CIRME 13TH INTERNATIONAL SCIENTIFIC MEETING

INTERNAL QUALITY CONTROL IN THE TRACEABILITY ERA

Estimating Measurement Uncertainty in Real Time

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Biography

Victoria (Vicki) Petrides

Personal

I live in suburban Washington, DC with my husband and three daughters. I enjoy swimming, walking, biking, and reading.

Career

I have 22 years experience as a statistician designing and analyzing analytical performance studies for laboratory tests.

I am also the diagnostic industry chair of AdvaMed's Statistical Working Group and an active participant in Clinical Laboratory Standards Institute (CLSI) document development committees.

Abbott

I am currently a Principal Research Statistician in R&D Data Analytics at Abbott Diagnostics.

My role over the last 22 years has included designing and analyzing clinical and analytical studies and providing statistically-related worldwide regulatory support of new product launches.

Academic

I received a bachelor of science in statistics from the University of Michigan in Ann Arbor and a master of science in applied mathematics with a concentration in statistics from the University of Cincinnati.

Uncertainty…

Leonardo Da Vinci. *The Last Supper*. 1490s. Santa Maria delle Grazie, Milano.

REAL TIME MEASUREMENT UNCERTAINTY

Value creation using measurement uncertainty

1 **Measurement Uncertainty**

What is measurement uncertainty and why is it important?

2 **When and How**

When and how often should we estimate measurement uncertainty?

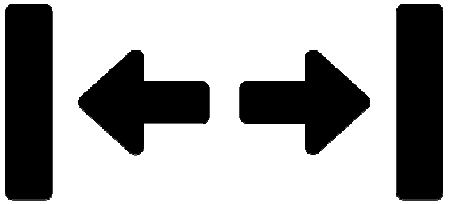
3 **Collaboration**

Measurement uncertainty in real time – examples from a collaboration

4 **Comments and Summary**

What is measurement uncertainty (MU)?

Measurement uncertainty is an expression of variability one can expect around an underlying "true" value of a sample.



Created by Adrien Coquet from Noun Project

What is measurement uncertainty?
ISO/TS 20914 officially defines MU for laboratories

ISO/TS 20914 *Definition*	Parameter characterizing the dispersion of the quantity values being attributed to a measurand, based on the information used.
Bias and Imprecision *Note 5*	All measurements have bias and imprecision … there is uncertainty as to which value should be reported
Interval of Values *Note 6*	MU provides an interval of values … to include the actual value of the measurand, with a stated level of confidence.
Calibrator Uncertainty *Note 7*	… typically comprise uncertainty of calibrator assigned values and long-term imprecision of IQC materials.

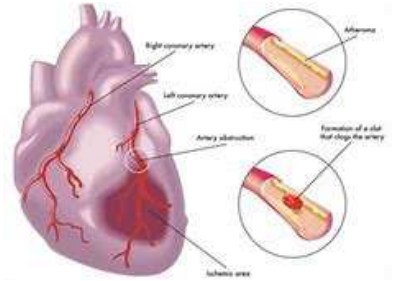
Why do we need MU?
ISO 15189 section 5.5.1.4 requires it

Determine measurement uncertainty	"The laboratory shall determine measurement uncertainty for each measurement procedure….
Define performance requirements	Define the performance requirements for the measurement uncertainty for each measurement procedure and
Regularly review estimates	regularly review estimates of measurement uncertainty.
Make estimates available	…Upon request, the laboratory shall make its estimates of measurement uncertainty available to laboratory users."

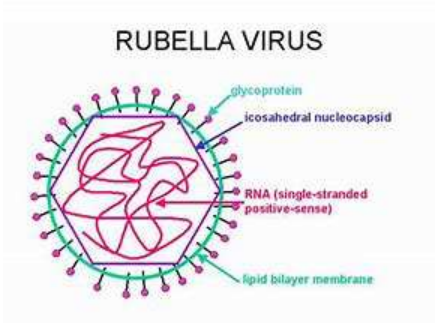
Why do we need MU?

Knowing the MU can lead to better patient outcomes

The PSA result of your patient is 4.3 µg/L, just above the medical decision limit of 4.0 µg /L. Should he be referred for biopsy?



The cardiac troponin results for your patient have risen. Are the levels and their differences significant enough to warrant intervention?



The rubella IgG result for your patient is in the equivocal zone. Should she be vaccinated?

How is MU estimated in the lab?

Add the manufacturer's calibrator uncertainty to the laboratory's long-term imprecision.

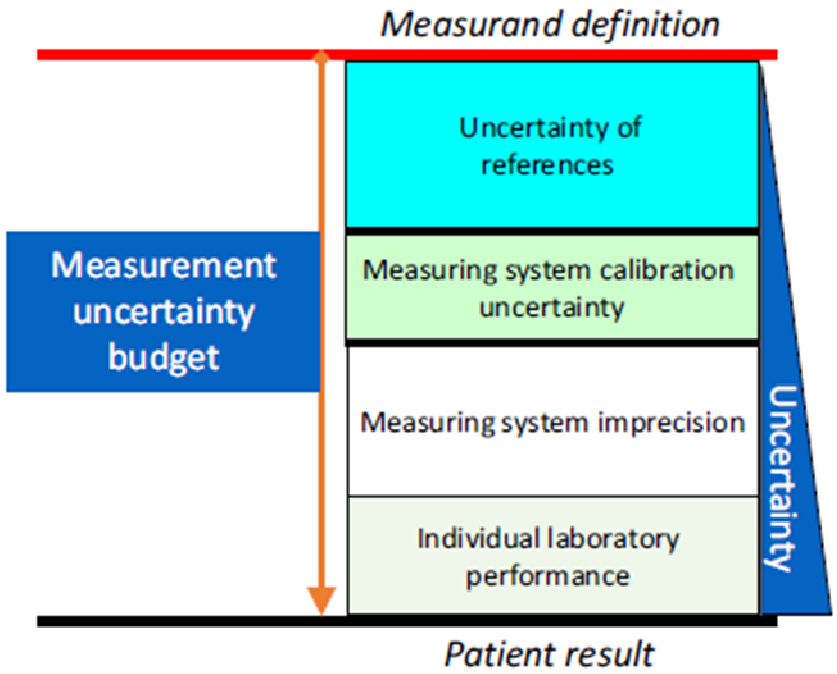


Fig. 1. Main components of the total uncertainty budget.

Reference method organization provides MU of reference material (**fixed MU estimate, ideally <1/3 of APS**)

Manufacturer uses reference method to create measuring system calibrators for commercial system and provides MU of calibrators (**fixed MU estimate, ideally <1/2 of APS**)

Lab uses commercial system with varying lots of calibrators, reagents, etc. to test patient specimens. (**varying MU estimate, ideally < APS**)

Braga F, Panteghini M. Defining permissible limits for the combined uncertainty budget in the implementation of metrological traceability. Clin Biochem. 2018;57:7-11.

When and how often should the lab estimate MU?

In REAL TIME

MEASUREMENT UNCERTAINTY IN REAL TIME

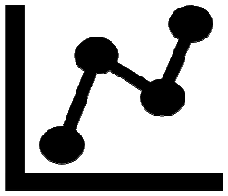
Examples from Collaboration

Setting for MU in real time
Reviewed routine IQC results from 3 assays

Testing Dates	July 1 – October 31, 2019
Testing Location	Research Centre for Metrological Traceability in Laboratory Medicine (CIRME), University of Milan
System	4 Abbott Alinity c systems
Assays	• Creatinine (enzymatic) • Glucose • Transferrin
Materials for each assay	• 2 – 3 calibration lots • 5 – 6 reagent lots • 1 internal quality control (IQC) lot

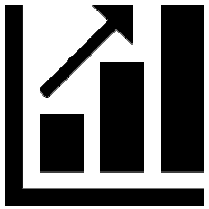
Comments and Summary

Knowing the MU can lead to better patient outcomes



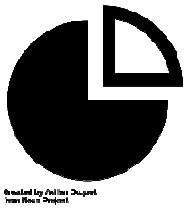
Rolling Estimates of Imprecision and MU

Examples reflected 30-day rolling results to illustrate the concept. In future applications, 180 day rolling results are preferred to better reflect long term imprecision.



Trends over Time

Dashboard #1 is helpful in visualizing trends over time and could be used to determine the MU on a given day.



Contributing Factors

Dashboard #2 is helpful in understanding the greatest contributors to variance.

Acknowledgements

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- Sara Pasqualetti

Abbott Diagnostics

- Tony Orzechowski
- Brian Renley
- Thom Rosiere
- Sharon Schneider
- Rich Scopp

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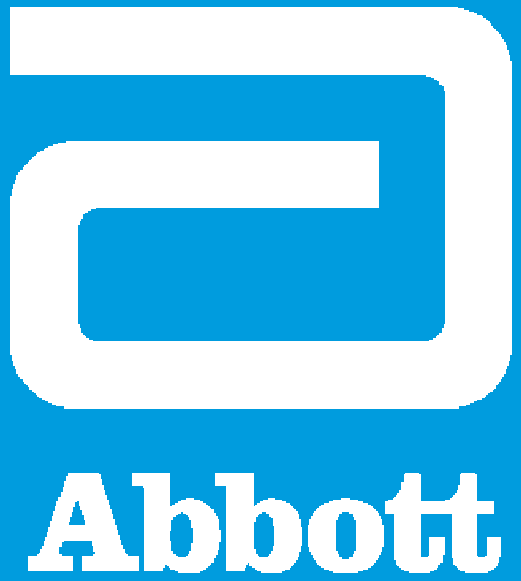
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