Setting the requirements for a method (including aspects of MU)

Bertil Magnusson, SP Technical Research Institute of Sweden

Eurachem Workshop Gent 2016

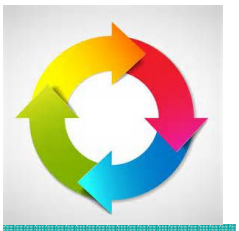
PART OF RI. SE

For a validation study we need to have several requirements…

- Target uncertainty
- Measurand
- Robustness

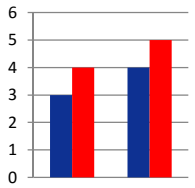
Focus on these 3 performance characteristics

- Sample types
- Measurement range
- Precision
- Trueness (bias)

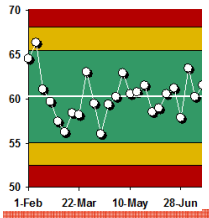


Measurement cycle

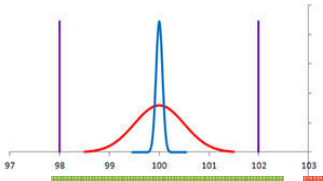
Requirements



Comparing



Process control



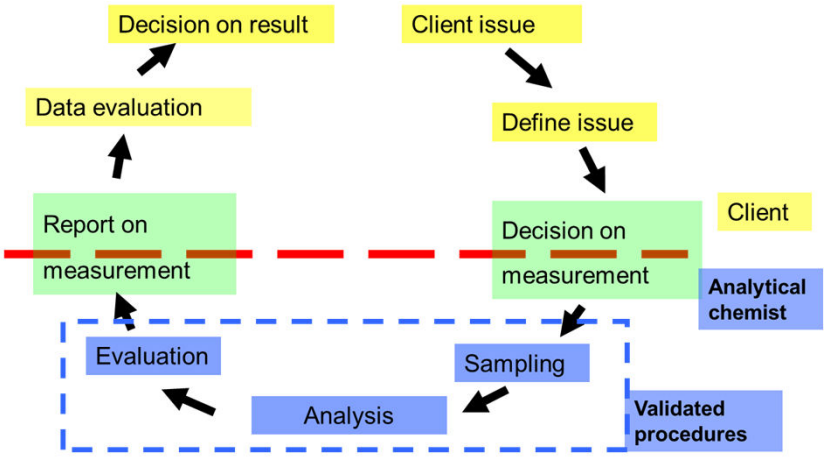
Specification

Legal limits

Translate requirements

With clear and distinct requirements on an analytical method we can assess fitness for purpose

Measurement cycle



The whole method validation process

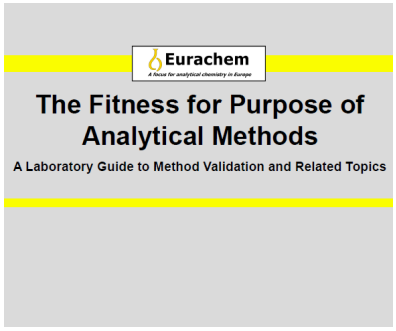
"from the customer problem

to the laboratory decision

on whether or not the customer request

can be carried out with an identified method"

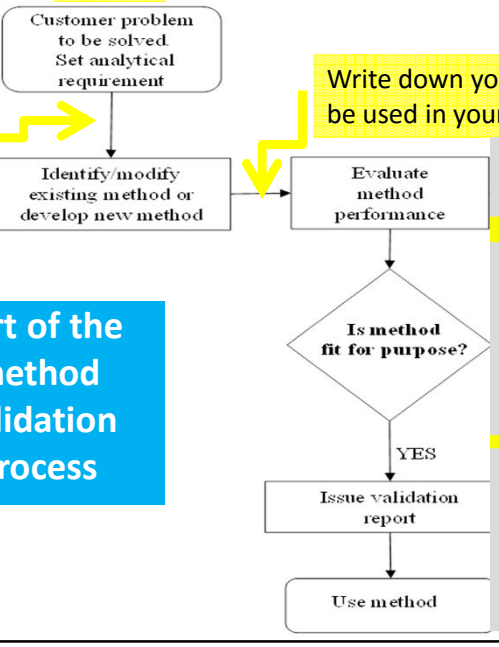
Text cited From Eurachem Guide Fitness for purpose of analytical methods, page 17



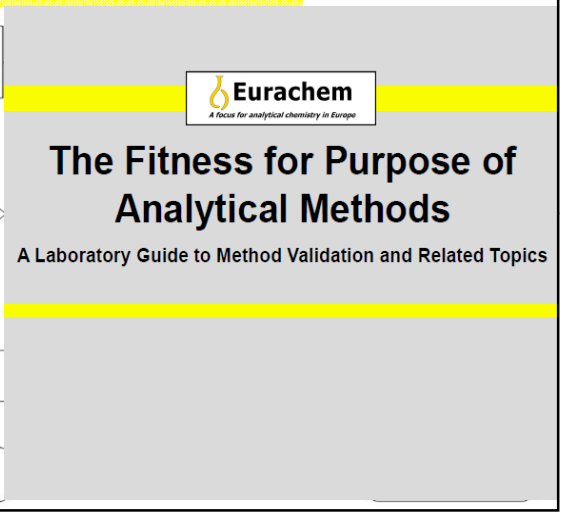
Step 1

Specify your measurand

Write down your method in detail to be used in your lab



Part of the method validation process



Requirements
Step 1 in the method validation process

Transferring the client issue
into analytical requirement
that can be used
in the validation study

Analytical requirements

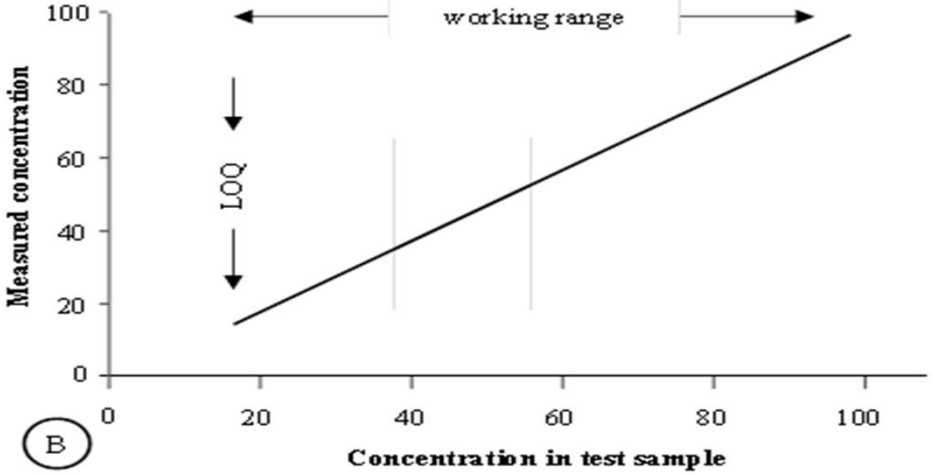
Specify the analytical requirement on ***performance characteristics*** *such as:*

- ***Measurement range***
- *Precision*
- *Trueness*
- *Measurement uncertainty*

Eurachem
A Focus for Analytical Chemistry in Europe

Chapter 6.3 Working range - method

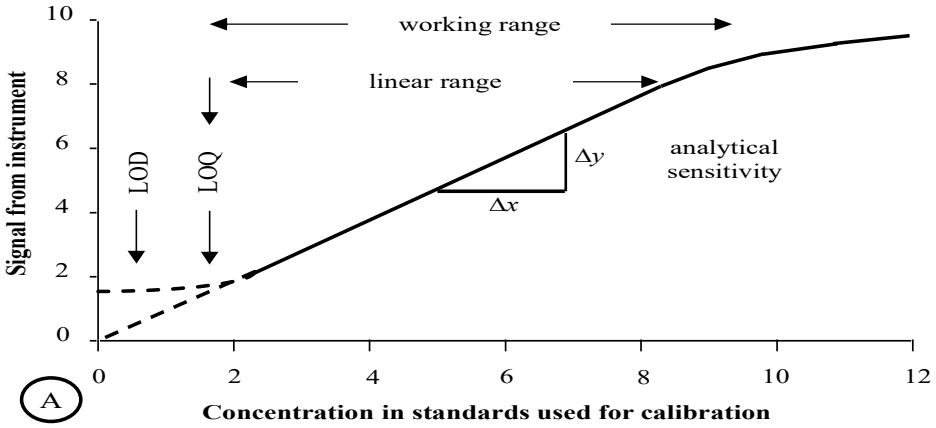
Instrument calibrated according to method/ procedure



9

Eurachem
A Focus for Analytical Chemistry in Europe

Chapter 6.3 Working range - instrument



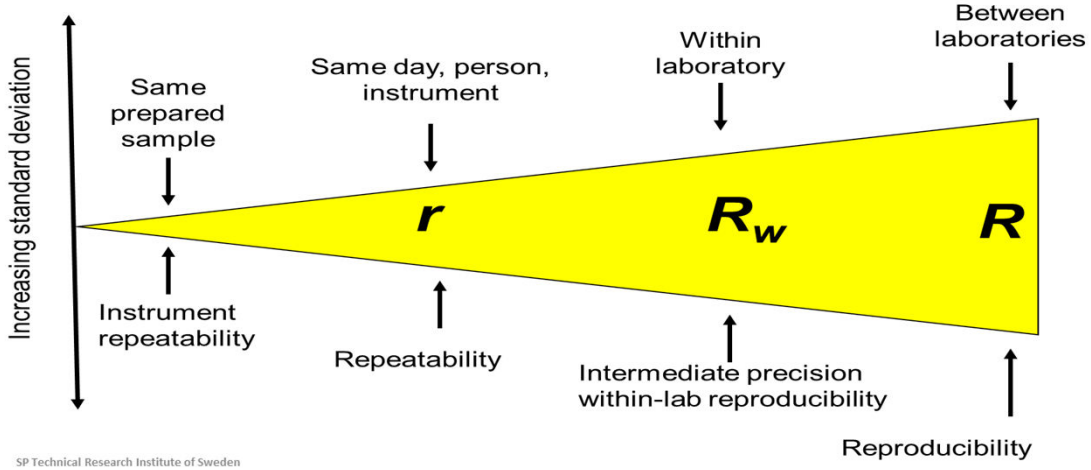
10

Analytical requirements

Specify the analytical requirement on performance characteristics such as:

- *Measurement range*
- *Precision*
- *Trueness*
- *Measurement uncertainty*

Precision



Analytical requirements

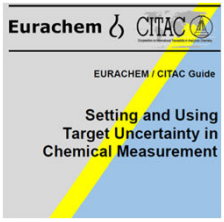
Specify the analytical requirement on ***performance characteristics*** *such as:*

- *Measurement range*
- *Precision*
- *Trueness*
  - *Specify max bias*
- *Measurement uncertainty*

Analytical requirements

Specify the analytical requirement on ***performance characteristics*** *such as:*

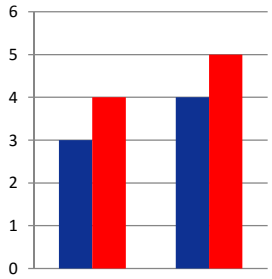
- *Measurement range*
- *Precision*
- *Trueness*
- ***Measurement uncertainty***
  - ***Set target uncertainty***
  - ***For validation – translate to precision and trueness***



Requirements when comparing

When comparing 2 results using the same method *precision limits* can be used

- Same lab – same day
  - **Repeatability limit**
- Same lab – different days
  - **Withinlab reproducibility limit**
- Different labs
  - Maybe **Reproducibility limit**



Precision limits

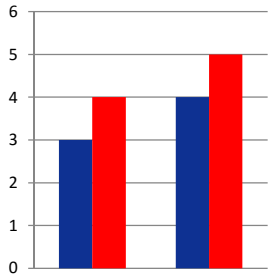
Precision limit

In 19 cases out of 20 the **difference** between 2 results will be less than…

e.g. the repeatability limit, *r*

$$r = k\sqrt{s_r^2 + s_r^2} = 2\sqrt{2s_r^2} = 2\sqrt{2}s_r$$

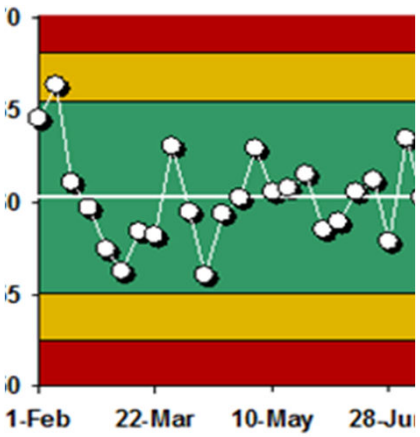
$$s_r = r/2.8$$



Process control

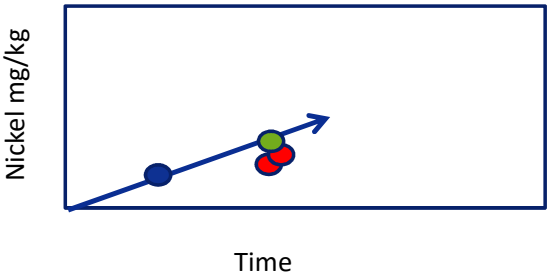
- Is the process under control?
- Demand on s_{Rw} at the level of interest

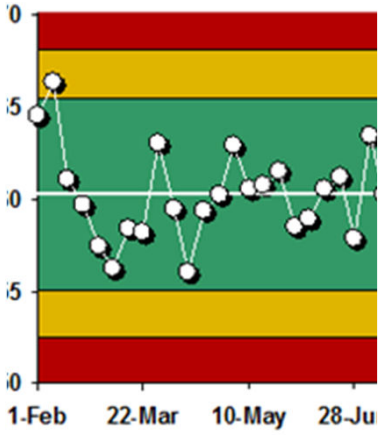
NOTE – to process from lab, communicate 95 % confidence interval i.e. 4 s_{Rw}



Process control

Fluid cracking catalyst poisoned by nickel in crude oil





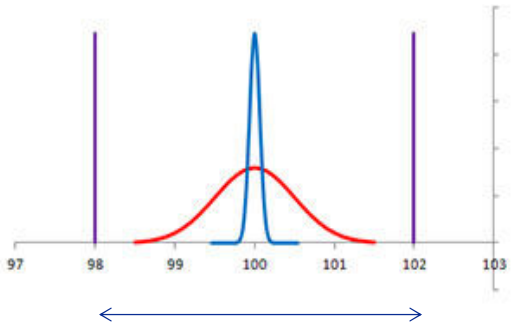
Specification

MSA – Measurement System Analysis – often physical measurement e.g. length

- Bias ≈ 0
- Acceptable s_{Rw} < 5 % of ***specification***
- Good s_{Rw} < 1,7 % of ***specification***

SPC – Statistical process control – Capability inded, C_p

- Acceptable $s_{process}$ < *10 %* of ***specification***
- Acceptable s_{Rw} < ?



Specification/Tolerance

Legal limits & EU directives

Directive 98/83/EC of 3 November 1998 on the **quality of water intended for human consumption**
At a given concentration level (parametric value) the **performance characteristics** for the method to be used are specified:

- Bias < 10 %
- Within-lab reproducibility, 2 s_{Rw} < 10 %
- LOD < 10 %

Legal limits & EU directives

Directive 2009/90/EC
regarding EU Water Framework Directive 2000/60/EC

At a given concentration level (environmental quality standard the **performance characteristics** for the method to be used are specified:

- Measurement Uncertainty, *U* < 50 %
- LOQ < 30 %

Legal limits – Danish law

Extensive list
Water
Ground, Drinking Surface, Marine Waste Swimming
Biota…
Soil
Sludge..

Requirements environmental measurements 2011*
Performance characteristics s_{Rw} CV_{Rw} LOD U_{abs} U_{Rel}
Example **Ground water**

Parameter	Enhed	$S_{T\,max}$	$CV_{T\,max}$	LD	U_{abs}	U_{rel}
Nikkel	µg/L	0,03	5%	0,03	0,1	20%
Selen	µg/L	0,03	5%	0,05	0,1	20%
Strontium	µg/L	3	5%	1	10	20%
Vanadium	µg/L	0,2	5%	0,2	0,5	20%
Zink	µg/L	0,3	5%	0,5	1	20%

Shellfish

Pesticider						
DDT pp'-	µg/kg VV	0,2	20%	0,05	1	50%
DDE pp'-	µg/kg VV	0,2	20%	0,05	1	50%

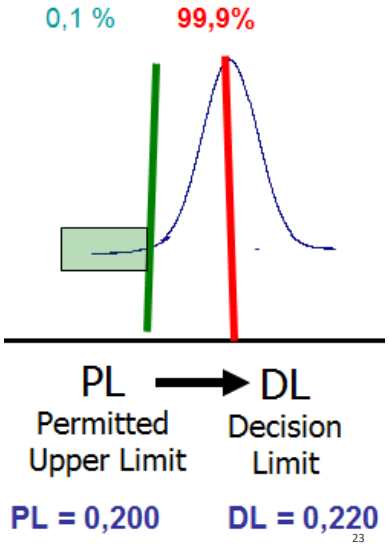
*www.retsinformation.dk/pdfPrint.aspx?id=174970

Legal limits - Blood alcohol

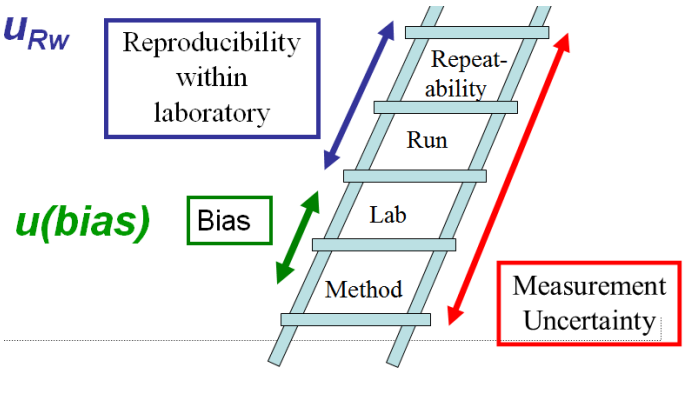
- **Measurand including measurement object** Concentration of EtOH in a blood sample delivered to the laboratory
- Upper limit 0,200 mg/g
- A **decision limit**. 0,220 mg/g

Target U calculated to be *0.026 mg/g

**The concentration above which it can be decided with a statistical certainty of 99.9 % that the permitted limit has been truly exceeded*



Translate requirements



Translate requirements From LOQ & U to s_{Rw}

The Trollbook – Nordtest Tr 565 proposes

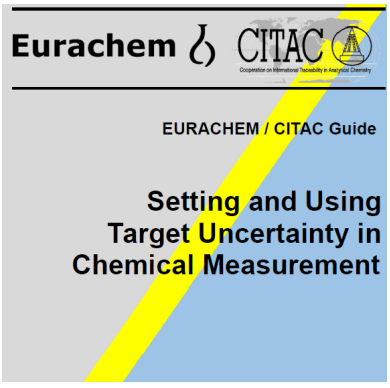
- Example 2 - LOQ
  - Acceptable within-lab reproducibility $s_{Rw} < LOQ/10$

Example 1 – Measurement uncertainty

- Acceptable within-lab reproducibility $s_{Rw} < U/4$

Setting requirements – target uncertainty

- Many more examples are given in our EURACHEM/CITAC guide



For a validation study we need to have several requirements…

Target uncertainty

Measurand

Robustness

With clear and distinct requirements on an analytical method we can assess fitness for pupose

Sample types

Measurement range

Precision

Trueness (bias)

PART OF RI. SE