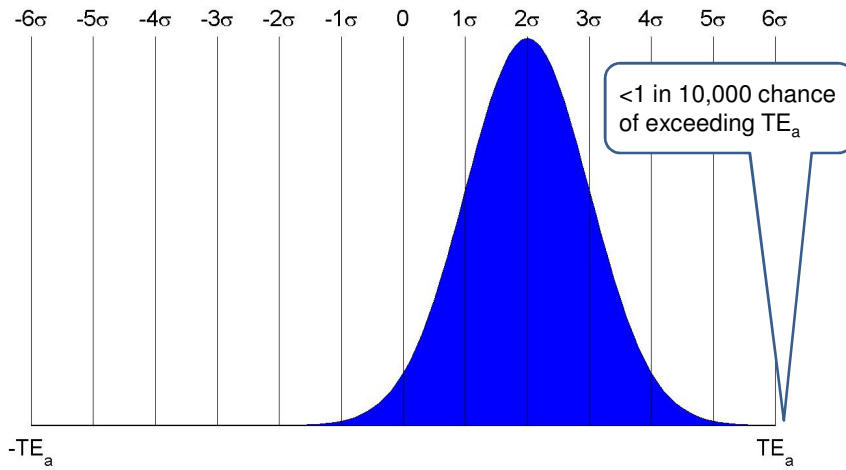
Recommendation #6

- For high sigma metric processes
  - Reduce the false rejection rate.
  - Reduce QC frequency (if recovery permits)
  - Strengthen your quality claim (use a smaller TE_a).

- For low sigma metric processes
  - Seek ways to reduce bias and imprecision.
  - Use more powerful QC rules and increase QC frequency.
  - Reassess the quality specification

29

Recommendation #7

Don't rely solely on sigma values to determine your QC strategy.

30

Recommendation #7

- Sigma-Metric Based QC strategy design
  - The number of QC's, the QC rule, and the QC frequency are selected based on the sigma metric (σ).

Performance	# QCs	Multi Rule	"Acceptable" Frequency
≥6 σ	2 QCs	1:3s QC rule	every 1000 specimens
≥5 σ <6	2 QCs	1:3s 2:2s R:4s	every 450
≥4 σ <5	4 QCs	1:3s 2:2s R:4s 4:1s	every 200
≥3 σ <4	6 QCs	1:3s 2:2s R:4s 4:1s 6x	every 45

Recommendation #7

Don't rely *solely* on Sigma values to determine QC frequency

They are just one factor that comes into play.

By John C. Yundt-Pacheco, MSCS, and Curtis A. Parvin, PhD

Laboratories know that appropriate quality control (QC) rule selection depends on the in-control performance of a test method (the Sigma value). Higher performing tests may allow "easier" rules, while lower performing tests require more powerful rules. In recent years, QC frequency has undergone a shift in thinking and approach related to patient risk-based QC design. That is, what we are asking now is, what is an appropriate QC frequency to assure that the risk of patient harm from an erroneous reported patient result is acceptable?

In that context, is the Sigma value for a test method all that is needed to determine an appropriate frequency for QC testing to adequately mitigate patient risk? The

unacceptable. What is clear is that out-of-control conditions occurring every two days have a very different impact than out-of-control conditions occurring every two years.

Time until clinician acts

Even if the QC rules are powerful enough to detect a significant out-of-control condition at the first QC event after the condition occurs, if patient results are being reported as soon as they are produced and verified, then there is the possibility that a number of erroneous patient results will have been reported between the occurrence of the out-of-control condition and its
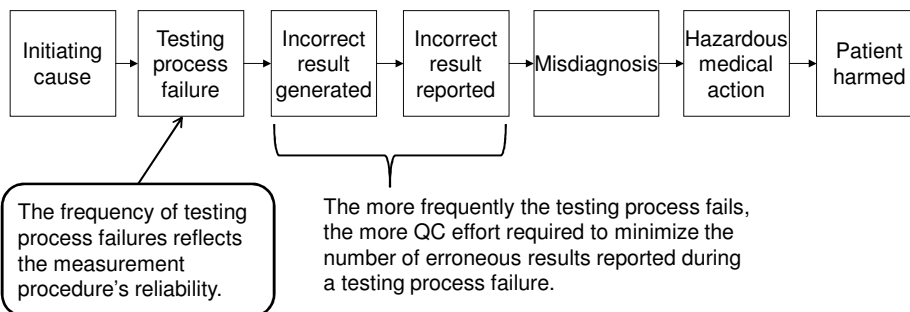
MLO, August 2018

Recommendation #8

Devote more QC effort to unreliable measurement procedures.

33

Recommendation #8

Sequence of Events Creating Risk of Harm for a Patient

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

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

The more frequently the testing process fails, the more QC effort required to minimize the number of erroneous results reported during a testing process failure.
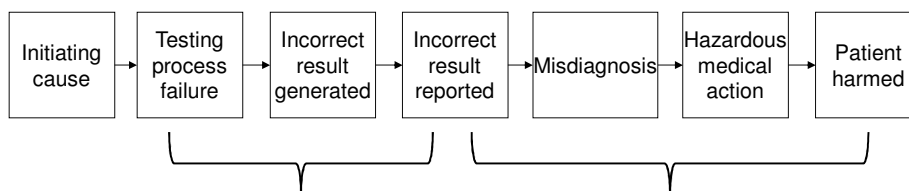
34

Recommendation #9

Devote more QC effort to analytes with high probability that erroneous results lead to patient harm.

Recommendation #9

Sequence of Events Creating Risk of Harm for a Patient

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

The higher the probability an erroneous result leads to patient harm, the more QC effort required to minimize the number of erroneous results reported.

Likelihood that incorrect reported results lead to patient harm

Recommendation #10

Devote more QC effort to analytes with high expected severity of patient harm from an erroneous result.

37

Recommendation #10

Risk Acceptability Matrix

	Severity of Harm				
Probability of Harm	**Negligible**	**Minor**	**Serious**	**Critical**	**Catastrophic**
Frequent	Unacceptable	Unacceptable	Unacceptable	Unacceptable	Unacceptable
Probable	Acceptable	Unacceptable	Unacceptable	Unacceptable	Unacceptable
Occasional	Acceptable	Acceptable	Acceptable	Unacceptable	Unacceptable
Remote	Acceptable	Acceptable	Acceptable	Acceptable	Unacceptable
Improbable	Acceptable	Acceptable	Acceptable	Acceptable	Acceptable

The higher the expected severity of patient harm, the more QC effort required to minimize reporting erroneous results that lead to harm.

38

27

Summary

- A laboratory'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 laboratory'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

- A number of simple QC practices are suggested that can help minimize patient risk.

39