
The tortuous
road to global
standardization
Creat Jaffe
Creat enzymatic
Creat dry chemistry

EC4 working group: IVD effects on the clinical use of creatinine

Remit dd June 7th 2004:

- Define current/expected problems regarding standardization and interpretation of creatinine data in blood and urine
- Assess discrepancies of IVD compatible data and formula's for creatinine clearance
- Assess problems to be expected in formula's for dosage
- Define solutions for the problems

EC4 working group on creatinine

Members:

- J Delanghe, Belgium, chairman
- M Panteghini, Italy
- M Galteau, France
- T Brinkmann, Germany
- A Harmoinen, Finland
- C Cobbaert, the Netherlands

Accuracy of creatinine measurement results: LIMITATONS OF THE AVAILABLE DATA!

- HPLC “reference method” is not JCTLM endorsed
- Commutability of EQA materials has not been proven
- Consequence: MAB data are disputable; similar situation for the other countries participating in the EC4 creatinine WG

→ **decision to study accuracy of creatinine measurement results after IVD implementation / international context!**

LESSON I

- The degree of commutability of the EQA-material highly affects method mean & frequency distribution width.
- Solely the use of commutable, liquid frozen controls enables EQAS organizers to get rid of peer group means and unmeaningful consensus means.

LESSON II

The right “tools” are needed to judge lab harmonization and reduction of interlaboratory variability correctly.

“ It’s time to care about the quality of the sample”

L. Thienpont et al.

LESSON III

- ***Value assignment*** of the commutable EQA enables its use as ***a trueness control***.
- Calibration 2000 brought along in 2003/2004
  - a significant reduction of the MAB to ≤ 5% for enzymes AND
  - a significant increase in the % of labs meeting the desirable bias criteria from 40% to > 75% for enzymes.

Creatinine International Trueness Verification Study

I. Aim
II. Participants
III. Study design
    A. Characteristics of the material
    B. Value assignment
    C. Trueness Verification Project
    D. Time schedule

I. Aim

- To verify trueness of creatinine measurements after implementation of the IVD 98/79/EC *across different instruments and methods from the major manufacturers*
- How well was the IVD conformity job done?

II. Participating laboratories

- Selected laboratories from Belgium, France, Italy,The Netherlands, Germany, Finland
  - Major manufacturers: Roche, Beckman, Dade Behring, OCD, Olympus, Abbott, Bayer
  - Methods: Jaffe, enzymatic, dry chemistry
  - Three labs per method group and/or per manufacturer and per country → > 3 (x 3) x 5 x 6 = > 90 labs
- Promoted by the EC4 WG members; organization through the national EQA coordinators
- International coordinator: J. Delanghe

III. Trueness Verification Project

A. Characteristics of the material developed for trueness verification:

- NCCLS C37A based (lab Weykamp, Winterswijk)
  - liquid frozen
  - commutable
- At three levels: 75; 150 and 300 μmol/L
- 0.5 mL vials
- Spiked with NIST 914a crystalline material

III. Trueness Verification Project

B. Value assignment

- By JCTLM-endorsed IDMS RM/RL
- Duplicate analyses in three independent runs
- Expanded uncertainty of ≈ 2%

- Also with “HPLC reference method” which was the accuracy base in the Netherlands for > 10 years

III. Trueness Verification Project

C. Project protocol

- Trueness verification material: transported and stored at - 80 °C; analyze within 4 weeks
- Instrument calibration and settings: exactly acc. to the manufacturer's instructions
- Analyse each level in 5-fold in one run.
- Complete result form and add the instrument settings used ---> send the completed form to the national and international coordinators

III. Trueness Verification Project

D. Time schedule

2004	2005		2006
Kick off meeting	Q1/2	Q3/Q4	Q1/Q2

Problem ident.→ Project proposal --> Trueness verification study

Nov., A'dam | May, Glasgow | In 6 countries / > 90 labs

Q3 2005

1. Preparation trueness verification material: July 2005 / ready
2. Value assignment
3. Sending to national coordinators: Sept 2005

Q4 2005 → Q2 2006

1. Analysis and reporting: Oct – Nov 2005
2. Central Data-entry and data verification
3. Statistical analysis
4. Results and concept publication

Conclusions

- IVD directive requires traceability
- JCTLM defines reference systems
- EC4 creat WG
  - Commutable materials: essential for bias assessment
  - Development of trueness controls - NCCLS C37A based to assess IVD conformity within the context of EC4 creatinine WG
  - Trueness Verification Study / international