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Eurachem Workshop Gent 2016

International Guidance - an overview

Presentation for the Eurachem Workshop

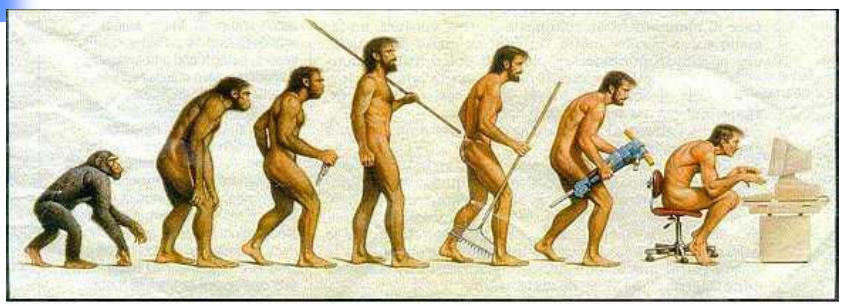
Method Validation in Analytical Science

Current Practices and Future Challenges

May 9 – 10 2016, Gent, Belgium

by/ Lorens P. Sibbesen, LAB Quality International
DENMARK

Development of Method Validation



- ✓ …from experimentally approaches to computerized models
- ✓ First ideas of formalizing method validation expressed back in the early 90'es
- ✓ But how do we actually do it – and how much?
- ✓ Good guidance is still needed

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Formal requirements in the early 90'es

- ✓ Requirement for accredited laboratories
- ✓ *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 procedures which are non-standard, these shall be fully documented

EN 45001 "General criteria for the operation of testing laboratories", CEN/CENELEC 1989

Pharmaceutical industry 1994/1996

- ✓ International Conference On Harmonisation Of Technical Requirements For Registration Of Pharmaceuticals For Human Use (ICH)
- ✓ Harmonised Tripartite Guidelines
  - Q2A: *Text on Validation of Analytical Procedures*
  - Q2B: *Validation of Analytical Procedures: Methodology*
  - Note: In 2005, combined to one guideline, Q2(R1)).
- ✓ "….a discussion of the characteristics for consideration during the validation of the analytical procedures…"
- ✓ "…provide some guidance and recommendations on how to consider the various validation characteristics for each analytical procedure."

- a lot of things has happened since !!!

- ✓ Technological development in analytical chemistry
- ✓ Demands for analytical measurements and microbiological tests increased (…in diversity and complexity)
- ✓ **Formal requirements** for quality assurance increased (e.g. for accredited laboratories)
- ✓ Understanding of measurement uncertainty in relation to the performance of a method
- ✓ **- but the basic requirements for delivering reliable results remain the same!!**
- ✓ Have led to a big number of various **guidelines and recommendations** on method validation over the years - more or less harmonised in approaches!

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Formal requirements today (Accr.)

- ✓ **ISO/IEC 17025:2005**
  General requirements for the competence of testing and calibration laboratories
  - 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. ….

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An early ISO standard on the subject!

- ✓ **ISO 5725, part 1-6** (1994; part 5 1998)
- ✓ ***Accuracy (trueness and precision) of measurement methods and results***
  - Part 1: *General principles and definitions*
  - Part 2: *Basic method for the determination of repeatability and reproducibility of a standard measurement method* ⇦ **Princ. for outlier testing!**
  - Part 3: *Intermediate measures of the precision of a standard measurement method*
  - Part 4: *Basic methods for the determination of the trueness of a standard measurement method*

(cont.)

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…standards on the subject! (cont'd)

- ✓ **ISO 5725, part 1-6**
  Accuracy (trueness and precision) of measurement methods and results
  - Part 5: *Alternative methods for the determination of the precision of a standard measurement method*
  - Part 6: *Use in practice of accuracy values*

⇨ Establishing Accuracy of measurement methods and results by collaborative/interlaboratory studies

- ✓ **ISO 21748** (2010)
  Guidance for the use of repeatability, reproducibility and trueness estimates in Measurem. Uncert. estimimation

⇨ Evaluation of MU using data optained from studies conducted in accordance with ISO 5725-2

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Various guidelines & recommendations

Some examples!
(out of a collection of > 60)

- ✓ **IUPAC Techn. Report** (1994)
  Protocol for the Design, Conduct and Interpretation of Method-Performance Studies
  ⇨ Early guideline on securing good method performance
- ✓ **IUPAC** (2002)
  Harmonized guidelines for single-laboratory validation of methods of analysis
  ⇨ Single lab. validation vs. collaborative trials!
- ✓ **DRAFT IUPAC Protocol** (under elaboration)
  Experiments for single-laboratory validation of methods of analysis: Harmonized Guidelines
  ⇨ Guidance on experimental designs for validation studies

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Examples from Pharmaceutical field (US)

- ✓ **Food and Drug Administration (FDA) / Center for Drug Evaluation and Research (CDER)** (2015)
  Analytical Procedures and Methods Validation for Drugs and Biologics . Guidance for Industry
  ⇨ Special application (Pharm.), special terminology (complements ICH Guidelines)
- ✓ **United States Pharmacopeia (USP)** (Current rev.)
  <1225> *Validation of Compendial Procedures*
  <1226> *Verification of Compendial Procedures*
  ⇨ Criteria for accept – and application – of Pharmacopeia Methods (US)

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Examples from Pharmaceutical field (EU)

- ✓ **European Medicines Agency (EMA)** (2011)
  Guideline on bio-analytical method validation

⇨ European answer to FDA!
NOTE: Special performance characteristics (e.g. "Carry-over", "Dilution Integrity" & Stability !!

- ✓ **OMCL (Europ. Network of Official Medicines Control Labs)** (2005)
  Validation of Analytical Procedures

⇨ Control of a regulated field

- ✓ **European Pharmacopoeia, 7th Ed.** (2015)
  Technical guide for the Elaboration of Monographs
  Part III: *Analytical Validation*

⇨ Criteria for accept – and application – of Pharmacopeia Methods (EU)

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Methods related to Food Safety

- ✓ **COUNCIL DIRECTIVE 96/23/EC of 29 April 1996**
  ...on measures to monitor certain substances and residues thereof in live animals and animal products..

⇨ Regulatory concern re. drug residues in meat

- ✓ **EU Commission, Decision 657 of 12 August 2002**
  Implementing Council Directive 96/23/EC concerning the performance of analytical methods and the interpretation of results

⇨ Recommend. for validation of specific methods (ANNEX)

- ✓ **Community Reference Laboratories Residues (CRLs)** (2010)
  Guidelines for the Validation of Screening Methods for Residues of Veterinary Medicines

⇨ Supplem. Com. Dec. re. valid. of screening methods

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Example of current development

- **SANCO/12495/2011**
  Method Validation and Quality Control Procedures for Pesticide Residues Analysis in Food and Feed
  ⇨ For laboratories involved in official EU control
- **SANCO/12571/2013**
  Guidance document on analytical quality control and validation procedures for pesticide residues analysis in food and feed
  ⇨ Supersedes SANCO/12495/2011
- **SANTE/11945/2015**
  Guidance document on analytical quality control and method validation procedures for pesticides residues analysis in food and feed.
  ⇨ Supersedes SANCO/12571/2013

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Various guidelines & recommendations

- **ISO/TR 13843** (2000)
  Water quality — Guidance on validation of microbiological methods
  ⇨ ISO Technical Report (entirely informative)
- **SAC-SINGLAS Guidance Note, C & B and ENV 002** (2002)
  Method validation of Microbiolobical Methods
  ⇨ Example of guideline from Accreditation Body
- **CEN Guide 13** (2008)
  Validation of environmental test methods
  ⇨ Related to EU regulation on environmental issues
- **AOAC International** (2012)
  Guidelines for Validation of Binary Qualitative Chem. Methods
  ⇨ Qualitative methods in the food/feed sector

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Various guidelines & recommendations

- **LABERCA**[1] (2005)
  Guide for the Validation of Analytical Methods for the Analysis of Residues and Contaminants in Biological Matrices and Foodstuffs by Mass Spectrometry

⇨ Example of very specific guideline

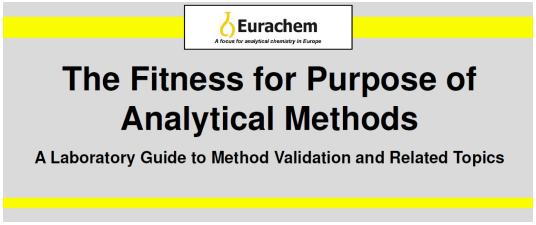
- **European Network of Forensic Science Institutes (ENFSI)** (2013)
  Guidelines for the single laboratory Validation of Instrumental and Human Based Methods in Forensic Science

⇨ Validation of forensic methods

- Etc. etc. etc.!
  - Requirements for labs. involved in various fields
  - Exchange of experience and inspiration for others!

LAB QUALITY INTERNATIONAL [1] LABoratoire d'Etude des Résidus et Contamin. dans les Aliments Eurachem Workshop Gent 2016

The Eurachem Guide



- 1st version in 1998
- Extremely popular over the years
  - 2nd most downloaded guide from the Eurachem website
- 2nd revised edition, October 2014!
- Generic approach (some references to sector-specific guidelines
- Downloadable for free from www.eurachem.org
  - Also in Farsi, Ukranian, Spanish, (..Turkish, Arabic… Czech..)

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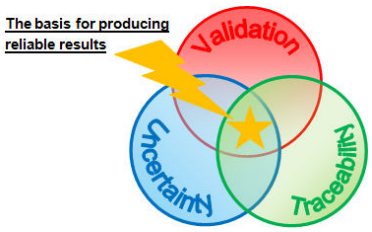
Related guidelines

- ✓ **Eurachem 2011**
  "Terminology in analytical Measurement" (TAM)
  - Introduction to the VIM " International Vocabulary of Metrology" (2008) for use in analytical chemistry
  - Important to have a common understanding of the terminology among stakeholders
- ✓ Areas related to method validation…
- ✓ …require their own specific guidelines



- ✓ See "Reading List" on www.eurachem.org.

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Eurachem MVWG is ongoing…

- ✓ Still a lot of challenges in the field
- ✓ Advanced/New techniques
  - New application of analytical principles
  - Multi-parameter methods
  - Multi-matrix methods
  - Verification of test kits/automated analysis (black box)
- ✓ Method validation/instrument qualification
- ✓ Calibration / Traceability in relation to method validation
- ✓ Setting performance requirements
  - Establishing Target Measurement Uncertainty?
- ✓ …etc. etc.

…join us ☺

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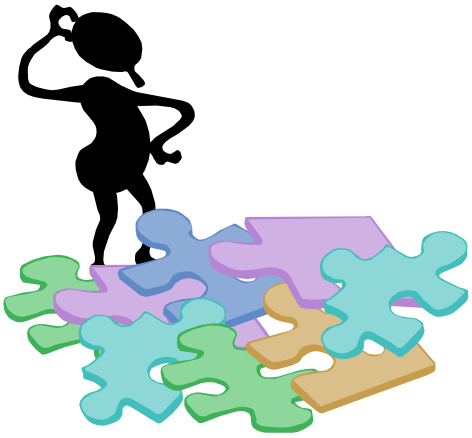
Thank you for your attention



… let's get started!

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