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From measurement uncertainty to everyday practice in medical laboratory

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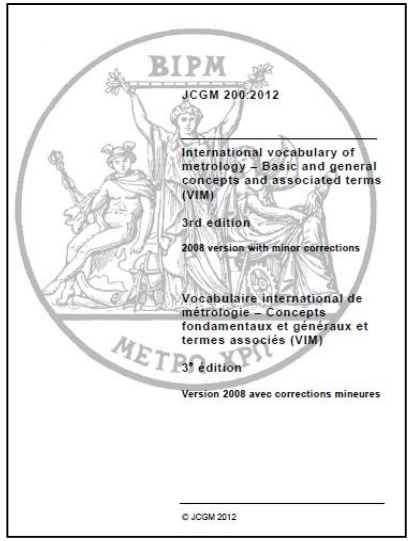
Measurement uncertainty essentials

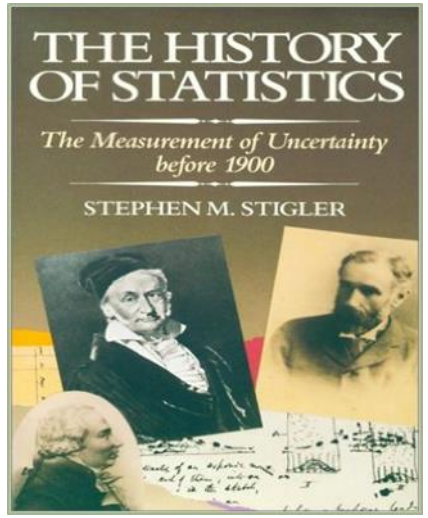
- ✓ Philosophy of metrology in laboratory medicine
- ✓ Error and measurement uncertainty
- ✓ World of guidelines
- ✓ Practical solutions
- ✓ Concluding remarks

metrology
science of **measurement** and its application

NOTE Metrology includes
all theoretical and practical aspects of measurement, whatever the **measurement uncertainty** and field of application.

Metrology dates back to the ancient world, but modern metrology is derived from the **politics French revolution,** where the standardisation of units was introduced.





Bureau International des Poids et Mesures

An international collaboration was instigated by the Bureau International des Poids et Mesures (International Bureau of Weights and Measures) in 1977 that resulted in an initial recommendation issued internally in 1980 and then published in 1981. (**Giacomo P.** Expression of experimental uncertainties. *Metrologia* 1981;17:73–74).

- **BIPM, IEC, IFCC, ISO, IUPAC, OIML.** *Guide to the Expression of Uncertainty in Measurement.* International Organization for Standardization, Geneva, First Edition (1993) reprinted and corrected (1995).
- **BIPM, IEC, ILAC, IFCC, ISO, IUPAC, OIML.** *Evaluation of Measurement Data— Guide to the Expression of Uncertainty in Measurement.* (2008).

- Estimation of measurement uncertainty in clinical chemistry and laboratory medicine

ISO 17025 , first edition 1999

(General requirements for the competence of the testing and calibration laboratories)

ISO 15189, first edition 2003

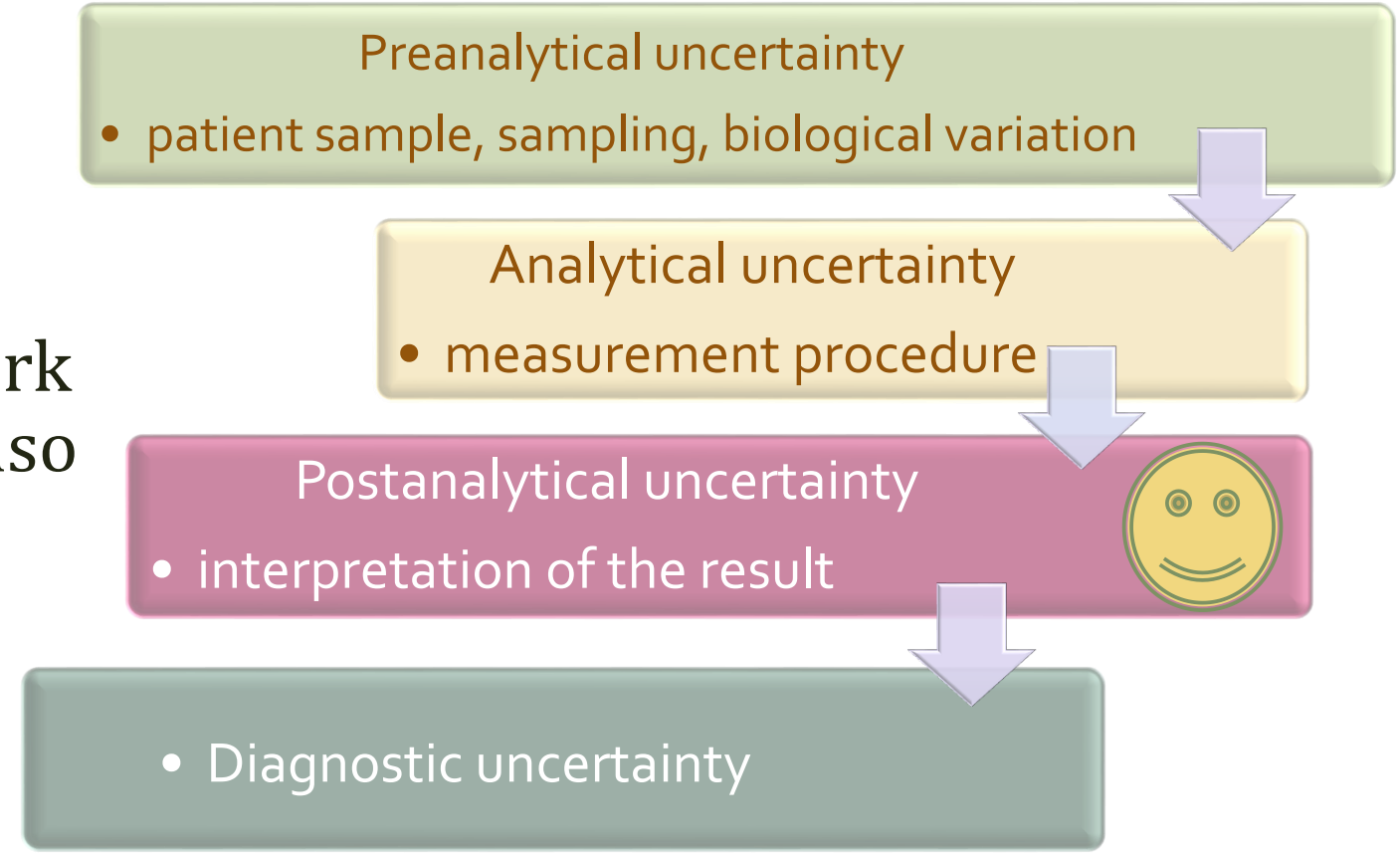
(Special requirements for the quality and competence of medical laboratories)

Revised issues:

- Standard requirement SRPS ISO/IEC 17025:2006, 17025:2017
- ISO 15189:2007, ISO 15189:2012 requirements

Measurement result is the ultimate product of the total process (testing chain) in laboratory medicine

- Work in medical laboratories depends on the same metrological principles as work in other laboratories, but is also focused on reducing and handling numerous other uncertainties.



Measurement uncertainty evolution starts with inventory of sources of Error!

Florent Vanstapel MD PhD, Clinical Chemistry
POCT Coordinator Laboratory Medicine UZ Leuven, Belgium

- Quality of measurement results depends on different measuring tools for assesment of assurance in medical laboratory and one of them is:

  - ✓Uncertainty
  - ✓Error
  - ✓Traceability
  - ✓Validation…

≈ *All measured values are wrong, but some are useful*

"Every measurement is subject to some uncertainty. **A measurement result is only complete if it is accompanied by a statement of the uncertainty in the measurement.** Measurement uncertainties can come from the measuring instrument, from the item being measured, from the environment, from the operator, and from other sources. **Such uncertainties can be estimated using statistical analysis of a set of measurements, *and* using other kinds of information about the measurement process.** There are established rules for how to calculate an overall estimate of uncertainty from these individual pieces of information. **The use of good practice – such as traceable calibration, careful calculation, good record keeping, and checking – can reduce measurement uncertainties.** When the uncertainty in a measurement is evaluated and stated, the fitness for purpose of the measurement can be properly judged."

Stephanie Bell, A Beginner's Guide to Uncertainty of Measurement, The National Physical Laboratory, http://www.npl.co.uk/publications/a-beginners-guide-to-uncertainty-in-measurement

➢Error vs Uncertainty

Total analytical error ≠ Measurement uncertainty of the result

➢*Error*

- is the difference between the measured value and the 'true value' of the measurand (depends mostly on *imprecision,* if *bias* is constant).

➢*Uncertainty (measurement uncertainty of the result)*

- is a quantification of the doubt about the measurement result.

- ➢ try to correct any known error (applying corrections from calibration certificates)
- ➢ any error whose value we do not know is a source of uncertainty (depends both on *imprecision* and *bias*).

✓ Error and measurement uncertainty

DE GRUYTER Clin Chem Lab Med 2018; aop

Opinion Paper

Ian Farrance*, Tony Badrick and Robert Frenkel[a]

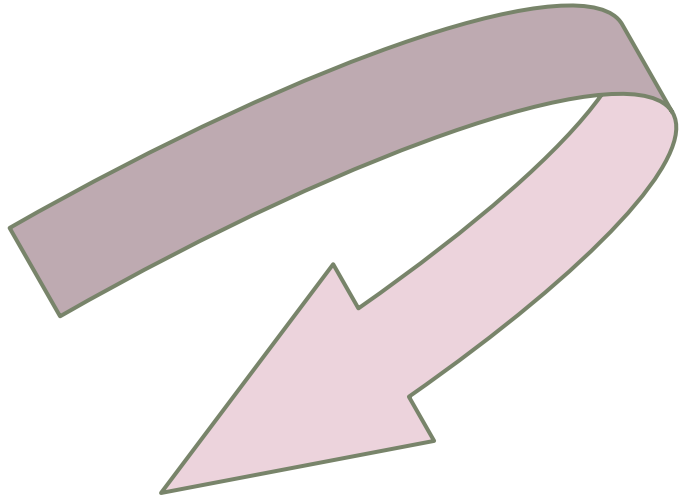
Uncertainty in measurement and total error: different roads to the same quality destination?

There is a risk that:

"Perfect becomes the enemy of good" (Pescetti 1603) in the choice between uncertainty and error methods.

„Error and uncertainty approaches should each be developed on its own merits as accepted but different philosophies and practical approaches to metrology."

E. Theodorsson. Uncertainty of measurement and total error: Tools for coping with diagnostic uncertainty. Clin Lab Med 37 (2017) 15–34



The GUM is Normative

GUM → ISO

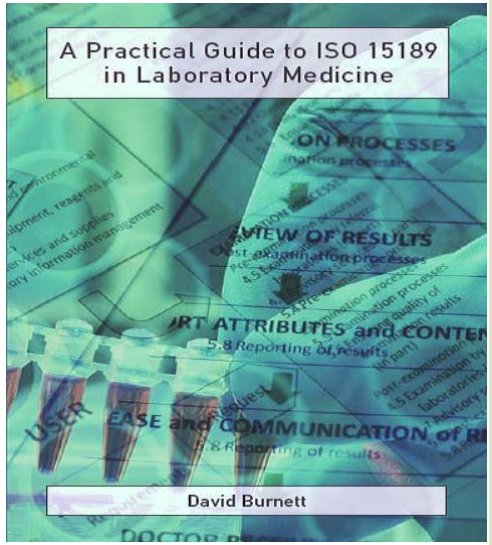
No ifs, ands or buts, you have to get this done correctly. In many venues, it's the law. And you had better do it the GUM way!

William R. Porter, PhD Peak Process Performance Partners LLC

GUM: 1.4. „It may therefore be necessary to develop particular standards based on this Guide that deal with the problems peculiar to specific fields of measurement or with the various uses of quantitative expressions of uncertainty. These standards may be simplified versions of this Guide but should include the detail that is appropriate to the level of accuracy and complexity of the measurements and uses addressed.“

„The evaluation of uncertainty is neither a routine task nor purely mathematical one; it depends on detailed knowledge of the nature of the measurand and of the measurement.“

BIPM, IEC, IFCC, ISO, IUPAC, OIML. Guide to the Expression of Uncertainty in Measurement. International Organization for Standardization, Geneva, First Edition (1993)



- Even ISO 15189 is a practical tool for management of quality in the medical laboratory it does not recommend methodology for calculation of measurement uncertainty

David Burnett

!! Despite the mandatory requirements for the measurement uncertainty and the time elapsed since the GUM published, a guide to the uncertainty of practical application has not yet been successfully adopted in medical laboratories.

!! Still no harmonisation in routine practice.

✓ World of Guidelines

✓ Practical solutions

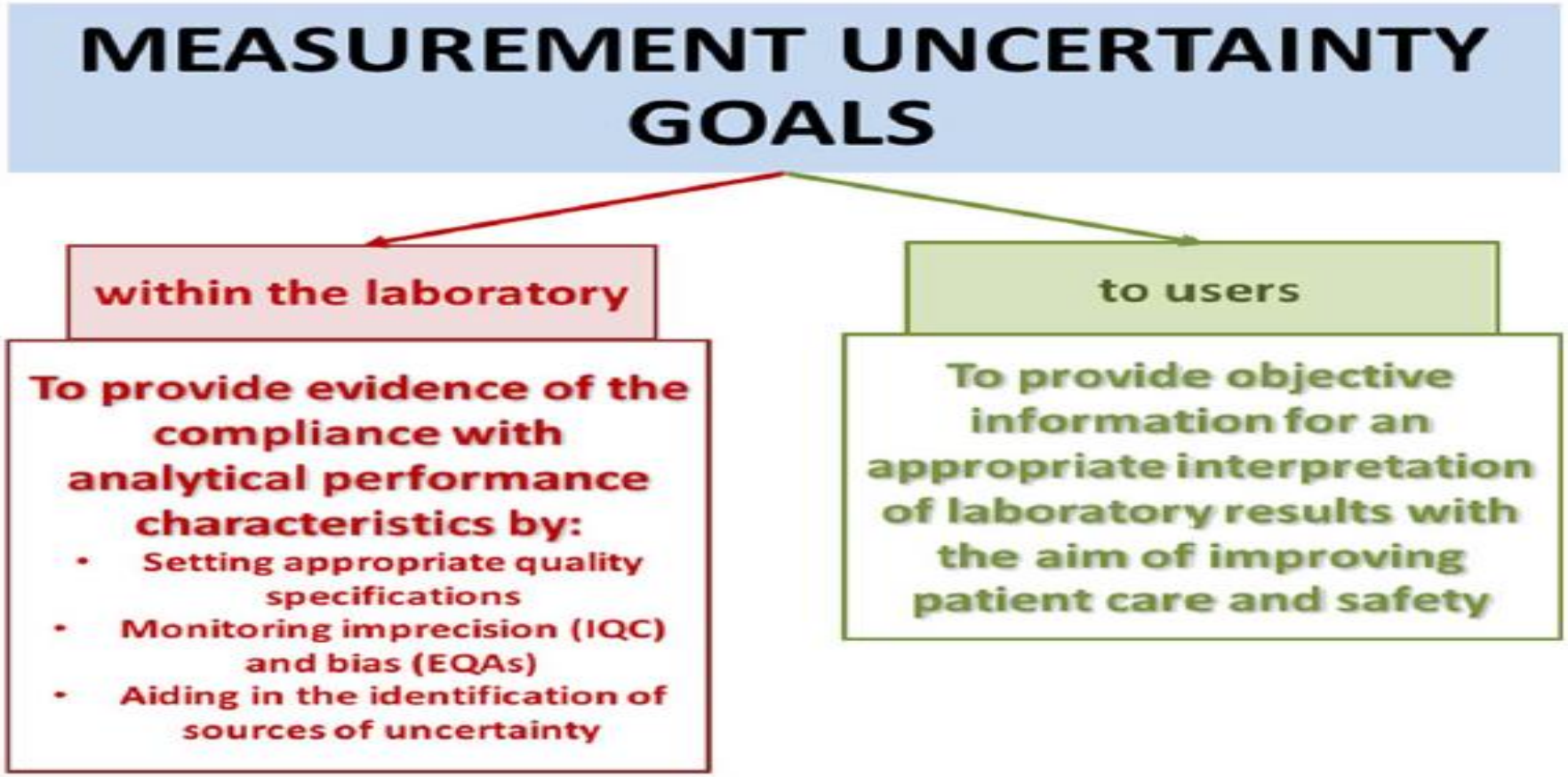
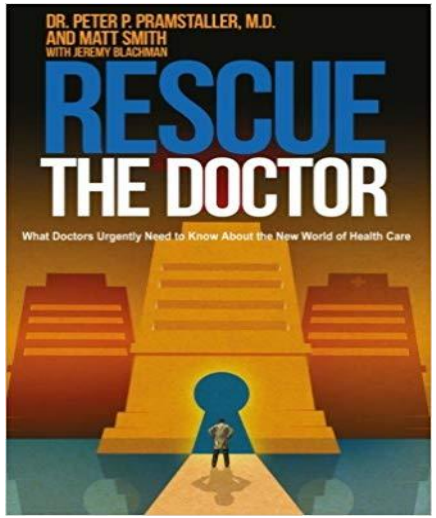


Fig. 1. Summary of the main goals of measurement uncertainty.

Mario, P., Clinical Biochemistry (2018), https://doi.org/10.1016/j.clinbiochem.2018.01.017



Evaluation of measurement data –

The role of measurement uncertainty in conformity assessment

ISO/IEC GUIDE 98-4:2012(E)

- well-characterised test method is used and sources of uncertainty are minimised by:

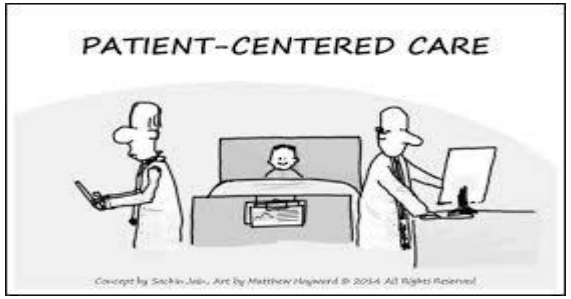
➢ use of measuring instruments with maximum permissible errors within specified limits,

➢ environmental influences, such as temperature and relative humidity, maintained within specified limits,

➢ well-documented control of laboratory procedures, and

➢ well-documented competency of measurement personnel

✓ Practical solutions



DE GRUYTER Clin Chem Lab Med 2016; aop

Opinion Paper

Graham Ross Dallas Jones*

Measurement uncertainty for clinical laboratories – a revision of the concept

- Measuring means comparing!
- „If the purpose of MU is to assist with interpretation of results, it is necessary to consider how numerical laboratory results are used for decisions on patient care.“
- All such results are interpreted by comparison with information derived from other measurements. The three main comparators are used for decision making.
- Traecability !!!

✓ Practical solutions

1. Comparison with a population reference interval. Reference intervals are provided on the report as an initial comparator for nearly all test results.
2. Comparison with a previous result on the same patient, i.e. to monitor a patient (increased, decreased, or remained stable analyte); calculate reference change value (RCV). (e.g. Troponin)
3. Comparison with a clinical decision point (diagnostic cut-offs). (e.g. Glucose)

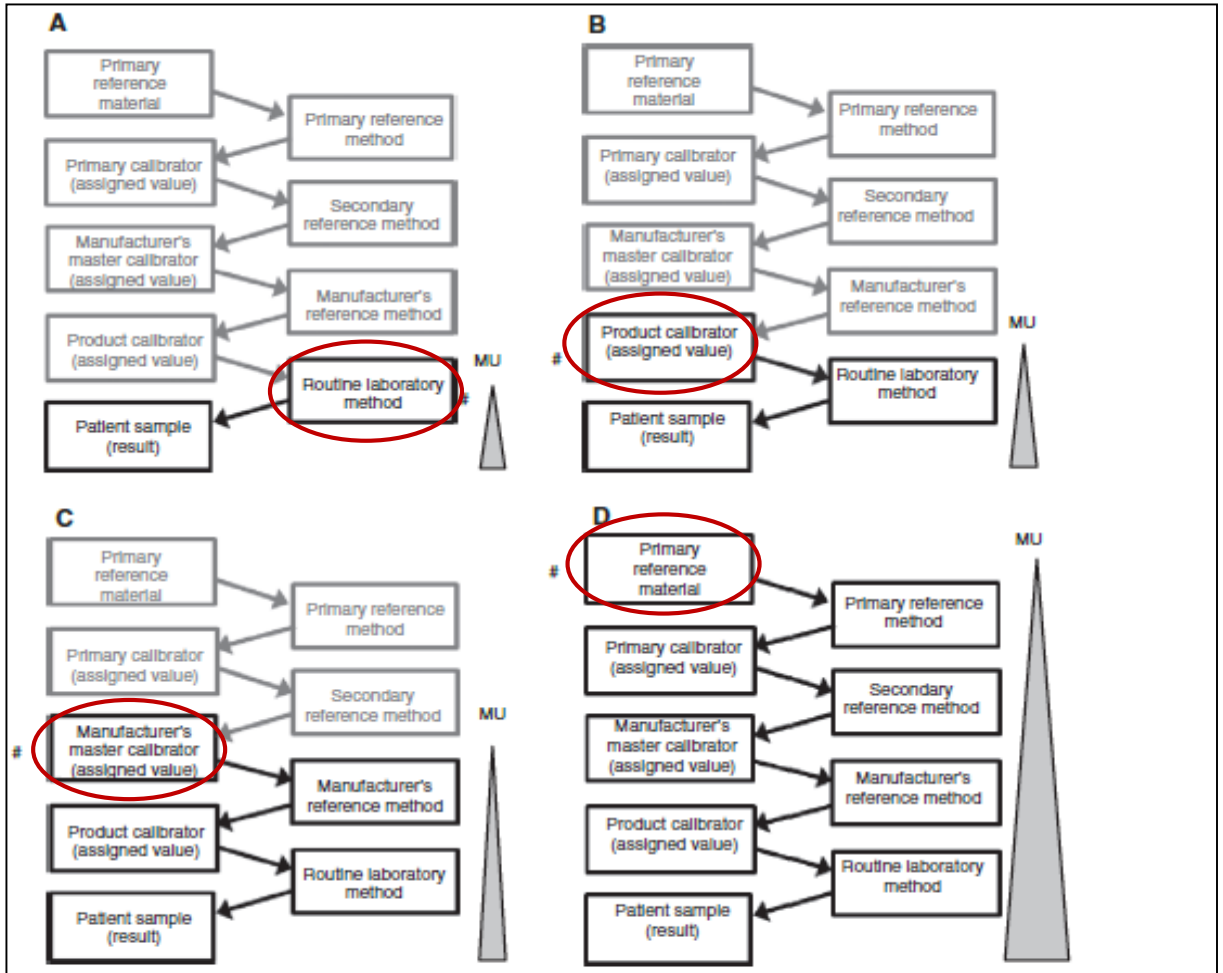
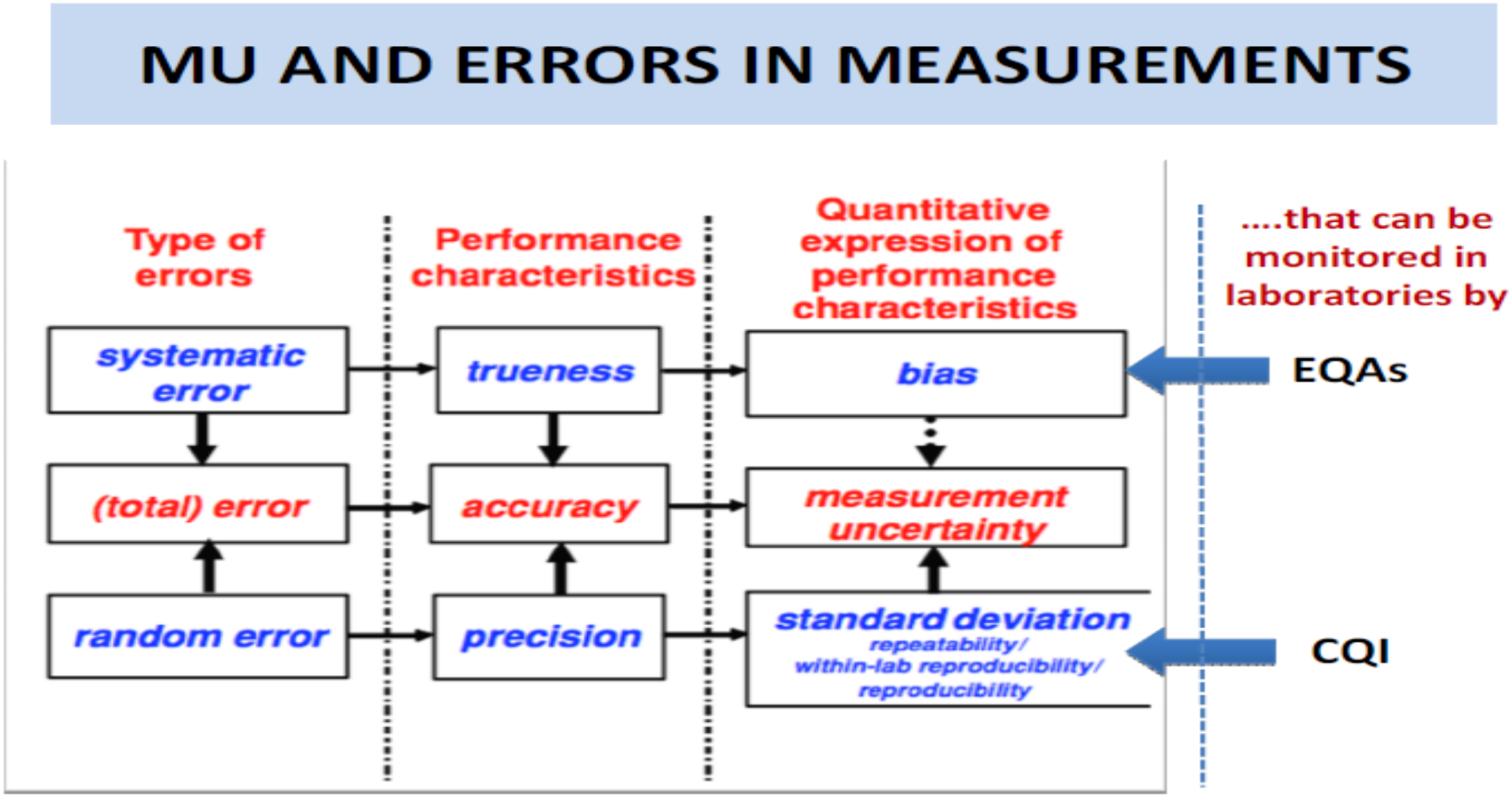


Figure 1: Traceability chains for scenarios 1–4.
(A) scenario 1; (B) scenario 2; (C) scenario 3; (D) scenario 4. The "true value" for estimation of MU is shown in each figure (#) and the components contributing to the uncertainty illustrated with the gray triangles and shown in black and those components not contributing to uncertainty for the relevant clinical decision in gray.

GRD Jones, Measurement uncertainty for clinical laboratories – a revision of the concept. CCLM, 2016



Modified from Menditto et al. Accred Qual Assur 2007; 12:45.

Mario, P., Clinical Biochemistry (2018), https://doi.org/10.1016/j.clinbiochem.2018.01.017

✓ Practical solutions

Test Purposes and Uncertainty: components to be included

Test purpose	Examples	Components to be included in measurement uncertainty
Test result if used in **comparison with a reference interval** either established in the same laboratory or verified by the laboratory by appropriated procedures	**e.g.** hormones	**Imprecision only** Jones GR. CCLM 2016; 54:1303
Test result is usually **compared with a clinical decision point**	**e.g.** glucose, ions	**Imprecision, bias and bias uncertainty** Jones GR. CCLM 2016; 54:1303
Test results is primarily used for **monitoring** patients over time	**e.g.** tumour markers, immunosuppressive drugs.	**Imprecision only** Jones GR. CCLM 2016; 54:1303 Tate J and Plebani M. CCLM 2016; 54:1277

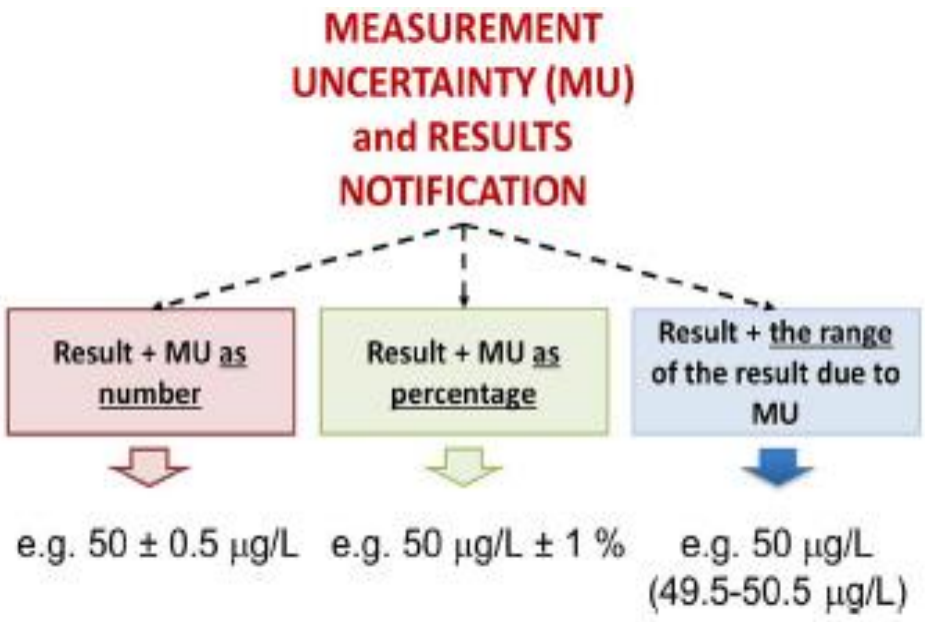


Fig. 4. Possible options to report measurement uncertainty in medical reports.

Mario, P., Clinical Biochemistry (2018), https://doi.org/10.1016/j.clinbiochem.2018.01.017

Concluding remarks

- MU is not a „fixed“ property of a result.
- MU can not ruine the good test and can not rescue the bad test.
- Estimates of long-term precision and on-going bias are the keys to providing realistic estimates of measurement uncertainty (different sources for those estimates of random and systematic errors at different times in the life-cycle of a testing process)
- To estimate MU is not enough!

Concluding remarks

- MU is not a finding to be calculated only to fulfil accreditation parameters and then immediately forgotten.
- Laboratory must define the performance specifications which can be improved on the MU value if these are not achieved.
- MU must become a key quality indicator in medical laboratories because it can be used to describe both the performance of an IVD measuring system and the laboratory itself.

An Ode to "Measurement Uncertainty"

Usha Anand*

1550 Clinical Chemistry 63:9 (2017)

So friends, let's not bury our heads in the sand or dwell in a fool's paradise.
Let us interact with experts in the field of metrology and seek their advice.
Once we learn how to calculate "measurement uncertainty" half the battle is won.
If we then ascertain if it affects the interpretation of our results, our job is almost done.