



Method performance, Quality Control, and Measurement Uncertainty

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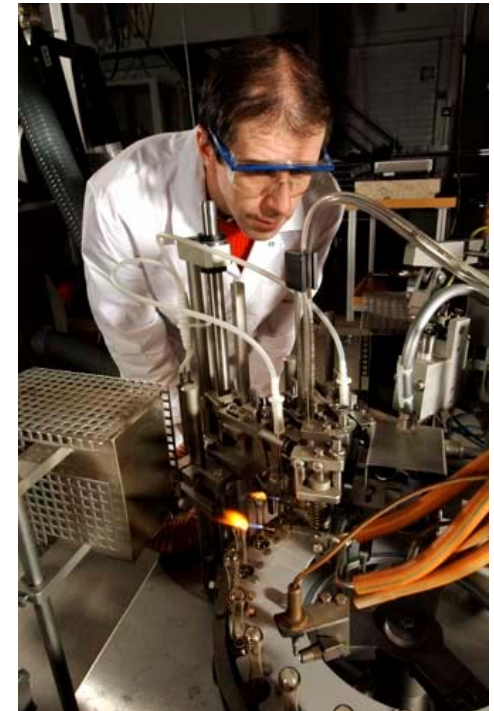
- **Introduction**
- **Method performance**
 - What characterises method performance?
- **Quality Control**
 - Why is QC important?
- **Measurement Uncertainty**
 - Do we really need to know?
 - Where do I find my MU?
- **Conclusions**

The role of JRC's Institute for Reference Materials and Measurements

The mission of the IRMM is to promote a common and reliable European measurement system in support of EU policies.

IRMM - CONFIDENCE IN MEASUREMENTS®

complementary to national activities:
providing quality assurance tools for all



The prime objective of JRC-IRMM is...

... to build confidence in measurements and ensuring their comparability.

- Method development and validation
- Validated data
- Reference measurements
- Production of reference materials
- Inter-laboratory comparisons
- Training

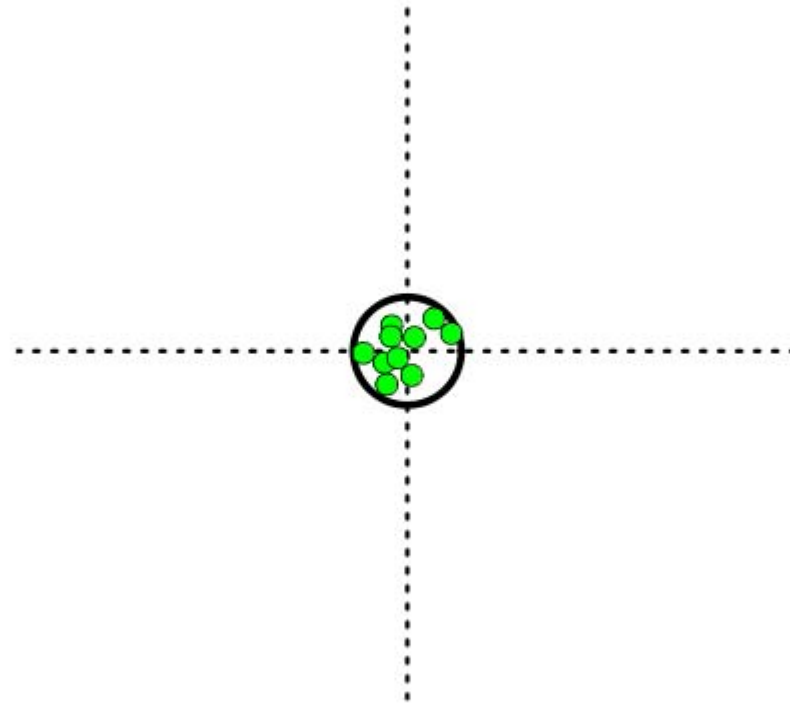


REGULATION (EC) No 882/2004 lists in Annex III:

1. Methods of analysis should be characterised by the following criteria:

- (a) accuracy;
- (b) applicability (matrix and concentration range);
- (c) limit of detection;
- (d) limit of determination;
- (e) precision;
- (f) repeatability;
- (g) reproducibility;
- (h) recovery;
- (i) selectivity;
- (j) sensitivity;
- (k) linearity;
- (l) measurement uncertainty;
- (m) other criteria that may be selected as required.

Precision + Recovery (trueness) = Accuracy



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- (a) accuracy;
- (b) applicability (matrix and concentration range);
- (c) limit of detection;
- (d) limit of determination;
- (e) precision;
- (f) repeatability; ← within laboratory (short time, single operator)
- (g) reproducibility; ← between laboratories
- (h) recovery;
- (i) selectivity;
- (j) sensitivity;
- (k) linearity;
- (l) measurement uncertainty;
- (m) other criteria that may be selected as required.

REGULATION (EC) No 401/2006

4. METHOD OF ANALYSIS TO BE USED BY THE LABORATORY AND LABORATORY CONTROL REQUIREMENTS

(g) Performance criteria for T-2 and HT-2 toxin

Level $\mu\text{g}/\text{kg}$	T-2 toxin		
	RSD _T %	RSD _R %	Recovery %
50-250	≤ 40	≤ 60	60 to 130
> 250	≤ 30	≤ 50	60 to 130

Level $\mu\text{g}/\text{kg}$	HT-2 toxin		
	RSD _T %	RSD _R %	Recovery %
100-200	≤ 40	≤ 60	60 to 130
> 200	≤ 30	≤ 50	60 to 130

Results of a collaborative trial to validate a method to determine the sum of T2 and HT2 toxins in cereals and baby food by immuno affinity clean-up and GC-MS:

Table 6: Performance parameters for the two toxins in cereal mix

		Mean	N	nc	outl.	n	r	s _r	RSD _r	R	s _R	RSD _R	HoR _{mod}
T-2	Blank	1.1	10	2	1	7	0.6	0.21	18	3.352	1.20	105	4.8
	Medium	9.4	10	0	1	9	1.38	0.49	5	2.91	1.04	11	0.5
	High	24.4	10	1	1	8	2.76	0.99	4	9.67	3.45	14	0.6
	App. recovery at 17 µg/kg	98	10	0	0	10	9.9	3.52	4	56.22	20	21	0.9
HT-2	Blank	3.6	10	1	0	9	3.39	1.21	34	6.05	2.16	60	2.7
	Medium	23.3	10	0	0	10	5.25	1.88	8	12.6	4.49	19	0.9
	High	52.2	10	1	1	8	7.58	2.71	5	23.2	8.29	16	0.7
	App. recover at 33 µg/kg	100	10	0	1	9	12.9	4.60	5	40.6	14.5	14	0.7

Legend: Mean – mean mass fraction [µg/kg] or mean percentage; N – number of labs; nc – non-compliant laboratories; outl. – outlying laboratories; n – number of laboratories used for statistics; r – repeatability [µg/kg], s_r – repeatability standard deviation [µg/kg], RSD_r – relative standard deviation under repeatability conditions [%]; R, s_R, RSD_R – the respective values for reproducibility, HoR_{mod} – the HorRat value for reproducibility modified after Thompson [11]

REGULATION (EC) No 401/2006

4.3.2. 'Fitness-for-purpose' approach

In the case where there are a limited number of fully validated methods of analysis, alternatively, a 'fitness-for purpose' approach, defining a single parameter, a fitness function, to evaluate the acceptability of methods of analysis may be used. A fitness function is an uncertainty function that specifies maximum levels of uncertainty regarded as fit for purpose.

Given the limited number of methods of analysis, fully validated by a collaborative trial, especially for the determination of T-2 and HT-2 toxin, the uncertainty function approach, specifying the maximum acceptable uncertainty, may also be used to assess the suitability (the 'fitness-for-purpose') of the method of analysis to be used by the laboratory. The laboratory may use a method which produces results within the maximum standard uncertainty. The maximum standard uncertainty may be calculated using the following formula:

$$Uf = \sqrt{(LOD / 2)^2 + (\alpha \times C)^2}$$

where:

- Uf is the maximum standard uncertainty ($\mu\text{g}/\text{kg}$)
- LOD is the limit of detection of the method ($\mu\text{g}/\text{kg}$)
- α is a constant, numeric factor to be used depending on the value of C. The values to be used are set out in the table hereafter
- C is the concentration of interest ($\mu\text{g}/\text{kg}$).

If the analytical method provides results with uncertainty measurements less than the maximum standard uncertainty the method shall be considered being equally suitable to one which meets the performance criteria given in point 4.3.1.

ISO/IEC 17025:2005 states:

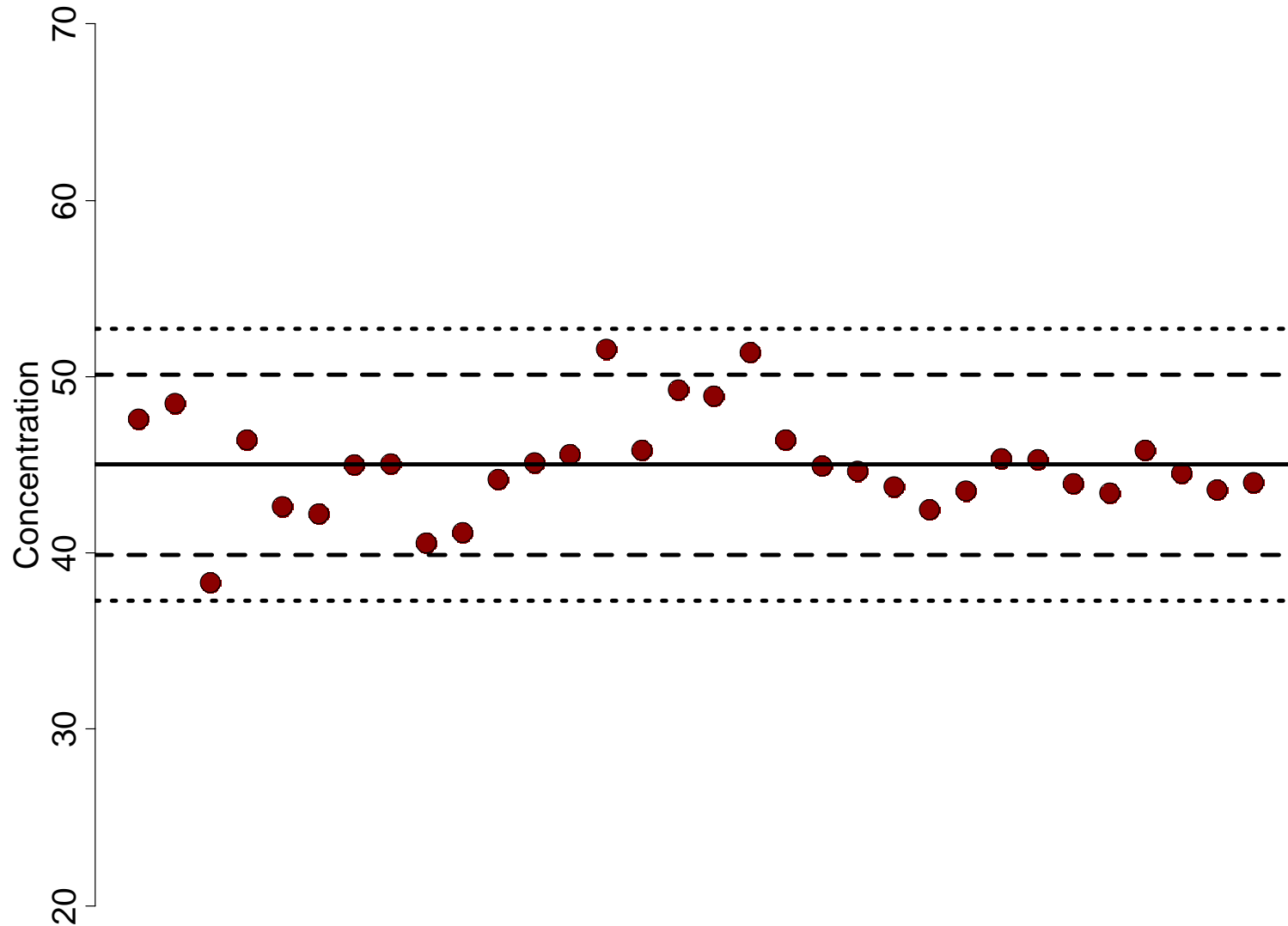
5.9 Assuring the quality of test and calibration results

5.9.1 The laboratory shall have quality control procedures for monitoring the validity of tests and calibrations undertaken. The resulting data shall be recorded in such a way that trends are detectable and, where practicable, statistical techniques shall be applied to the reviewing of the results. This monitoring shall be planned and reviewed and may include, but not be limited to, the following:

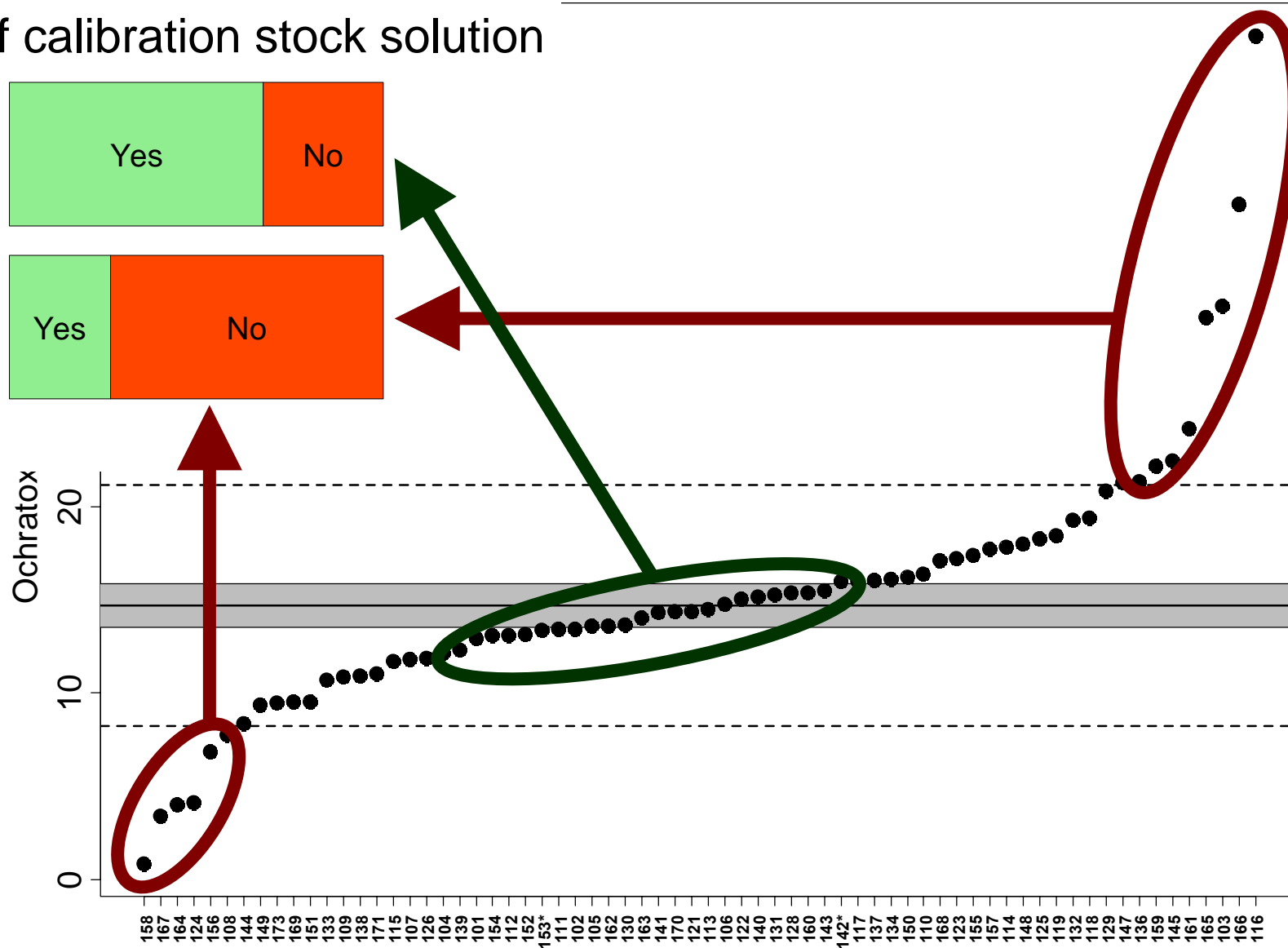
- a) regular use of certified reference materials and/or internal quality control using secondary reference materials;
- b) participation in interlaboratory comparison or proficiency-testing programmes;
- c) replicate tests or calibrations using the same or different methods;
- d) retesting or recalibration of retained items;
- e) correlation of results for different characteristics of an item.

NOTE The selected methods should be appropriate for the type and volume of the work undertaken.

Quality Control Chart:



Check of calibration stock solution



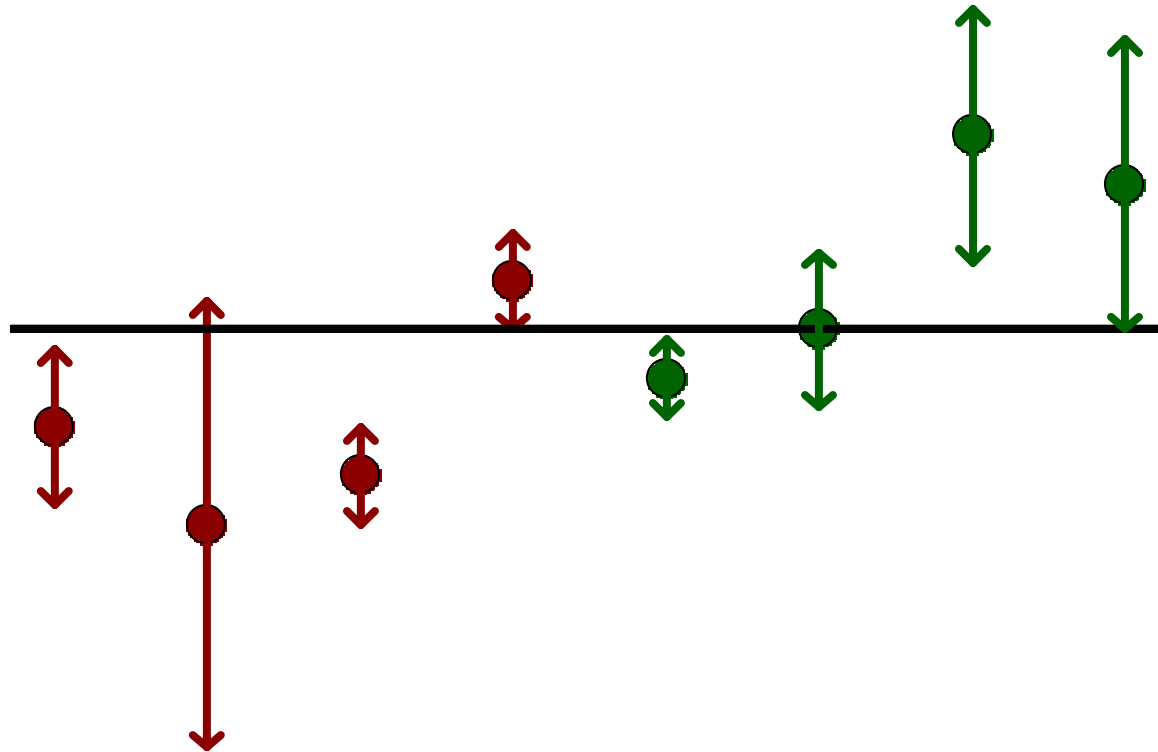
ISO 21748 states:

“Knowledge of the uncertainty of measurement results is essential to the **interpretation of the results**.”

Without quantitative assessments of uncertainty, it is impossible to **decide** whether observed differences between results reflect more than experimental variability, whether test items **comply with specifications**, or whether laws based on limits have been broken.

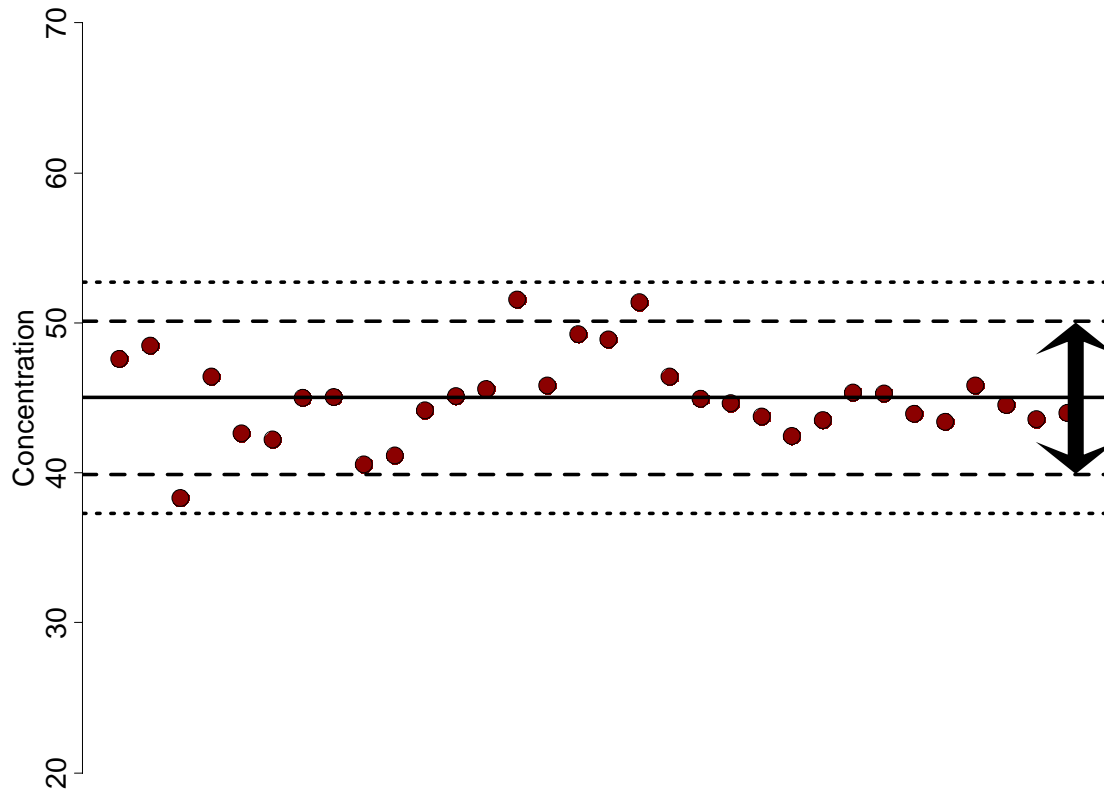
Without information on uncertainty, there is a real risk of either over- or under-interpretation of results.

Incorrect decisions taken on such a basis may result in unnecessary expenditure in industry, incorrect prosecution in law, or adverse health or social consequences.”

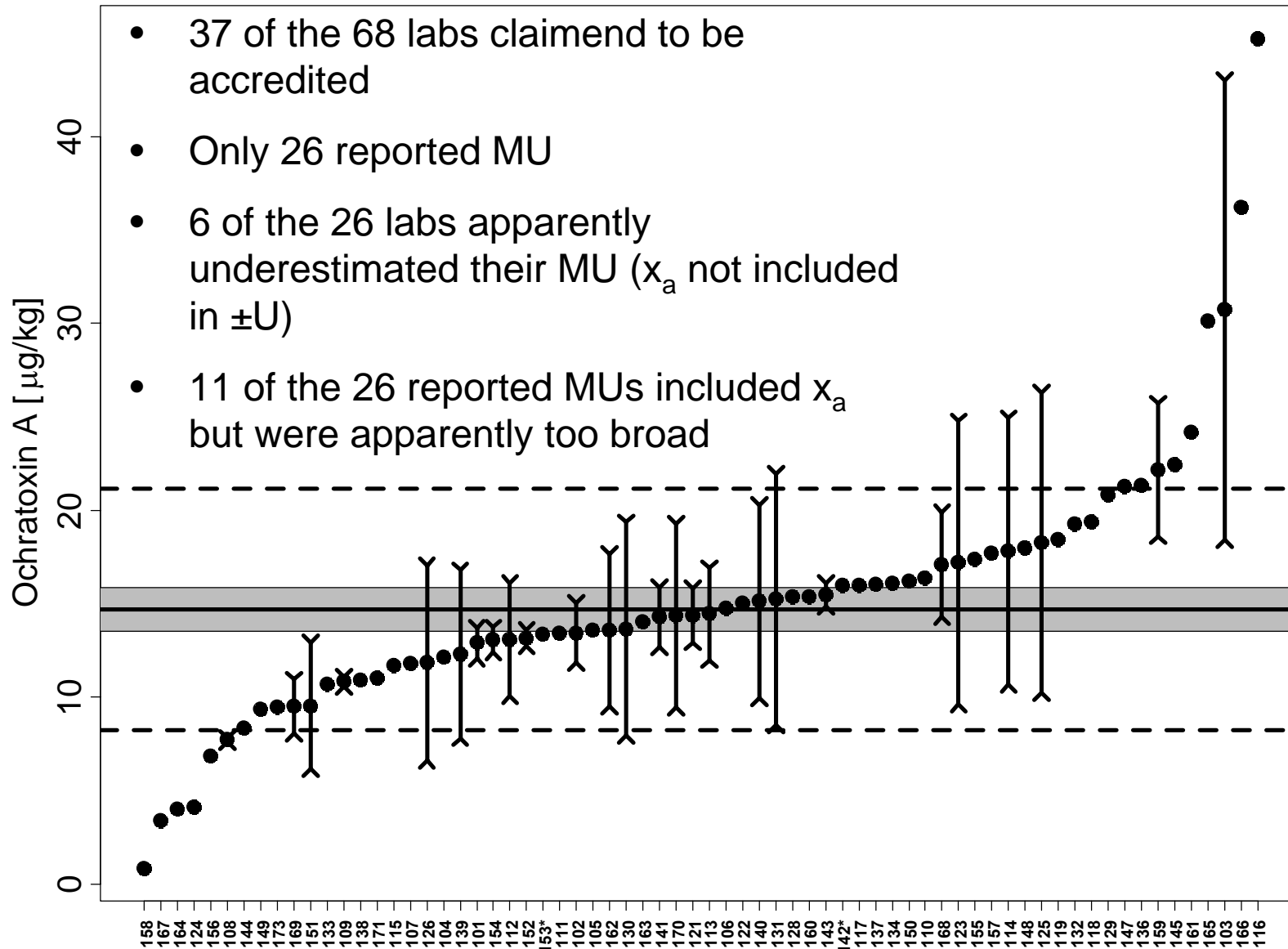


Estimation of MU can be done:

- in a “bottom-up” approach acc. to GUM
- in a “top-down” approach acc. to ISO 21748
- using method validation and quality control data from your own work



$2s$ range = 2 x Intermediate precision



- **EuroLab** TR No. 1/2007; *Measurement uncertainty revised: alternative approaches to uncertainty evaluation*
http://www.eurolab.org/docs/technical_report/Technical_Report_Measurement_Uncertainty_2007.pdf
- **Nordtest** Report TR 537 (2003); *Handbook for calculation of measurement uncertainty in environmental laboratories*
<http://www.nordicinnovation.net/nordtestfiler/tec537.pdf>
- **ISO 21748** (www.iso.org) *Guide to the use of repeatability, reproducibility and trueness estimates in measurement uncertainty estimates*
- **ISO 5725 – 6** (www.iso.org); “*Accuracy (trueness and precision) of measurement methods and results*”
- **ISO - GUM** (www.iso.org) “*Guide to the expression of uncertainty in measurements*”
- **QUAM** (2000)Eurachem guide “*Quantifying Uncertainty in Analytical Measurements*”
<http://www.eurachem.org/guides/QUAM2000-1.pdf>
- Commission Decision **2002/657/EC** concerning the performance of analytical methods and the interpretation of results (*cf. google*)

Measurements and legislation

- millions of measurements are performed every year to implement European directives and regulations
- important risk management decisions are taken based on those measurements – need confidence in measurements
- need for harmonising policy implementation in EU27+: building consensus

→ EU and global dimension of harmonisation



Who needs confidence in measurements?

The risk manager

- Making difficult choices on the basis of measurements results:
False + or False -?
Who is right? Are the results comparable and reliable?
Are they obtained with the good technique?

The citizens

- Who is checking the safety of our food and our environment?
- What is the quality of the controls being made?

The industrial operators

- Are we being controlled by competent laboratories?

Rapid Alert System for Food and Feed (RASFF) Border rejections (Week 39):

DATE	NOTIFIED BY	REF.	REASON FOR NOTIFYING	ACTION (TO BE) TAKEN
23/09/2008	Germany	2008.BMP	aflatoxins (B1 = ND; Tot. = ND / B1 = 4.0; Tot. = 4.4 / B1 = 11.7; Tot. = 12.9 µg/kg - ppb) in pistachio nuts with shell from Iran	product (to be) re-dispatched
24/09/2008	Italy	2008.BMQ	parasitic infestation with Anisakis of European hake (Merluccius merluccius) from Croatia	product (to be) destroyed
24/09/2008	Germany	2008.BMR	unauthorised colour Sudan 4 (25.7; 2.1 mg/kg - ppm) in palmoil from Togo	product (to be) destroyed
24/09/2008	Finland	2008.BMS	Salmonella Thompson (6,7:k:1,5) in broccoli from Thailand	product (to be) detained
25/09/2008	France	2008.BMT	aflatoxins (B1 = 2.9; Tot. = 5.5 / B1 = 2.2; Tot. = 3.5 / B1 = 4.0; Tot. = 5.8 µg/kg - ppb) in dried figs from Turkey	product (to be) re-dispatched
25/09/2008	Spain	2008.BMU	mercury (2.2 mg/kg - ppm) in frozen hammerhead shark (Sphyrna zygaena) from Japan	product (to be) redispached or destroyed
25/09/2008	Italy	2008.BMV	migration of nickel (0.26 mg/kg - ppm) from BBQ grid from China	product (to be) destroyed
25/09/2008	Italy	2008.BMW	migration of nickel (2.066 mg/kg - ppm) from stainless skewers from China	product (to be) redispached or destroyed
25/09/2008	Italy	2008.BMX	aflatoxins (B1 = 3.9; Tot. = 6.4 / B1 < 0.1; Tot. < 0.1 / B1 < 0.1; Tot. < 0.1 µg/kg - ppb) in Brazil nut kernels from Brazil	physical treatment - sorting
25/09/2008	Italy	2008.BMY	migration of chromium (0.427 mg/kg - ppm) from strainer sets from China	product (to be) re-dispatched
26/09/2008	Cyprus	2008.BMZ	unauthorised use of colour E 127 - erythrosine in individually packed mint candies from the United States	product (to be) redispached or destroyed
26/09/2008	Italy	2008.BNA	aflatoxins (B1 = 19.25; Tot. = 23.9 / B1 = 0.39; Tot. = 0.97 / B1 = 16.6; Tot. = 17.5 µg/kg - ppb) in shelled pistachio nuts from United States	product (to be) re-dispatched

Joint Research Centre (JRC)

Robust science for policy making

