Estimation of the measurement uncertainty based on method validation according to alternative models

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„What are we doing?"

General:
Risk management and communication in the sector of food safety and consumer protection

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Dept. 5 → EURL:
Harmonisation of food and feed analysis to make our daily food safer
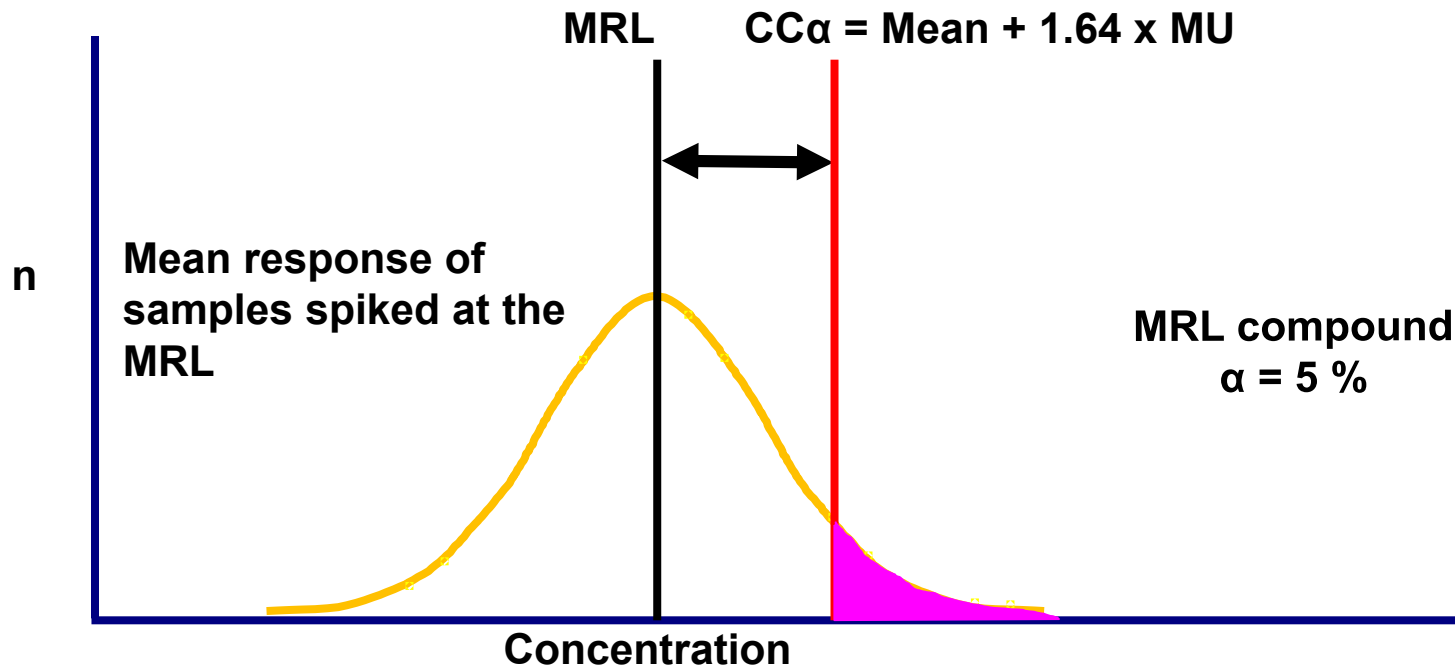
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Accreditation ISO 17025, ISO 17043

Veterinary drug residues:

- **Authorised compounds → proof for exceedance of maximum residue limits (MRL)**

- **Forbidden compounds → proof of presence**

CCα includes measurement uncertainty

MRL   **CCα = Mean + 1.64 x MU**

n

Mean response of samples spiked at the MRL

MRL compound α = 5 %

Concentration

How to implement measurement uncertainty?

"Bottom up" approach: MU for every single source of error or uncertainty

"Top down" approach: MU for combined contributions of error or uncertainty sources which comes from validation data

"Bottom up" + "top down" approach: MU from validation data + sources of error or uncertainty not covered by validation data

Non<u>s</u>teroidal <u>a</u>nti-<u>i</u>nflammatory <u>drugs</u> in milk

- **Development of a multi method for 34 <u>NSAIDs</u> in milk**

- **In-house validation is according to alternative models (Commission Decision 657/2002/EC)**

Validation study

Nonsteroidal anti-inflammatory drugs in milk

- **Blank milk spiked at 5 concentration levels**
  → maximum residue limits, recommended concentration
- **Blank milk originating from a different cow was analysed**
- **Validation was conducted on 8 different days**
- **48 samples analysed in total**
- **Duration of whole validation study: 2 months**
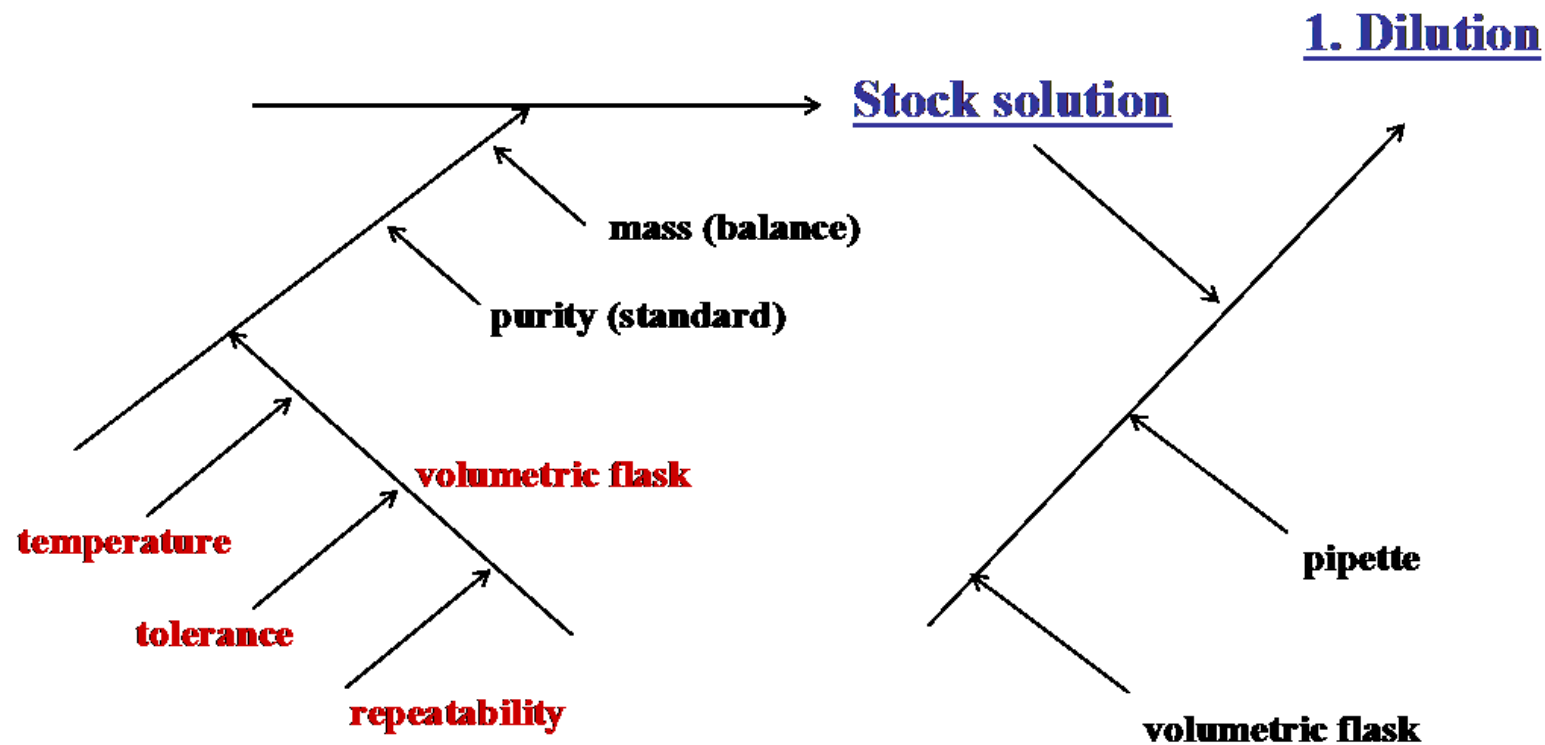
"Top down" approach

Run
Matrix   uncertainty
Repeatability

Experimental plan

„Top down" approach

Run	Matrix	Factor-level combination			
		Operator	Texture of milk	Storage time	HPLC column
1	P160094	unexperienced	lyo	directly	batch A
2	P160104	experienced	liquid	after 2 - 3 days	batch A
3	P160096	unexperienced	liquid	after 2 - 3 days	batch B
4	P160185	experienced	lyo	directly	batch B
5	P160106	unexperienced	liquid	directly	batch B
6	P140433	experienced	lyo	after 2 - 3 days	batch B
7	P140428	unexperienced	lyo	after 2 - 3 days	batch A
8	P160109	experienced	liquid	directly	batch A

InterVal 3.4.0.0, QuoData

„Bottom up" approach

Total measurement uncertainty

"Bottom up" + "top down" approach

$$u_{total}(x) = \sqrt{u^2_{matrix}(x) + u^2_{run}(x) + u^2_{repeat}(x) + u^2_{standard}(x)}$$

Salicylic acid

Indometacin
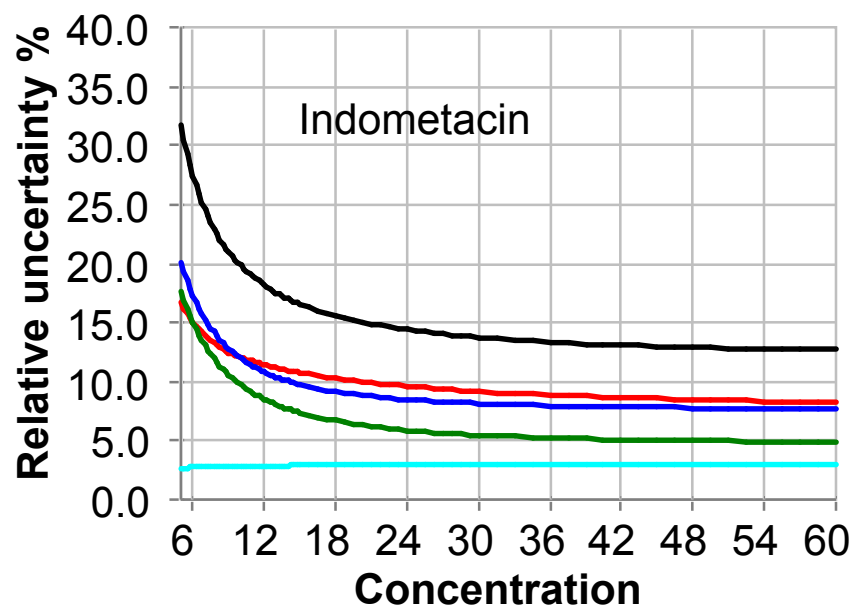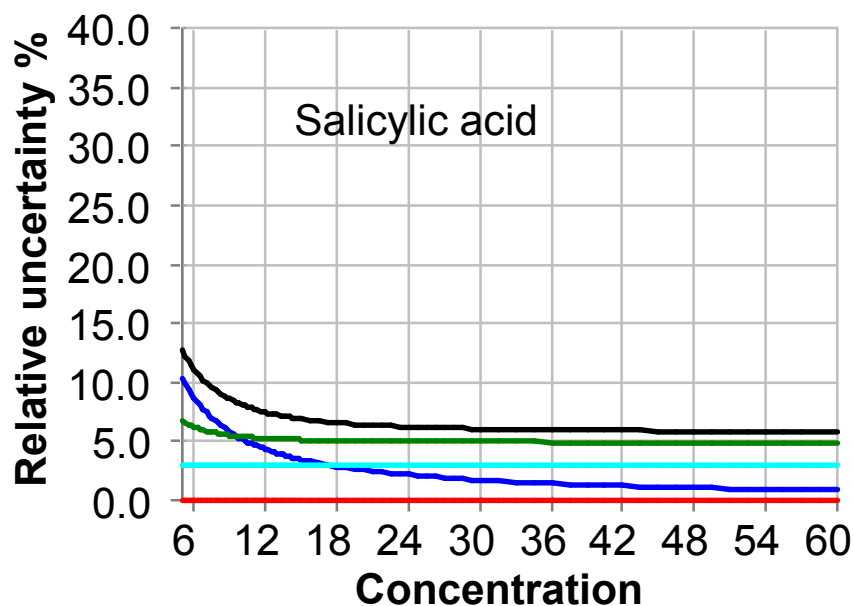
Rel. matrix uncertainty
Rel. standard solution uncertainty
Rel. run uncertainty
Rel. total uncertainty
Rel. repeatability uncertainty

InterVal 3.4.0.0, QuoData

Advantage of experimental design

"Bottom up" + "top down" approach

Random and systematic factor variations are considered in an efficient way due to experimental design based validation

Non defined effects	Defined effects
Random effects	Storage conditions
Time effects	Effects due to the operator
Correction of blank	Deviations due to instrumentation
	Influences of samples (matrix, stability)

Bias contribution to measurement uncertainty is not considered, but can be derived from other sources.

Take away message

- **Combining "Bottom up" + "top down" approach → risk of missing significant uncertainty contributions is minimized**

- **Application of experimental design → estimation of individual components of the total measurement uncertainty possible**
  - Influencing factors on method ruggedness are revealed
  - Importance for method transfer and extension

- **Sample matrix can contribute significantly to total uncertainty → consideration in uncertainty estimation required**

Thank you for your attention!

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