Measurement uncertainty and acceptance sampling: CXG 50 and CXG 54

CCMAS

Web-seminar

27 May 2022

quo data

*QUALITY & STATISTICS!

Introduction

Measurement uncertainty, CXG 54 and the Information document

- Following the publication of ISO/IEC 17025:2017, test laboratories face increased scrutiny regarding measurement uncertainty (MU) and its application in conformity assessment (for individual items).

7.6 Evaluation of measurement uncertainty

7.6.1 Laboratories shall identify the contributions to measurement uncertainty. When evaluating measurement uncertainty, all contributions that are of significance, including those arising from sampling, shall be taken into account using appropriate methods of analysis.

7.6.2 A laboratory performing calibrations, including of its own equipment, shall evaluate the measurement uncertainty for all calibrations.

7.6.3 A laboratory performing testing shall evaluate measurement uncertainty. Where the test method precludes rigorous evaluation of measurement uncertainty, an estimation shall be made based on an understanding of the theoretical principles or practical experience of the performance of the method.

NOTE 1 In those cases where a well-recognized test method specifies limits to the values of the major sources of measurement uncertainty and specifies the form of presentation of the calculated results, the laboratory is considered to have satisfied 7.6.3 by following the test method and reporting instructions.

NOTE 2 For a particular method where the measurement uncertainty of the results has been established and verified, there is no need to evaluate measurement uncertainty for each result if the laboratory can demonstrate that the identified critical influencing factors are under control.

NOTE 3 For further information, see ISO/IEC Guide 98-3, ISO 21748 and the ISO 5725 series.

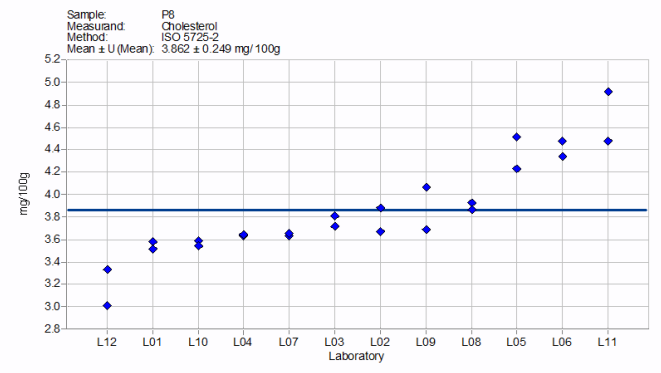
- Given the wide range of approaches for determining MU, CXG 54 and the Information Document will provide orientation and contribute to achieving harmonization.

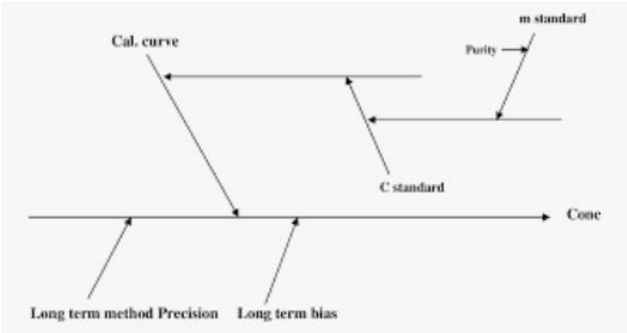
Introduction

Measurement uncertainty, CXG 54 and the Information document

The new CXG 54 is an update of the Guideline 54 from 2009. It is intended to provide basic information and orientation regarding:

- The definition of MU
- Why MU is important
- Relevant terminology
- The normative context
- The different approaches to determining MU





$$u_c = \sqrt{u(R_w)^2 + (u(bias))^2}$$

- $u(R_w)$, mean of SDs obtained from the replicate of each analytical run for two SRM levels divided by the respective mean of means (M):

$$u_{Rw} = \frac{\sum SD}{M} \times 100$$

- u(bias), three components contributed to the standard uncertainty of bias

$$u(bias) = \sqrt{(bias)^2 + \left(\frac{s_{bias}}{\sqrt{n}}\right)^2 + u(Cref)^2}$$

bias variability

NIST SRM 967a

Introduction

Measurement uncertainty, CXG 54 and the Information document

- The aim of CXG 54 is provide basic information and orientation *while remaining concise*.

- For this reason, it was proposed to make available a second document in order to provide a more in-depth treatment. This second document is the Information Document.

Introduction

Measurement uncertainty, CXG 54 and the Information document

Among other things, the Information Document provides

- Background information regarding the pivotal concepts
- Elucidations regarding the relationship between different approaches to determining MU
- A comprehensive list of all possible uncertainty components
- Worked-out examples showing how to evaluate individual uncertainty components.

Introduction

Measurement uncertainty, CXG 54 and the Information document

The instructions from CCMAS regarding the scope of CXG 54 and the Information Document were to consider only uncertainty sources *within* the laboratory:

- subsampling within the laboratory (obtaining a test sample from the laboratory sample)
- sample preparation
- analytical procedure *per se*
- In particular: the instructions were to exclude *sampling uncertainty* from the scope of these two documents.

What stage is the work at?

CCMAS41:

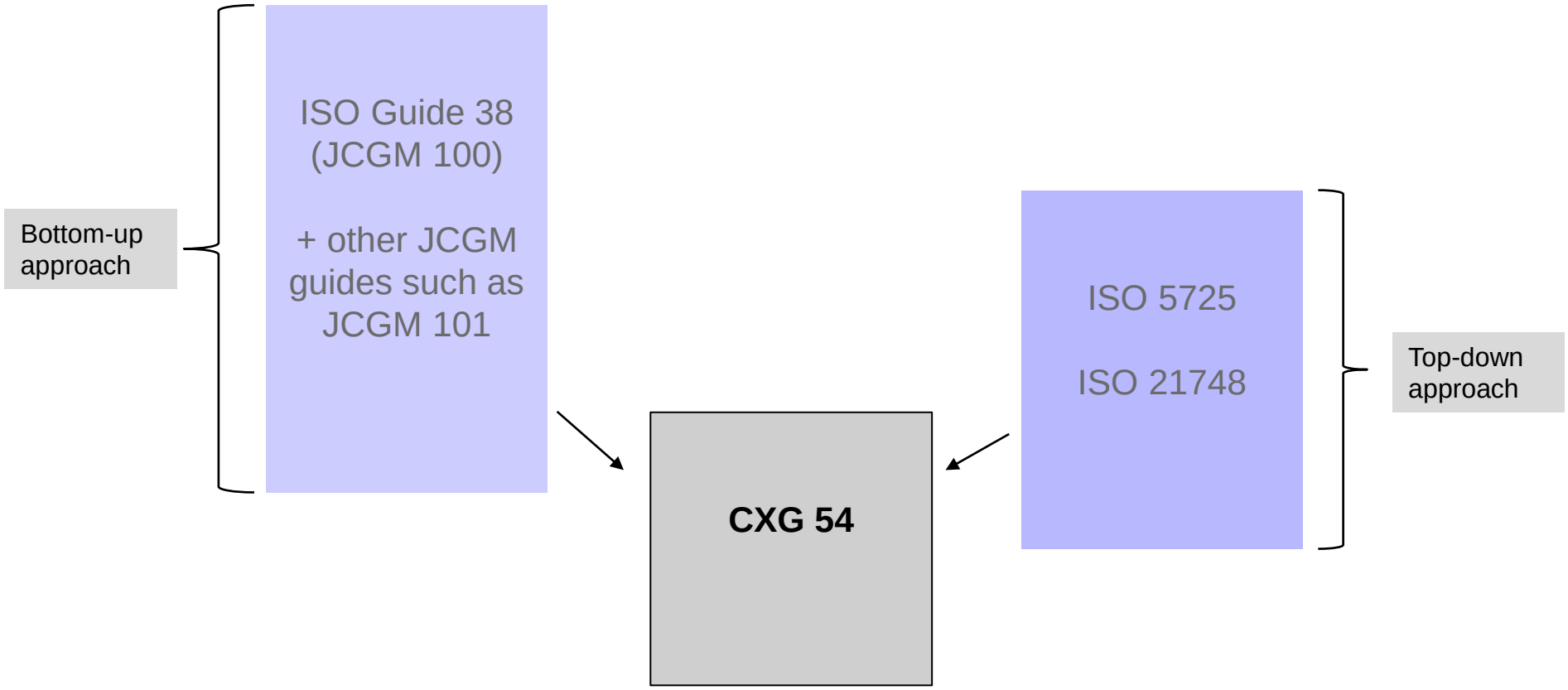
i. to advance the revised Guidelines to Step 8 for adoption by CAC44 (Appendix III); and

ii. to request Germany to revise the information document taking into account the comments and decisions made at the session, for circulation for comments and consideration by CCMAS42.

CAC44 (November 2011):

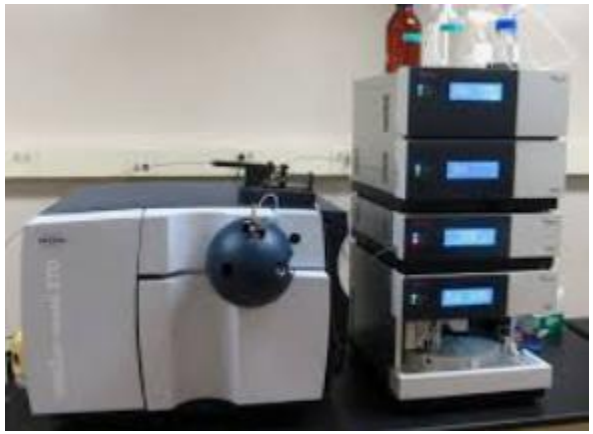
CXG 54 was adopted as revised and is now available online.

Relationship between CXG 54 and ISO standards



Measurement uncertainty

Is it still necessary to determine the measurement uncertainty? Analytical methods have improved considerably in recent decades. Is measurement uncertainty not negligible?

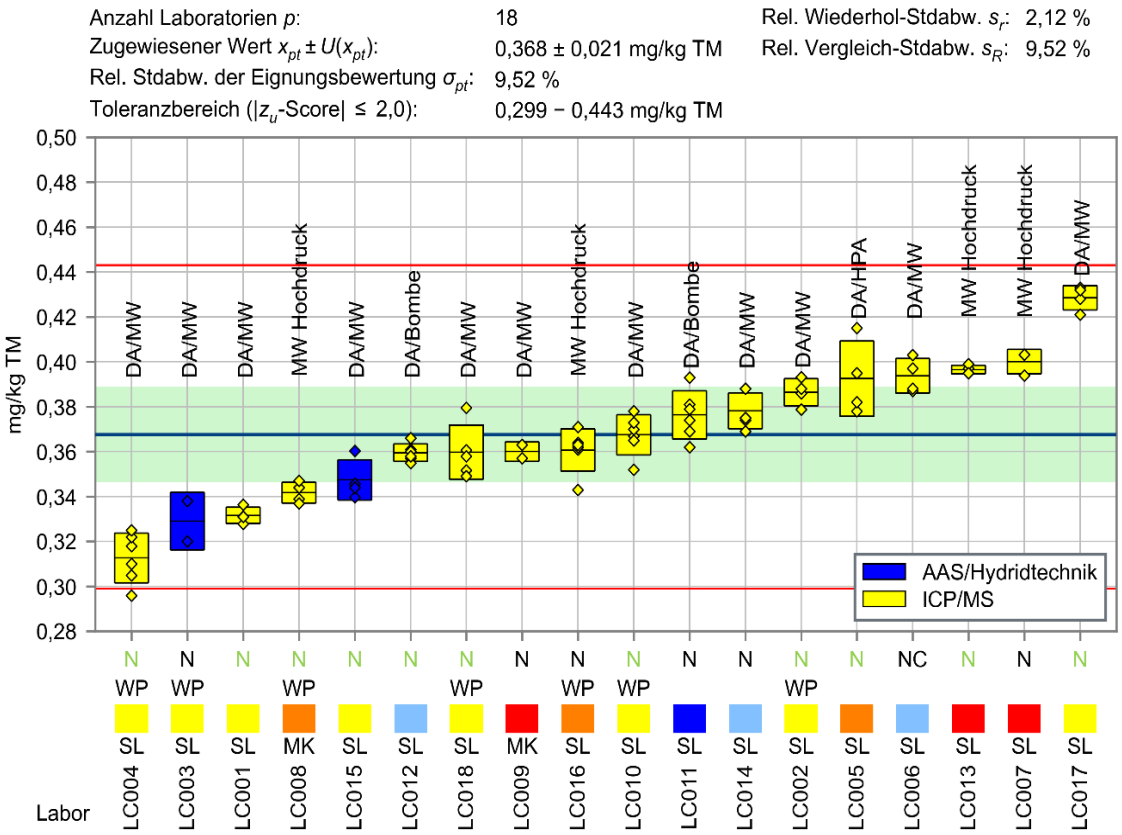


Measurement uncertainty

In interlaboratory studies, it is often observed that different laboratories obtain different results for the same samples.

In other words, the dispersion of values that could reasonably be attributed to the measurand is not negligible.

In other words, the MU is not negligible

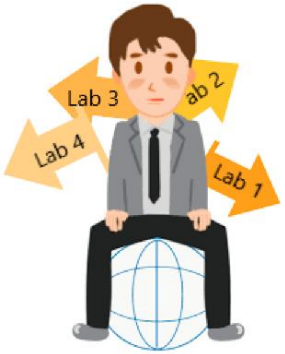


Arsenic in chicken egg powder (2021)

Measurement uncertainty

Interlaboratory tests have a long history since 1915 (at least)

Question asked at an ASTM symposium in 1958: “Will round robin testing *(interlaboratory tests)* increase or decrease in the future? Will it continue to be frustrating? When will it become ancient history?”



Comparison leads to frustration.
Frustration leads to disrespect.
Disrespect leads to division.
Never compare yourself with someone.
D. Gautam

???

Response at the 1958 symposium: “Round robin testing will have to exist until somebody comes up with something a lot better. It will always be frustrating. I do not think any one of us will live long enough to see it become ancient history. **The old idea of running a lot of tests, or of having a lot of people run a lot of tests, and then trying to correlate the data, still holds pretty well**.”

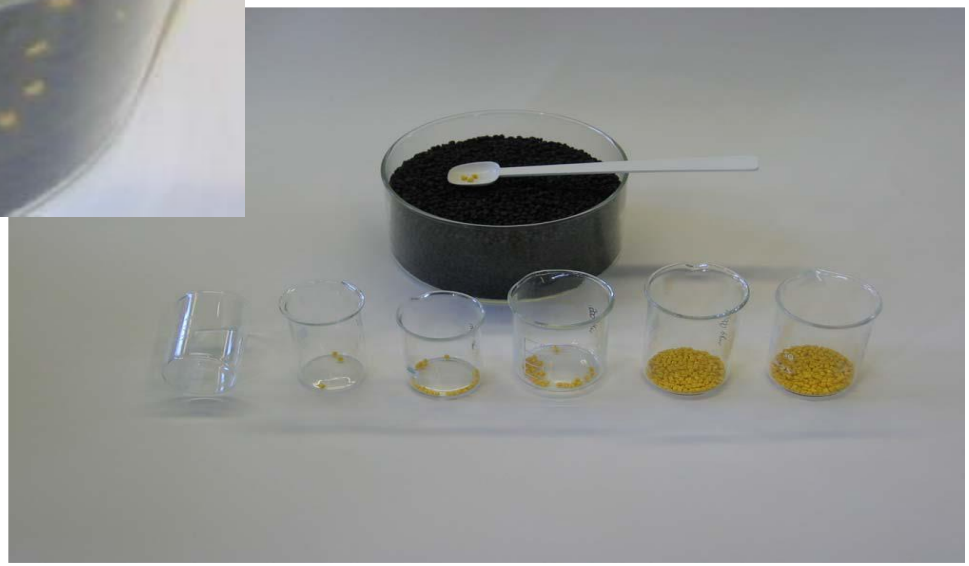
Measurement uncertainty

Why is MU non-negligible? What are the main sources of error?

- **Fundamental variability**
- **Matrix mismatch**

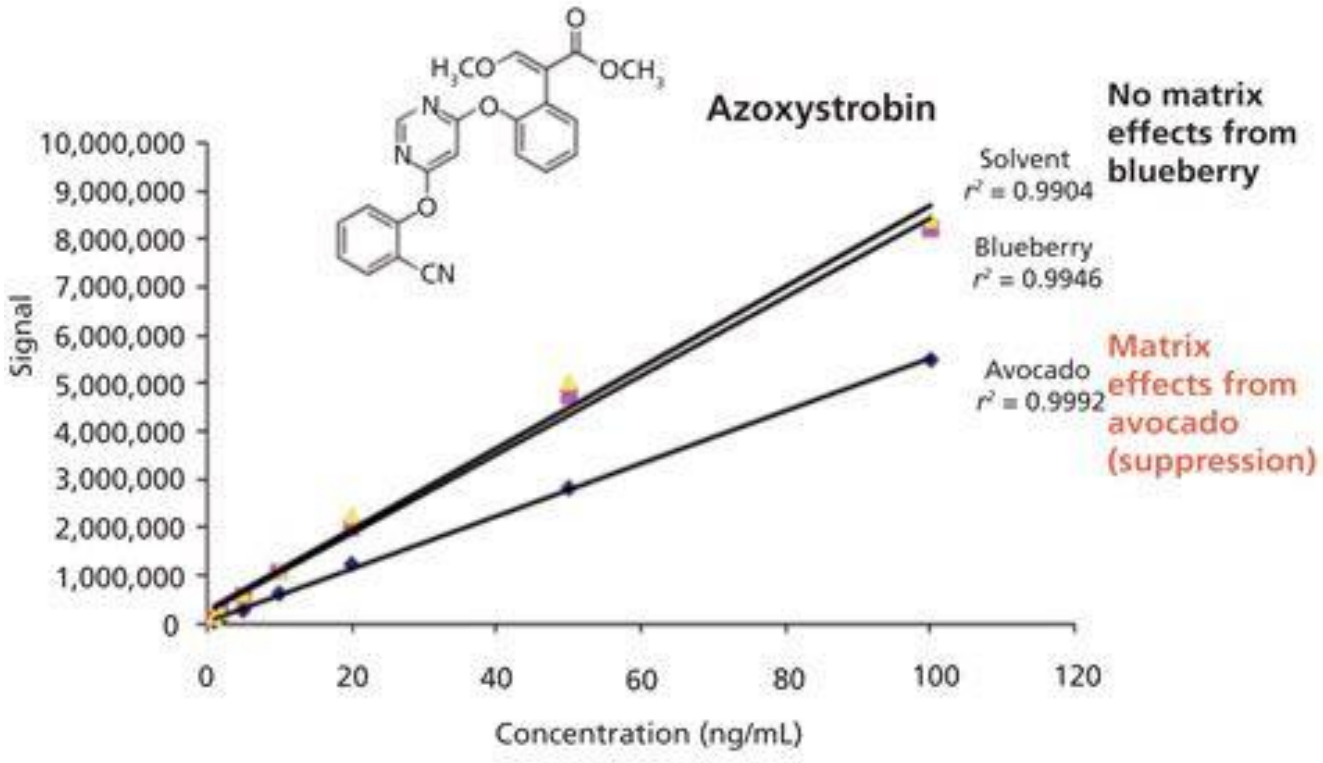
Measurement uncertainty

Fundamental variability



(Barrenstein 2019)

Although both LC–MS and GC–MS are highly selective, they are both vulnerable to matrix effects.



(Zhang et al. 2017)

Measurement uncertainty

Matrix mismatch

- Another example: different coffee samples
- Interlaboratory study 1
  - around 15 labs
  - HPLC
  - 8 different types of coffee
  - 2 analytes: 16-OMC and kahweol
  - For each analyte and coffee type: mean value across labs, repeatability and reproducibility
- Interlaboratory study 2
  - around 10 labs
  - NMR
  - Same analytes and coffee types and interlaboratory study 1

Question 1: what is the ratio between the HPLC and NMR mean values for each analyte and coffee type?
Question 2: how much do the ratios vary across coffee types for a given analyte:?

Measurement uncertainty

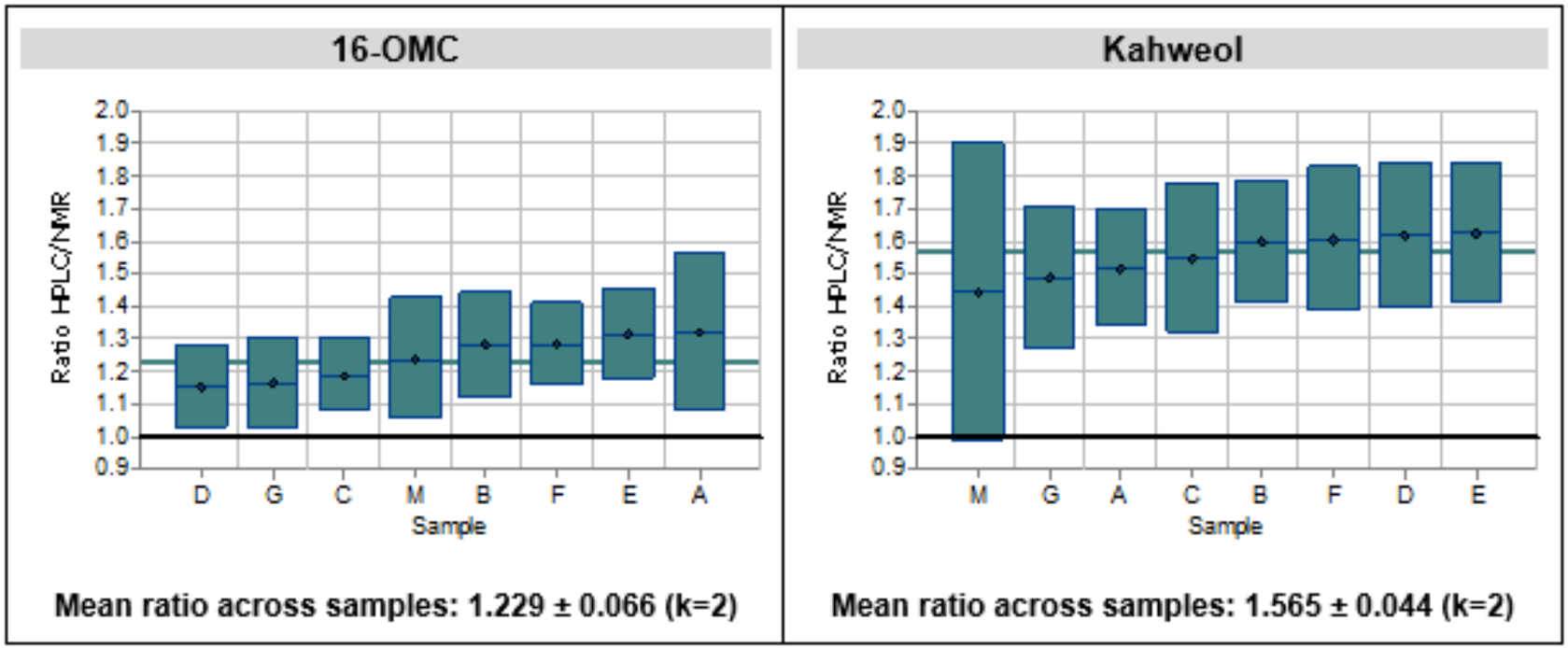
Matrix mismatch

16-O-methylcafestol (16-OMC) and kahweol were determined in eight coffee samples by both HPLC and NMR analysis.

Sample	HPLC					NMR					Ratio HPLC/NMR	
	Number of laboratories	Mean [mg/kg]	Repeata-bility SD [mg/kg]	Reproduci-bility SD [mg/kg]	Standard error of the mean [mg/kg]	Number of laboratories	Mean [mg/kg]	Repeata-bility SD [mg/kg]	Reproduci-bility SD [mg/kg]	Standard error of the mean [mg/kg]	Mean	Standard error of the mean
16-OMC												
A	14	21.82	4.89	7.65	1.70	11	16.55	2.11	3.29	0.83	**1.32**	**0.12**
B	14	41.38	3.35	8.26	2.07	11	32.32	3.92	5.48	1.29	**1.28**	**0.08**
C	14	58.23	3.93	8.95	2.21	10	49.02	3.63	5.25	1.33	**1.19**	**0.06**
D	15	76.23	6.42	16.04	3.79	11	66.05	4.46	6.97	1.70	**1.15**	**0.06**
E	13	441.94	10.13	76.92	21.01	11	336.22	10.82	29.77	8.52	**1.31**	**0.07**
F	15	602.21	49.79	109.37	25.72	11	469.82	15.76	43.59	11.92	**1.28**	**0.06**
G	16	816.96	101.47	200.28	44.30	11	702.51	36.37	62.64	16.32	**1.16**	**0.07**
M	16	1502.54	93.93	272.32	64.62	11	1213.99	69.17	247.25	75.86	**1.24**	**0.10**
Kahweol												
A	13	6397.25	1689.64	1960.58	361.91	9	4222.67	150.33	246.38	66.15	**1.51**	**0.09**
B	12	6555.85	416.12	1325.68	368.28	9	4102.03	72.63	274.51	84.50	**1.60**	**0.10**
C	12	6167.47	286.83	1603.37	451.58	9	3991.18	86.22	219.84	62.75	**1.55**	**0.12**
D	11	6235.72	353.20	1435.10	422.76	9	3854.82	154.68	231.50	59.70	**1.62**	**0.11**
E	12	5307.17	255.65	1171.16	331.99	8	3267.09	97.14	235.29	73.25	**1.62**	**0.11**
F	12	4591.42	382.09	1102.51	299.70	8	2854.54	77.81	244.29	73.70	**1.61**	**0.11**
G	13	3453.92	423.17	974.12	243.97	8	2317.59	117.17	179.98	47.01	**1.49**	**0.11**
M	13	134.71	33.59	38.34	6.93	9	93.44	20.84	43.49	12.91	**1.44**	**0.23**

Measurement uncertainty

Matrix mismatch



Analyte	Number of samples	MU Hampel estimator			
		Mean ratio HPLC/NMR	Standard error of mean ratio	Dark noise related to matrix effects	standard uncertainty (k=1) of conversion factor (including matrix related effects)
16-OMC	8	1.229	0.028	0.018	0.033
Kahweol	8	1.565	0.022	0.000	0.022

You are asked to determine the measurement uncertainty for a given measurand (measurand = quantity to be measured in a specific matrix or sample).

Where do you start?

Choosing the right approach for the calculation of measurement uncertainty

- Paragraphs 13 and 14 in CXG 54 provide an overview of different approaches.
- In particular: distinction between top-down and bottom-up
- Further information: Section 2 of the Information document

Bottom-up approach

- Described in JCGM documents (GUM)
- **Starting point:** equation describing the physical or chemical mechanism (or, more generally, the relationship between input variables and the measurement result), along with uncertainty values for each input variable
- On the basis of uncertainty values of the input variables, the uncertainty of the measurement result (combined uncertainty, uncertainty budget) is obtained:
  - via linear approximation (partial derivatives)
  - via simulation (Monte Carlo method, gold standard)
- Requires a model (equation) for each measurand
- Requires uncertainty values for each input variable
- Number of input variables can be considerable

Top-down approach

- Described in ISO 21748 (design and modelling of precision experiments is described in ISO 5725)
- **Starting point:** available precision data (*reproducibility* SD, usually two variance components: *repeatability* and *between-lab*), obtained e.g. via an interlaboratory validation study
- The repeatability component can be considered to characterize random variation inside a given lab.
- The between-lab component can be considered to characterize the range of lab bias.
- No model (equation) is required.
- Number of variance components depends on the experimental design of the validation study

Determine whether bias needs to be taken into account

- In GUM it is assumed that if an estimate of bias is available, then a bias correction is performed. It is the uncertainty of the bias correction which is then included as a component of measurement uncertainty.
- This is touched on in Paragraphs 10 and 25 in CXG 54.
- As far as the top-down approach is concerned, according to the model described in Section 3 of the Information document, there are three components of bias:
  - Method
  - Lab
  - Matrix
- The between-lab component of reproducibility precision from an interlaboratory (collaborative) validation study characterizes the range of lab bias (lab bias depends on the measurement conditions inside the participating laboratories and may vary over time)
- Paragraph 15 in CXG 54 addresses the case that an in-house (single-lab) study rather than an interlaboratory study was conducted. In such case, lab bias can be estimated via a separate recovery study.

Determining the contribution of fundamental variability to measurement uncertainty

- Fundamental variability is briefly discussed (and distinguished from grouping and segregation error) in Footnote 1 to Paragraph 4 in CXG 54.
- Section 9.4 of the Information document describes a simple procedure for calculating fundamental variability:
  - 20 tests are performed with routine test portion size
  - 20 tests with k-fold (e.g. twofold or threefold) increase in test portion size
  - the estimate of FV is obtained from the difference between the respective variances

	Experiment 1 Original test portion size Test result [mg/kg]	Experiment 2 Test portion size is tripled Test result [mg/kg]
Sample 1	14.0	15.1
Sample 2	11.9	13.8
Sample 3	10.5	11.8
Sample 4	14.9	14.0
Sample 5	13.1	11.4
Sample 6	9.5	15.7
Sample 7	15.6	12.4
Sample 8	18.3	11.5
Sample 9	12.5	12.1
Sample 10	16.4	13.7
Sample 11	18.0	15.8
Sample 12	14.0	12.5
Sample 13	13.0	12.8
Sample 14	20.8	15.1
Sample 15	10.2	11.8
Sample 16	21.5	10.6
Sample 17	13.9	11.1
Sample 18	17.8	12.9
Sample 19	7.7	11.4
Sample 20	12.2	16.3

s_1^2	s_2^2	s_1^2/s_2^2
13.54	3.05	4.44

$$s_F = \sqrt{\frac{3}{2} \cdot (s_1^2 - s_2^2)} = 3.97.$$

CXG 54: Practical applicability

Fundamental variability

A **1-tonne** container contains one single carrier particle, translating to 1 ng/kg analyte concentration. (This one particle contains 1 µg of the analyte.)

A **100 g** laboratory sample is collected from the container. Thus, with 99.99 % probability, the laboratory sample will contain no carrier particle, and there will be no fundamental variability in the lab. However, with 0.01 % probability, the laboratory sample will contain the single carrier particle.

In such a case, if a **1 g** test portion is taken from the laboratory sample, then the analyte concentration in the test portion will be either 0 mg/kg (99 % probability) or 1 mg/kg (1 % probability). This corresponds to a (Poisson) standard deviation of 10 ng/kg – which clearly constitutes a disproportionate estimate in relation to the situation in the container.

What conclusions can be drawn?

Determining the contribution of matrix mismatch to measurement uncertainty

- Matrix mismatch is briefly discussed in Paragraph 15 of CXG 54.
- Section 9.2 of the Information document describes a simple procedure for calculating the matrix SD:
  - Analysis of variance
  - Two components: within- and between-matrix

	Test result 1 [mg/kg]	Test result 2 [mg/kg]
Matrix 1	114.51	112.24
Matrix 2	120.25	111.59
Matrix 3	88.46	86.62
Matrix 4	118.93	102.35
Matrix 5	74.06	80.91
Matrix 6	117.50	102.69
Matrix 7	120.96	109.35
Matrix 8	96.05	92.92
Matrix 9	98.43	87.09
Matrix 10	107.99	117.42
Matrix 11	117.34	126.87
Matrix 12	76.56	109.79