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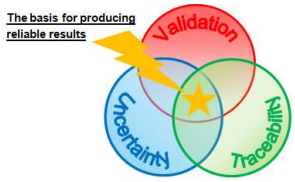


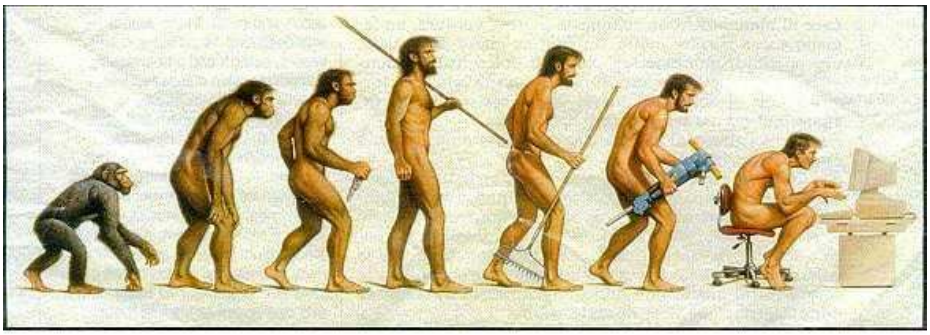

# *Validation*
# *Traceability*
# *Measurement Uncertainty*
## *Challenges for the 21st Century's analysts*

**What has happened in the area of analytical method validation since the issue of the "Fitness for Purpose" Guide in 1998?**

by/ Lorens P. Sibbesen, LAB Quality International
DENMARK



## Development!! ???



**… what have we achieved – really???**

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## - a lot of things has happened !!!

- within the areas of….

- ✓ Technological development in analytical chemistry
- ✓ Demands for analytical measurements
- ✓ Formal requirements for quality assurance (e.g. for accredited laboratories)
- ✓ Understanding of measurement uncertainty in relation to the performance of a method
- ✓ A number of various guidelines and recommendations

  \+ any correlations between the factors above
- ✓ **- but the basic requirements for delivering reliable results remain the same!!**
- ✓ Giving new challenges for the 21st century's analysts! ☺

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## Technological developments

- ✓ More advanced (and sensitive) technologies
  - Although the basic analytical principles are mostly the same - they have been more and more refined
    E.g. by new combinations of separation and detection techniques (E.g. HPLC ⇨ LC-MS-MS)

  ⇨ More specific methods, multi-methods, lower levels etc.
  How do we secure validity?
- ✓ Automation
  - Præparation often done automatically by advanced auto-samplers, robots etc.
    (E.g. automized dynamic headspace !!)

  ⇨ Smaller samples needed, "analytical machines"
  How can we validate?

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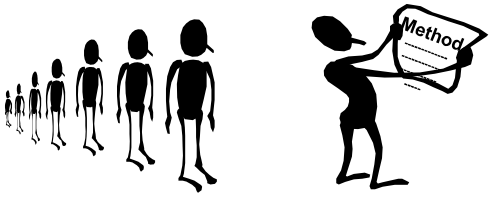
## Demands from clients/customers

- ✓ The market demands more and more
  - Specific analysis
  - For many different parameters
  - On very low levels
  - With low (acceptable!?) uncertainty
  - - and as quick and cheap as possible!!!

⇨ Are we fully knowledgable of the real requirements for our methods – and how can we secure that these require-ments are fulfilled?

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## Formal requirements

- ✓ 1998: EN 45001 – the basis for accreditation!
  - 5.4.1 *Test methods and procedures*
    The testing laboratory shall have adequate documented instructions on the use and operation of all relevant equipment, on the handling and preparation of test items (where applicable), and on standard testing techniques, where the absence of such instructions could jeopardize the efficacity of the testing process
  - The testing laboratory shall reject requests to perform tests according to test methods that may endanger an objective result or have low validity [!]
    Where it is necessary to employ test methods and proce-dures which are non-standard, these shall be fully documented

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## Formal requirements

- ✓ 2012: ISO/IEC 17025:2005
  - 5.4.5 *Validation of methods*
    Validation is the confirmation by examination and the provision of objective evidence that the particular requirements for a specific intended use are fulfilled.
    The laboratory shall validate non-standard methods, laboratory-designed/developed methods, standard methods used outside their intended scope, and amplifications and modifications of standard methods to confirm that the methods are fit for the intended use.
    The validation shall be as extensive as is necessary to meet the needs of the given application or field of application. ….
- ✓ Increasing emphasis on participation in PT schemes !

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## MU & MV !!!

- ✓ Measurement Uncertainty ⇔ Method Validation
- ✓ Major development on understanding and handling of MU since 1998!
  - Still debatable!
  - And still under development!
- ✓ Setting specific requirements for a method – or just (!) some ”general” requirements for the uncertainty on the results from that method!!
- ✓ Confusion among many laboratories
  - and certainly among their customers/clients

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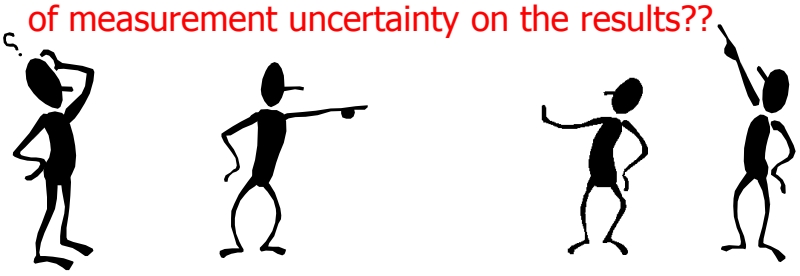
## MU & MV !!!

- ✓ To evaluate the fitness of purpose of analytical methods, overall measurement uncertainty estimation is more and more applied
- ✓ But can validity of a method be measured only in terms of measurement uncertainty on the results??



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## Various guidelines & recommendations

**Some examples!**

- ✓ 1998
  - Eurachem Guide: *The Fitness for Purpose of Analytical Methods. A Laboratory Guide to Method Validation and Related Topics*.
- ✓ 1999
  - AOAC/FAO/IAEA/IUPAC: *Guidelines for Single-Laboratory Validation of Analytical Methods for Trace-level Concentrations of Organic Chemicals*

  ⇨Specific application
- ✓ 2001
  - FDA: *Guidance for Industry: Bioanalytical Method Validation*

  ⇨Special application (Pharm.), special terminology

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## Various guidelines & recommendations

- ✓ 2002
  - IUPAC: *Harmonized guidelines for single-laboratory validation of methods of analysis*

    ⇨Single laboratory validation vs. collaborative trials!
  - EU Commission, Decision of 12 August 2002, "*Implementing Council Directive 96/23/EC concerning the performance of analytical methods and the interpretation of results*"

    ⇨Regulatory concern!!
- ✓ 2005
  - OMCL (EUROPEAN NETWORK OF OFFICIAL MEDICINES CONTROL LABORATORIES): *Validation of Analytical Procedures*

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## Various guidelines & recommendations

- ✓ 2009
  - European Commission, JRC, "*Guidelines for performance criteria and validation procedures of analytical methods in controls of food contact materials*"
  - ⇨Specifying the regulatory concern!!
- ✓ 2011
  - European Medicines Agency (EMA), "*Guideline on bio-analytical method validation*"
  - ⇨European answer to FDA!
    NOTE: Special performance characteristics
    (e.g. "Carry-over", "Dilution Integrity" & Stability !!!
- ✓ I.e. a number of various guidelines existing !!

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## So – what now!!!

- ✓ A lot of new challenges coming up re. validation of analytical methods in the 21st century!
- ✓ The issue of validating analytical methods still of major concern – in many areas, in many ways!

- ✓ **Does Eurachem have a role to play in all this???**
- ✓ - that's the challenges we are facing taking the responsibility of developing a new/revised Eurachem guide in the area of method validation
- ✓ - and where we need you help and input during this workshop!

**Thank you!**

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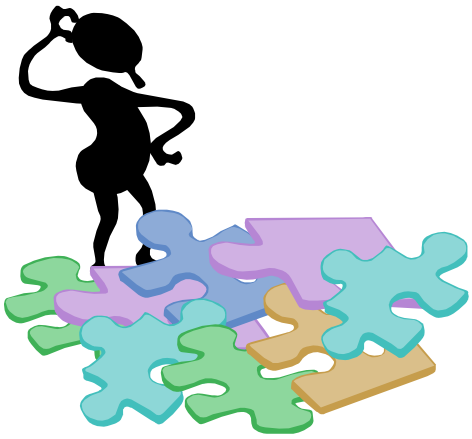
## … let's get started!



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