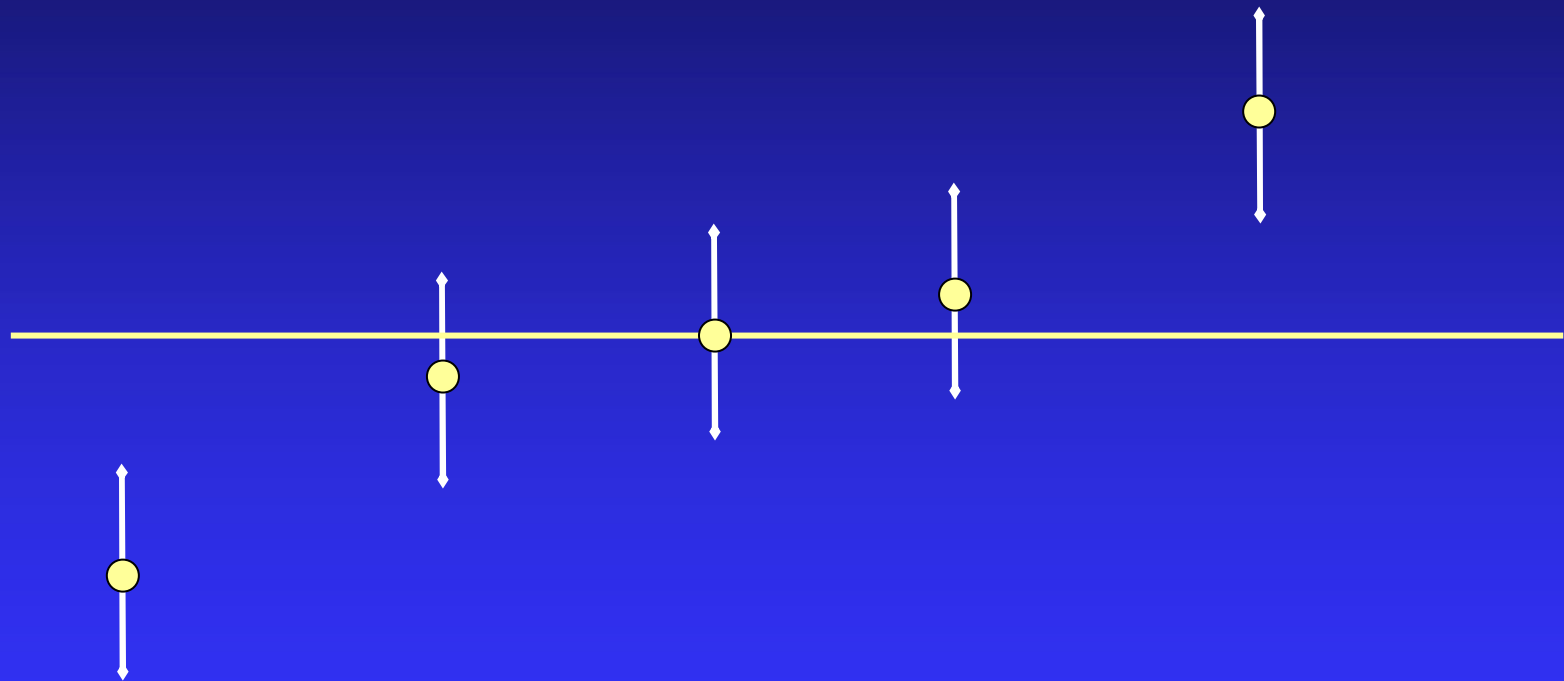


# Introduction to EURACHEM/CITAC Uncertainty Guide 2<sup>nd</sup> edition

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# Why Measurement Uncertainty



# Why Measurement Uncertainty



- Doping Cases
  - ◆ MU has to be considered to judge misconduct
    - ◆ Frank de Boer
    - ◆ Edgar David
- GMO Soya with Limit of 1%
  - ◆ Switzerland Government paid € 500'000.- from a € 1'000'000.- damage because of neglecting MU

# History

- 1977 Lack of international consensus on the expression of uncertainty in measurement (CIPM)
- 1980 Recommendation INC-1 Expression of Experimental Uncertainties (CIPM; 1981& 1986)
- 1993 Guide to the Expression of Uncertainty in Measurement (ISO)
- 1995 Quantifying Uncertainty in Analytical Measurement (Eurachem/CITAC)
- 2000 Quantifying Uncertainty in Analytical Measurement Second Edition (Eurachem/CITAC Guide)

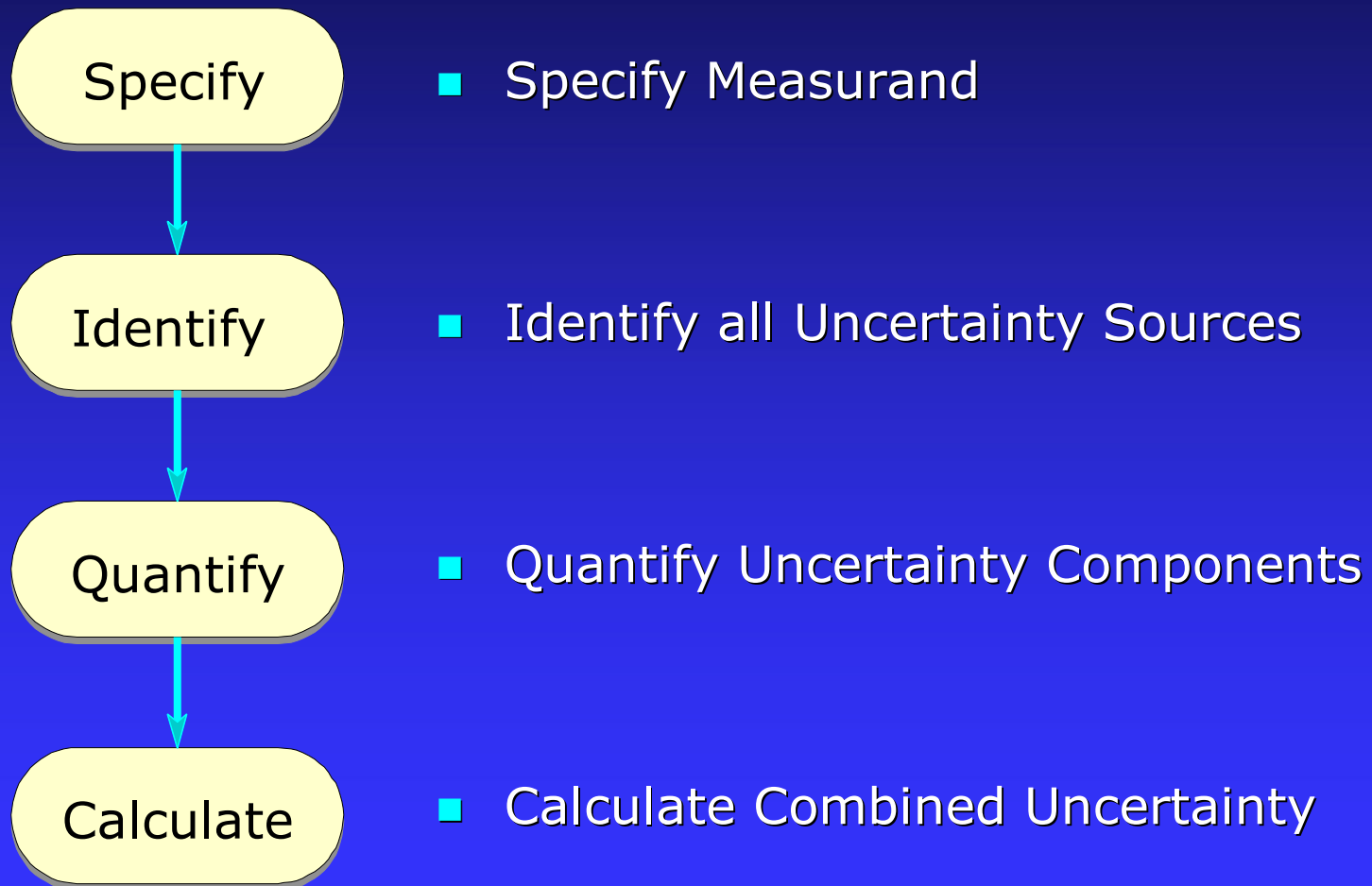
# Scope and Field of Application

- The principles of this Guide may be applied:
  - ◆ Quality control and quality assurance in manufacturing industries
  - ◆ Testing for regulatory compliance
  - ◆ Testing utilising an agreed method
  - ◆ Calibration of standards and equipment
  - ◆ Measurements associated with the development of reference materials
  - ◆ Research and development

# Scope and Field of Application

- Additional guidance will be required for:
  - ◆ Reference material value assignment using consensus methods (including multiple measurement methods)
  - ◆ Use of uncertainty estimates in compliance statements
  - ◆ Expression and use of uncertainty at low levels
  - ◆ Uncertainties associated with sampling operations are not explicitly treated

# Process of Uncertainty Estimation



# Step 1. Specify Measurand

- Write down a clear statement of what is being measured, including the relationship between the measurand and the input quantities (*e.g.* measured quantities, constants, calibration standard values *etc.*) upon which it depends.
- Where possible, include corrections for known systematic effects.
- The specification information should be given in the relevant Standard Operating Procedure (SOP) or other method description.

## Step 2. Identify Uncertainty Sources

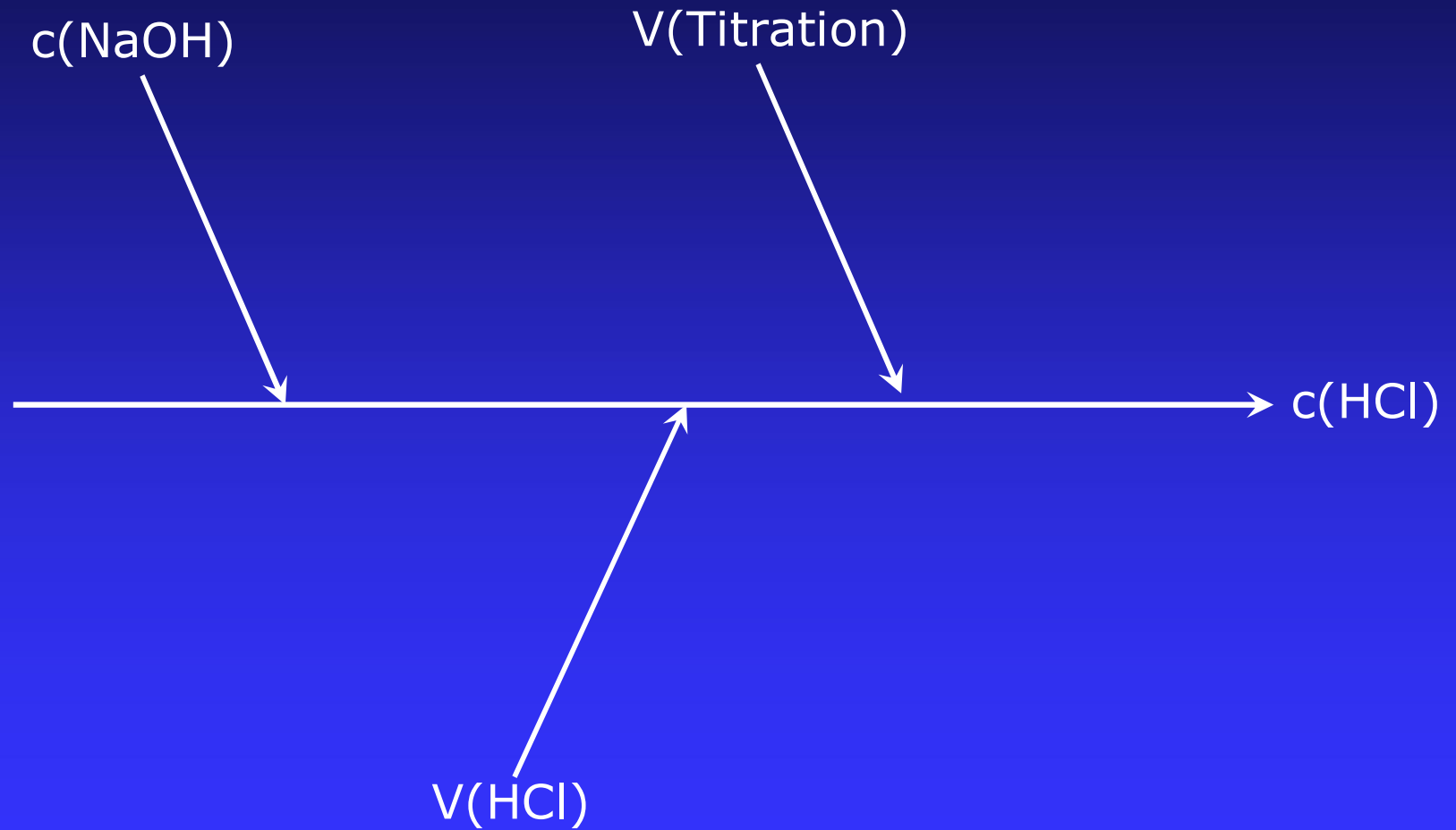
- List the possible sources of uncertainty. This will include sources that contribute to the uncertainty on the parameters in the relationship specified in Step 1, but may include other sources and must include sources arising from chemical assumptions.
- Tool for forming a structured list is the Cause and Effect diagram.
- Appendix D. Analysing Uncertainty Sources based on S. L. R. Ellison, V. J. Barwick; *Accred. Qual. Assur.* **3** 101-105 (1998)

# Example

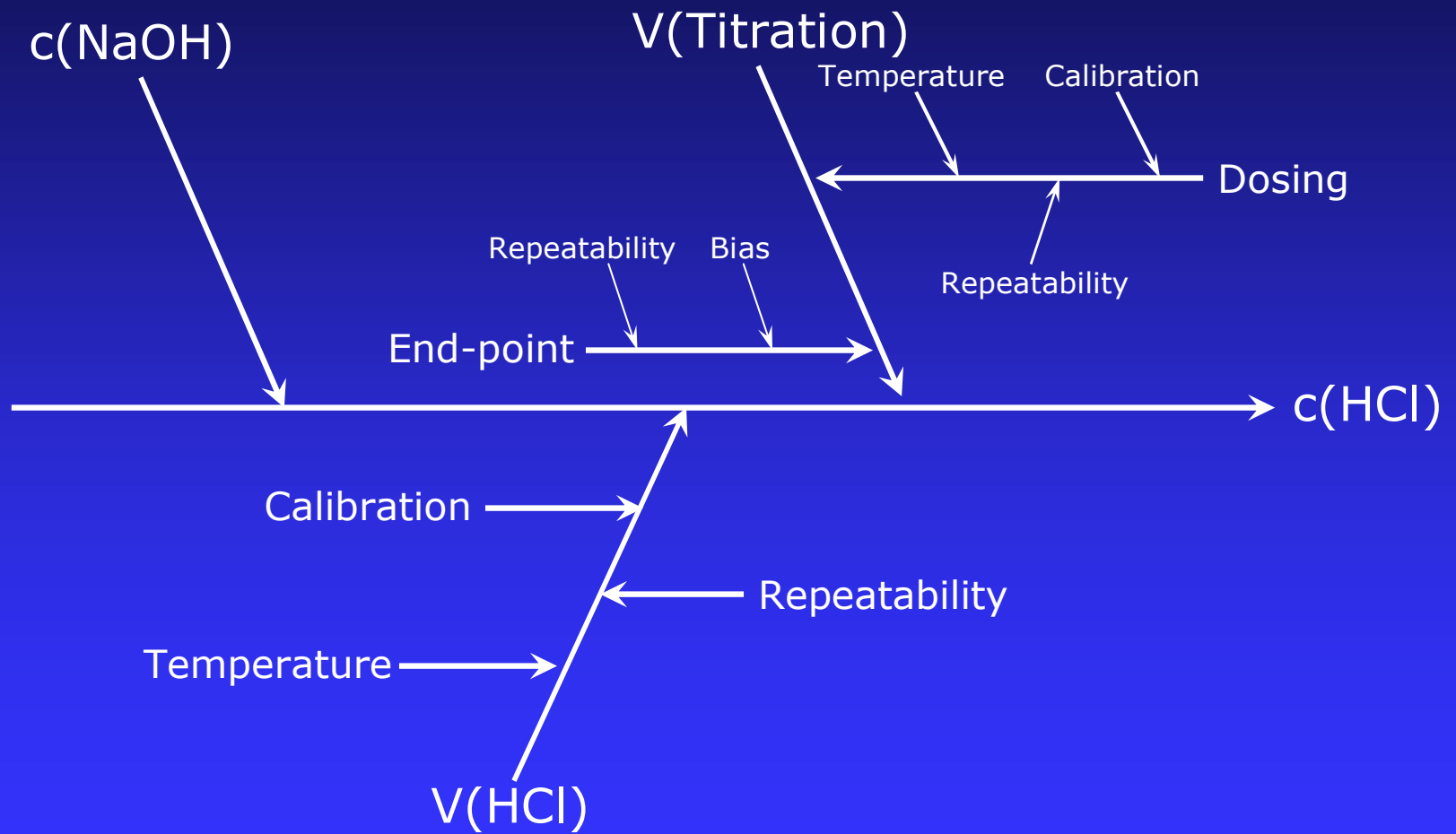
Determine the concentration of an HCl solution with the titration of 10 ml sample using a freshly prepared and standardized 0.1 mol/l NaOH solution.

$$c_{HCl} = \frac{V_{Titration}}{V_{HCl}} \cdot c_{NaOH} \quad (\text{mol/l})$$

# Cause and Effect Diagram



# Cause and Effect Diagram



## Step 3. Quantify Uncertainty Components

- Measure or estimate the size of the uncertainty component associated with each potential source of uncertainty identified.
- It is often possible to estimate or determine a single contribution to uncertainty associated with a number of separate sources.
- It is also important to consider whether available data accounts sufficiently for all sources of uncertainty.
- If necessary plan additional experiments and studies carefully to ensure that all sources of uncertainty are adequately accounted for.

# Quantify Uncertainty Components

Simplify by grouping sources covered by existing data



Quantify grouped components



Quantify remaining components

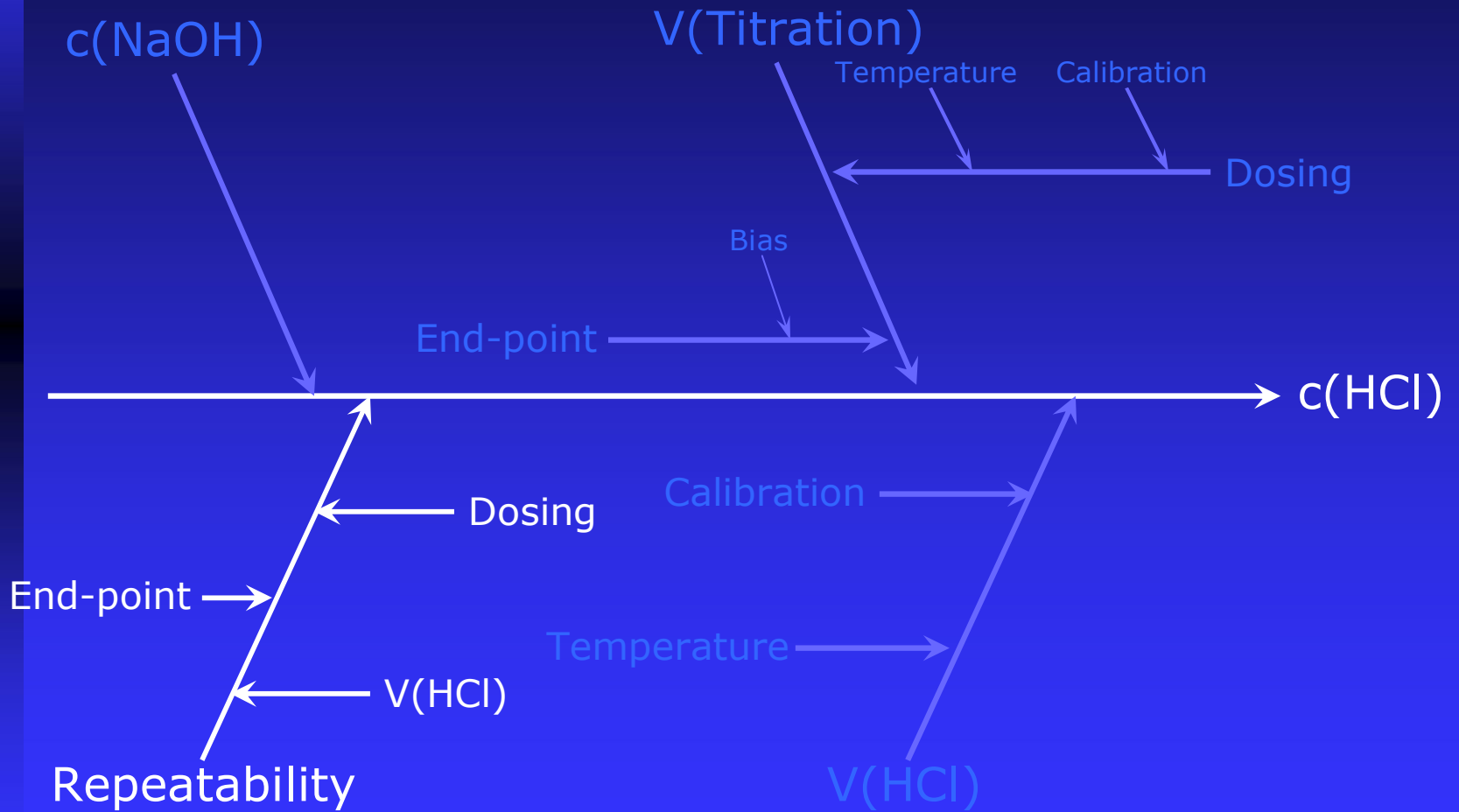


Convert components to standard deviations

- Cause and Effect Diagram
- Validation
- Validation; Robustness








# Simplify by grouping sources



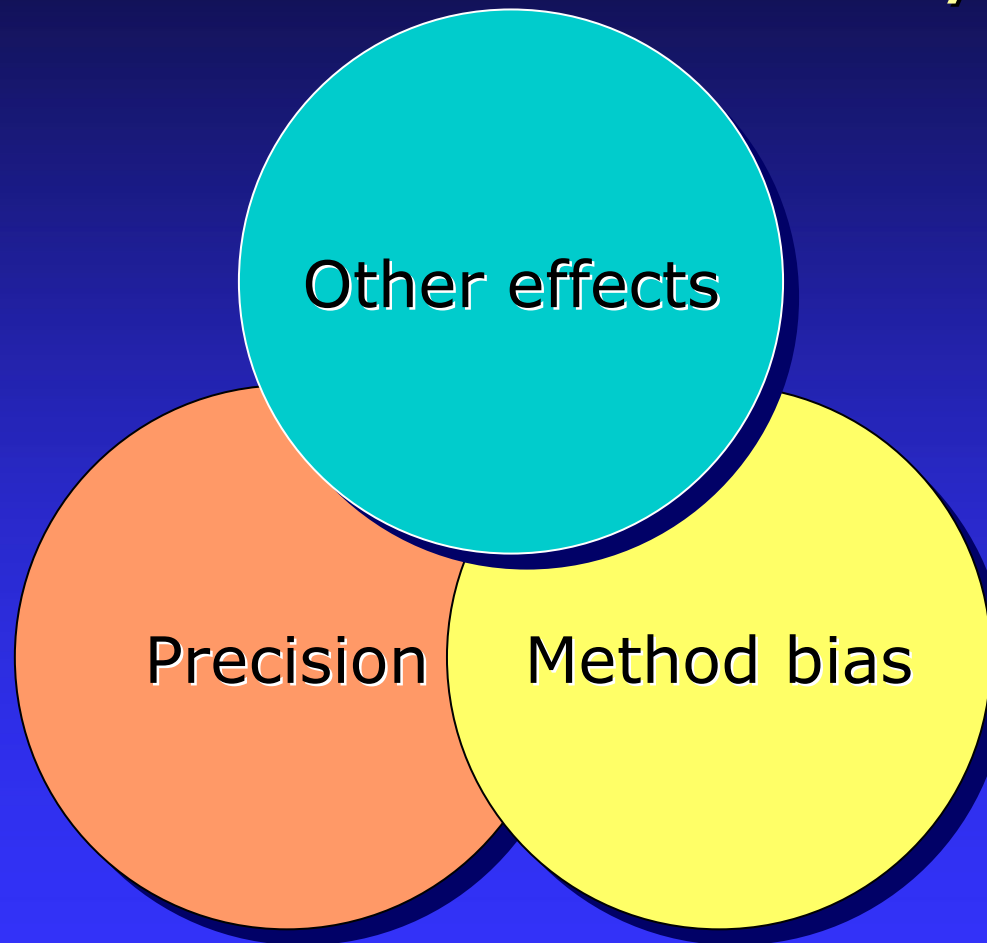
# How to quantify grouped components

- Uncertainty estimation using prior collaborative method development and validation study data
- Uncertainty estimation using in-house development and validation studies
- Evaluation of uncertainty for empirical methods
- Evaluation of uncertainty for ad-hoc methods

# Collaborative method validation

- **Sampling:** Collaborative studies rarely include a sampling step 
- **Pre-treatment:** In most studies, samples are homogenised, and may additionally be stabilised, before distribution 
- **Method bias:** Method bias is often examined prior to or during interlaboratory study 
- **Variation of conditions:** Laboratories participating in a study may tend towards the mean of allowed ranges of experimental conditions 
- **Changes in sample matrix:** Matrix composition and levels of interferences are rarely varied 

# In-house validation study



# Conduct of experimental studies of method performance

- **Representativeness** is essential. Studies should be conducted to provide a realistic survey of the number and range of effects operating during normal use of the method.
- Representative variation: Influence parameter must take a distribution of values appropriate to the uncertainty in the parameter in question.
- Systematic studies can quickly establish the size of an effect.
- With random variation takes over 30 determinations to establish an uncertainty contribution to about 20% relative accuracy.

# Relevance of prior studies

- Demonstration that a comparable precision to that obtained previously can be achieved.
- Demonstration that the use of the bias data obtained previously is justified, typically through determination of bias on relevant reference materials, by appropriate spiking studies, or by satisfactory performance on relevant proficiency schemas.
- Continued performance within statistical control as shown by regular QC sample results and the implementation of effective analytical quality assurance procedures.

# Evaluation of uncertainty for empirical methods

- An 'empirical method' is a method agreed upon for the purposes of comparative measurement within a particular field of application where the measurand characteristically depends upon the method in use.
- The method accordingly defines the measurand.
- Bias associated with the method is defined as zero.

# Evaluation of uncertainty for empirical methods

- Bias estimation needs relate only to the laboratory performance.
- Whether to demonstrate negligible bias or to measure bias should be conducted using reference materials certified using the particular method.
- Where reference materials so characterised are unavailable, overall control of bias is associated with the control of method parameters affecting the result.

## Step 4. Calculate the combined uncertainty

First order approximation (GUM)

$$\text{From } Y \approx f(\mu_1, \dots, \mu_n) + \sum_{i=1}^n \frac{\partial f}{\partial X_i} (X_i - \mu_i) + O((X_i - \mu_i)^2)$$

we obtain

$$E[Y] \approx f(\mu_1, \dots, \mu_n)$$

$$\text{Var}(Y) \approx \sum_{i=1}^n \left( \frac{\partial f}{\partial X_i} \right)^2 \text{Var}(X_i) + \sum_{j=1}^n \sum_{i=1}^n \frac{\partial f}{\partial X_i} \frac{\partial f}{\partial X_j} \text{Cov}(X_i, X_j)$$

## Step 4. Calculate the combined uncertainty

	A	B	C	D	E
1			P	m	V
2		value	0.9999	100.28	100.00
3		uncertainty	0.000058	0.05	0.07
4					
5	P	0.9999	0.999958	0.9999	0.9999
6	m	100.28	100.28	100.33	100.28
7	V	100.0	100.00	100.00	100.07
8					
9	c(Cd)	1002.69972	1002.75788	1003.19966	1001.99832
10	u(y,x)		0.05816	0.49995	-0.70140
11	<sup>2</sup>	0.74529	0.00338	0.24995	0.49196
12					
13	u(c)	0.9			

# Appendix A. Examples

1. Preparation of a calibration standard
2. Standardising a sodium hydroxide solution
3. An Acid/Base titration
4. Uncertainty estimation from in-house validation studies; *Determination of organophosphorus pesticides in bread*

## Appendix A. Examples

5. Determination of cadmium release from ceramic ware by atomic absorption spectrometry
6. The determination of crude fibre in animal feeding stuffs
7. Determination of the amount of lead in water using double isotope dilution and inductively coupled plasma mass spectrometry

## Quantifying Uncertainty in Analytical Measurement

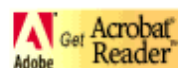
### Project

Members of the CITAC/ Eurachem working group measurement uncertainty have decided to support the utilisation of the completely revised Guide Quantifying Uncertainty in Analytical Measurement by setting up this web-site. It is hosted by EMPA St. Gallen (Switzerland) and Dr. Matthias Rösslein, who launched the project, is leading a small team, which builds and supports it.

You will find the following content on this site:

- **Guide:** A full html-version of the guide. The full text can be searched using an excite search engine.
- **Examples:** You may submit your uncertainty evaluations and seek comments on them in the forum. These examples will be posted here, but there will be no guarantee that they fully comply with the content of the guide.
- **Glossary:** Definition of terms we need to understand each other.
- **FAQ:** Frequently Asked Questions.
- **Forum:** Here you can ask questions, ask for advice and comment on published examples. It is you, who will keep this forum active.
- **Info:** Contact, Information, Links, Feedback, ...
- **Workshop** on Measurement Traceability and Uncertainty in Analytical Chemistry. June 16 - June 18, 2002 in Luzern/Switzerland

If you would like to have a hard copy of this guide you can download the [pdf-file](#). You need to have an [Acrobat Reader](#) to be able to view or print the pdf-version of the guide.



There is also a [text-only Acrobat Reader](#) download page

### News

30. May 2002 Deadline for [Workshop](#) until 10. June 2002

23. May 2002 There is [a new example](#) about Gravimetry.

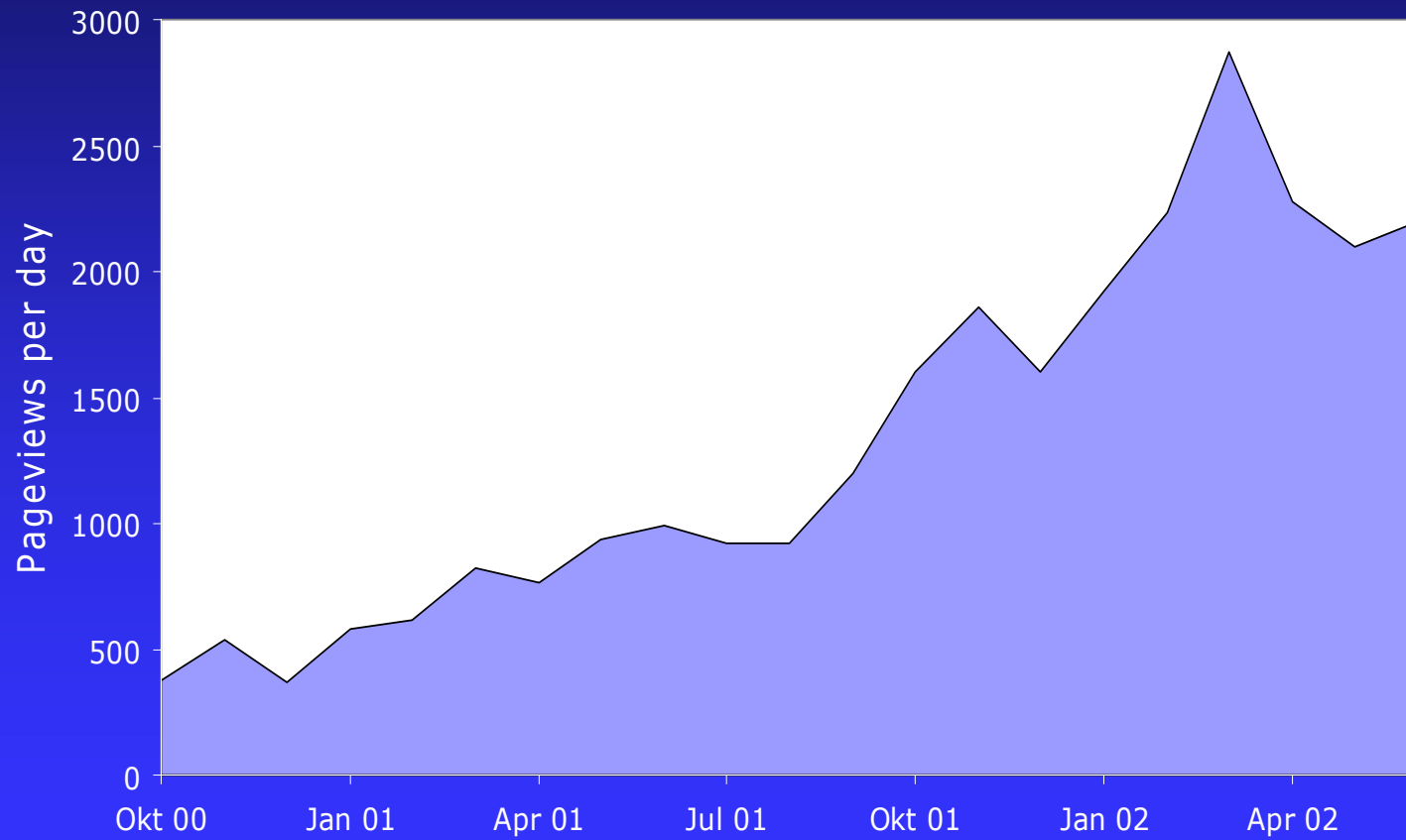
14. February 2002 [Online Payment with Credit Cards](#) for workshop fee is possible

3. January 2002 [Workshop](#) section is fully functioning. It will be updated continal. Online registration is possible.

30. November A new HPLC method in the section [additional](#)

# www.measurementuncertainty.org

www.measurementuncertainty.org



# Conclusion

- Excellent guide to fulfil the demands of 17025
- Limitations listed in scope of guide
- Method – concentration range  $\Leftrightarrow$  MU evaluation – one concentration
- Currently validation studies are rarely adequate to fulfil needs of MU evaluation
- Representativeness and Relevance of prior studies