
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