The CCQM, What It Does, What It Has Achieved and Why It is Important to You

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CCQM President Emeritus
Immediate Past Secretary CIPM
Honorary Member of the CIPM

Symposium on Chemistry and the International System of Weights and Measures
Symposium at ACS National Meeting, Boston, MA, August 19, 2015
Contents

- Global need for comparable measurement results through traceability
- Metrological traceability and the Traceability Chain
- The role and deliverables of the NMIs and DIs
- The global metrological infrastructure and the CCQM
- What are the problems and what goes wrong
- How do the NMIs/DIs and the CCQM work
- CIPM Mutual Recognition Arrangement – CIPM MRA, Quality Chain
- Joint Committee on Traceability in Laboratory Medicine – JCTLM
Need for globally comparable and accepted measurement results for sustainable competitiveness, innovation, better quality of life

  - 80% affected by standards/norms and regulation
  - compliance costs ~10% of production costs

• Industrial, energy, food (>1,2 trillion USD), pharmaceuticals (>461 billion USD), cosmetics, and all other products from everywhere

• Global spread of diseases and global environmental and climate issues

• Global security, forensics and anti doping

• “soft/perceptive” metrology (smell, taste, blends, color, glance, form, etc.) physiological measurements

• Requires comparable, traceable measurements
Demanding Metrological Traceability

- Legislators, Regulators (fair trade, carbon trading, food, health, pollution, police)
- Joint Committee on Traceability in Laboratory Medicine - JCTLM (BIPM, IFCC, ILAC, WHO, in-vitro diagnostics industry)
- Codex Alimentarius Commission, HACCP, micro-biology
- Animal health, plant protection, bio-diversity
- WMO Global Atmospheric Watch, climate change
- Pharmacopeia (USP, EDQM, JP, pharmaceutical industry)
- Sports and World Anti Doping Agency – WADA
- Forensics authorities and security authorities
- VAMAS, materials metrology
- And many others, such as of course industry, traders, laboratories

Addressing metrological traceability and measurement uncertainty

CIPM and BIPM cooperate with all organizations through workshops and in the CIPM Consultative Committees, such as the CCQM with all its Working Groups
“Once measured, everywhere accepted” requires Comparability through **Traceability**

**Metrological traceability**

Property of a **measurement result** whereby the result can be related to a reference **through an unbroken chain** of calibrations, each contributing to the **measurement uncertainty**

JCGM 200:2008 (VIM 3)

Traceability to the SI, or if not (yet) possible to another internationally agreed reference (e.g. hardness, pH, WHO International Units)
Traceability chain
(by courtesy of ISO (ISO 17511) and BIPM)

Every step increases measurement uncertainty

NMIs/DIs
(by law)

Manufacturer and other accredited calibration and CRM producer laboratories

Routine Test & Meas. Laboratories
(accredited and non-accredited)
Traceability to the SI (bio-)chemical measurements

Traceability to the mole or other SI units

- Amount of substance: mol
- Amount fraction: mol/mol
- Amount concentration: mol/m³
- Mass concentration: kg/m³
- Amount content: mol/kg
- Mass fraction: kg/kg
- Surface analysis: nm

(or expressed in multiples or sub-multiples)

In cases of traceability to e.g. WHO International Standards (CRMs) and Units; no traceability to the SI, and no long term stable references
The National Metrological Infrastructure
National measurement standards are a public good; so government responsibility and resources

Dissemination of traceability to the SI

NMIs

Accredited Calibration labs & CRM prod.

Testing and industrial/field laboratories (accredited and non-accredited)

Products and services (certified and non-certified)

Traceability to the SI
Services to be delivered by National Metrology Institutes and other Designated Institutes

- **Calibration** of (transfer) measurement standards and capability to assign values to physical, bio and chemical reference samples
- **Certified Reference Materials** (production, certification)
- **Reference value assignment of Proficiency Testing** samples (own PT schemes and/or third party PT schemes)
- **Validation of measurement methods/procedures**
- Delivering traceability to industry and ILAC Arrangement accredited calibration and testing laboratories, CRM producers and PT providers
- Delivering traceability to sector specific reference laboratories (clinical and food reference laboratories, WMO reference laboratories, a.o.)
Metre Convention
1875

General Conference on Weights and Measures
( CGPM )
meets every four years and consists of delegates from Member States

International Committee for Weights and Measures
( CIPM )
consists of eighteen individuals elected by the CGPM
It is charged with supervision of the BIPM and affairs of the Metre Convention
The CIPM meets annually at the BIPM

Consultative Committees
( CCs )
Ten CCs each chaired by a member of CIPM; to advise the CIPM; act on technical matters and take important role in CIPM MRA; comprise representatives of NMIs and other experts.

Bureau International des Poids et Mesures
( BIPM )
International centre for metrology
Laboratories and offices at Sèvres with an international staff of about seventy

Associate States and Economies of the CGPM

Diplomatic Treaty
Governments of Member States
International organizations
National metrology institutes ( NMIs )
CCQM – the Beginning

- A Working Group on Metrology in Chemistry was established by the CIPM at its 80th meeting in September 1991
  - Study I, metals in solution (coordinated by NIST)
    - lead (and cadmium) in natural water
      - 1st study 1992-1994 not satisfactory
      - 2nd study 1995-1998 acceptable results
  - Study II, measurement of gases (coordinated by VSL)
    - Carbon dioxide in nitrogen

- In 1993 CIPM decided to endorse the Working Group’s recommendation that a permanent Consultative Committee for Amount of Substance be formed
How to establish global comparability through traceability?

The 1st meeting of the CCQM in 1995

Still many scientists outside the CCQM doubting whether it will ever be possible to establish traceability in chemistry
CCQM – Metrology in Chemistry and Biology

President: W. May  (Past President: R. Kaarls, 1993-2013)
Executive Secretary: R. Wielgosz (BIPM)

~ 45 Member and Observer Organizations
~ 250 experts active in the CCQM WGs

Some WGs meeting twice per year

CCQM Working Groups

- Chairpersons/Strategic Planning  
  NIST  W. May
- Key Comparisons and CMC Quality  
  GLHK  W.M.(Della) Sin
- Organic Analysis  
  NMIA  L. Mackay
- Inorganic Analysis  
  LGC  M. Sargent
- Gas Analysis  
  KRISS  J.S. Kim
- Electro-chemical Analysis  
  SMU  M. Mariassy
- Surface Analysis  
  BAM  W. Unger
CCQM – Metrology in Chemistry and Biology

CCQM Working Groups (continued)

- Nucleic Acids
  - LGC
  - H. Parkes
- Proteins
  - KRISS
  - S-R. Park
- Cells
  - NIST
  - A. Plant

CCQM ad hoc Steering Group

- Microbiology
  - NIST
  - J. Morrow
- Identity WG
  - NIST/IRMM
  - J. Morrow/H. Schimmel
- Quantity WG
  - NMIA/NIM
  - D. Clarke/Wang Jing

CCQM ad hoc Working Group

- Redefinition SI
  - PTB
  - B. Güttler
- CIPM MRA and CMC database review
  - CIPM/CCQM
  - R. Kaarls
CCQM Metrology in (Bio-)Chemistry

- **High purity Chemicals** (inorganic and organic compounds, **metals**, isotopes, other)
- **Inorganic solutions** (elemental, anionic, other)
- **Organic solutions** (PAHs, PCBs, pesticides, other)
- **Gases** (high purity, environmental, fuel, forensic, medical, other)
- **Water** (fresh water, contaminated water, sea water, other)
- **pH**
- **Electrolytic conductivity**
- **Metals and Metal alloys** (ferrous metals, non-ferrous metals, precious metals, other)
- **Advanced materials** (semiconductors, superconductors, polymers and plastics, ceramics, other)
CCQM Metrology in (Bio-)Chemistry

- Biological fluids and materials (blood serum, renal fluids, hair, tissues, bone, botanical materials, other)
- Food (nutritional constituents, contaminants, GMOs, other)
- Fuels (coal and coke, petroleum products, bio-mass, other)
- Sediments, Soils, Ores and Particulates (sediments, soils, ores, particulates, other)
- Other Materials (cements, paints, textiles, glasses, thin films, coatings, insulating materials, rubber, adhesives, other)
- Surfaces, films and engineered nanomaterials (inorganic, organic, biomaterials, other)
- Micro-biological pathogens (bacteria, viruses, fungi, yeast, mould)
Priority areas in the USA (NIST)

• Energy (biofuels, hydrogen fuel, solar, wind) green, renewable
• Environment and climate change (WMO GAW) long term future
• Healthcare better healthcare, cost reduction
  • Diagnostics (EU IVD directive driven)
  • Therapeutic (WHO)
  • Pharmaceuticals (USP, a.o.)
• Food safety and nutritional value (FDA, EU, etc.) better food quality, more healthy people, reducing the economic costs of food borne illnesses and waste of food
• Homeland security/forensics safer society
Priority areas in the EU (EURAMET)

European Metrology Research Programme (FP 7 and art.185) and EMPIR on Innovation and Research (EU Horizon 2020)

• **Health care** (Virtual human modelling system, Reference measurements and materials (JCTLM), Diagnostic and Therapeutic instrumentation (imaging, microscopy, NMR, ultrasound) better health care, innovative products

• **Energy** (New and renewable energy resources, Smart energy networks) green and renewable energy

• **Environment and climate change** (Detecting change and monitoring climate, Carbon dioxide sequestration) a cleaner and long term future

• **Fundamental metrology** (SI, Nanotechnology, Security related metrology) fundamental measurement standards, and safe nanotechnology and a safer society
CCQM stakeholder and expert cooperation

- BIPM (scientific and industrial metrology), OIML (legal metrology)
- MoU with WHO, WMO, IAEA, ILAC, JCTLM (IFCC and ILAC)
- Regulators, Industrial Societies, Sector Specific Reference Laboratories, EQAS, PT providers, a.o.
- Addressing the “Grand Challenges” in society and economy (EU, APEC, USA, Japan, a.o. with focus areas on food safety, health care, environmental control/climate change, energy, advanced and nano materials, and security/forensics)
Parameters for Bioethanol to be included in MRC

As presented in the White Paper

Equally for Bio Diesel – FAME, many organic components

- Density
- Sulfate content
- Sulfur content
- Copper content
- Iron content
- Sodium content
- Ethanol content
- Acidity
- Phosphorus content
- pH
- Chloride content
- Water content
Ocean salinity

- Salinity is one of the most important input quantity of climate models and of Tsunami warning systems.

- Standards are maintained and disseminated on behalf of International Association for the Physical Sciences of the Oceans (IAPSO) by OSIL.
Forensics

- Crime Scene Investigations
- Standards for Drunk Driving Testing
- Drugs of Abuse in Urine and Hair
- Sports Medicine
- DNA-based Human Identification
- Explosives Detection
- Estimating Drug use within the Population

Very good results of a comparison of 4 NMIs/DIs, which deliver traceability, carried out in cooperation with the WADA
Surface and Micro/NanoAnalysis (SNMA) at the Interface

SMNA resides in a number of NMIs in one or more different Divisions, depending on local histories – so the light may shine in different directions in the NMIs.
Why need of reliable micro-biological measurements?

- Already for many years requested by a number of NMIs
- 2013 world export volume of food products > 1200 billion USD
- Estimated that 20% to 30% of total world food production is lost due to microbial spoilage
- USA CDC statistics on food-borne illnesses indicate:
  - 48 million illnesses per year due to food-borne pathogens, of which
  - 128 000 hospitalizations and 3000 deaths
  - It means every year 1 in 6 Americans are affected
- Food poisoning in the EU (EFSA 2009 figures)

<table>
<thead>
<tr>
<th></th>
<th>EU 2009</th>
<th>USA 2011 estimated</th>
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<tbody>
<tr>
<td>Salmonella</td>
<td>108 614</td>
<td>1 027 561</td>
</tr>
<tr>
<td>Campylobacter</td>
<td>198 252</td>
<td>845 024</td>
</tr>
<tr>
<td>Listeria</td>
<td>1 645</td>
<td>255 death</td>
</tr>
<tr>
<td>VTEC E.coli</td>
<td>3 573</td>
<td>2 100 hospitalized</td>
</tr>
</tbody>
</table>

(sources CDC statistics and Campden BRI)
CCQM-P39 and IMEP-20: Pb in tuna fish

Graph showing the deviation from the median in % for different methods: GF-AAS, ICP-IDMS, and ICP-MS. The graph includes data from various laboratories: IAEA_AAS, BNM-LNE, LGC, IRMM, NMIJ, and ENEA. The results are presented in mg/kg and show deviations from the certified value in %.
Reference Value or Consensus Value

- A good example of the outcome.
- Apparent bias was found in recent APLAC Accreditation PT program.
- ‘PAH in Sediment’
- Corrective actions needed
- Demonstrates the advantage of an assigned reference value instead of a consensus value
Changes in ratings of laboratories PT performance if use reference value instead of consensus value

<table>
<thead>
<tr>
<th>Effect on Rating</th>
<th>Number of Labs.</th>
<th>Percent</th>
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</thead>
<tbody>
<tr>
<td>'Acceptable' &gt;&gt;</td>
<td>17</td>
<td>37</td>
</tr>
<tr>
<td>'Unacceptable'</td>
<td></td>
<td></td>
</tr>
<tr>
<td>'Unacceptable' &gt;&gt;</td>
<td>9</td>
<td>20</td>
</tr>
<tr>
<td>'Acceptable'</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No change to rating</td>
<td>20</td>
<td>43</td>
</tr>
</tbody>
</table>
Current major measurement problems in (bio-)chemistry

- Impossibility to address all possible analyte-matrix combinations
- Lack of pure, primary calibrators/reference materials
  Quantification and Identification!
- Measurand not understood (insufficient knowledge of what the measurand, intended to be measured, should be, and not sure what is really measured)
- Measurand is method/procedure defined (need global harmonization of procedure)
- “reference” methods/procedures are not metrologically sound
- Insufficient global harmonization of measurement methods (e.g. moisture in grains and cereals; in cooperation with OIML, ISO, Codex Alimentarius, legislators)
- Measurement uncertainty
- No calibration chain/hierarchy
- Lack of CRMs
- Commutability problems
CIPM, CCQM, BIPM, RMOs and bilateral comparisons in the scope of the CIPM MRA

Some 1200 Key- and Supplementary-Comparisons carried out and planned

Scheme for Key Comparisons

- BIPM
- NMI participating in CIPM key comparisons.
- NMI participating in CIPM key comparisons and in RMO key comparisons.
- NMI participating in RMO key comparisons.
- NMI participating in ongoing BIPM key comparisons.
- NMI participating in a bilateral key comparison.
- International organization signatory to MRA.
WGs Conducting Key Comparisons that Interrogate Measurement Competencies that Cover a Broad Range of Application Areas … including the following examples:

**Health**
- clinical diagnostic markers
- electrolytes \((Na, K, Ca)\), Pb in blood
- anabolic steroids in urine

**Food**
- Pesticides, antibiotics hormones
- vitamins and minerals
- drinking water
- ethanol in “Adult Beverages”

**Environment**
- air, soil, sediments
- biological tissues
- waste water

**Advanced Materials**
- semiconductors, alloys, polymers

**General Studies**
- pH and electrolytic conductivity
- purity assessment
- calibration solutions mixtures

**Forensics**
- drugs, breathalyzer \((ethanol-in-air)\)
- explosive residues
- DNA profiling

**Commodities**
- emissions trading, sulfur in fossil fuels
- natural gas
- cement

**Biotechnology**
- DNA quantification
- protein quantitation
- GMO
Amount of Substance fraction of CO$_2$ in Stack gas

Degrees of equivalence, offset $D_i$ and expanded uncertainty ($k=2$)
$U_i$ expressed in mmol/mol
CCQM-K18 and K18.1 - pH of carbonate buffer (~10), temperature 25 °C
Degrees of equivalence: $D_j$ and expanded uncertainty $U_j (k = 2)$

$D_{\text{exp}} = 0.0663$
$U_{\text{exp}} = 0.0105$

Red diamonds: participants in CCQM-K18
Green triangles: participants in CCQM-K18.1
Open symbols represent values for laboratories in Associate States and Economies of the CGPM

The BIPM key comparison database, September 2008
Ca in Herba Ecliptae
CCQM-K67
Composition of a Fe-Ni alloy film: atomic fraction of Fe
Degrees of equivalence, $D_i$, and expanded uncertainty $U_i$ ($k = 2$)

$x_R = 50.02$ atomic %
$U_R = 2u_R = 1.23$ atomic %
CIPM Mutual Recognition Arrangement – CIPM MRA

- Covering all physical, chemical and biological measurement areas
- In total > 24 000 CMCs published (March 2015), based on on-site peer reviewed capabilities and competences \((\text{ISO/IEC 17025 and ISO Guide 34})\)
- \(\sim 5800\) (bio-)chemical Calibration and Measurement Capabilities
- From \(\sim 249\) NMIs/DIs in 93 countries/economies, and IAEA, EU JRC (IRMM and ISPRA), WMO (3 reference labs) and ESA-ESTEC.
- Chemical and biological comparisons
  - 187 CCQM Key Comparisons
  - 178 CCQM Pilot Study comparisons
  - 25 additional comparisons, including Microbial Identity and Cell Counting
  - 47 RMO Key- and Supplementary Comparisons
BIPM and the Mutual Recognition Arrangement

Key Comparisons

Calibration and Measurement Capabilities

<table>
<thead>
<tr>
<th>Matrix or material</th>
<th>Analyte or component</th>
<th>Dissemination range of measurement capability</th>
<th>Range of certified values in reference materials</th>
</tr>
</thead>
<tbody>
<tr>
<td>nitrogen</td>
<td>nitrogen monoxide</td>
<td>Amount-of-substance fraction in mmol/mol</td>
<td>Amount-of-substance fraction in mmol/mol</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Relative expanded uncertainty in %</td>
<td>Relative expanded uncertainty in %</td>
</tr>
<tr>
<td>1 to 10</td>
<td>0.2 to 0.1</td>
<td>1 to 10</td>
<td>0.2 to 0.1</td>
</tr>
</tbody>
</table>

Mechanism(s) for measurement service delivery: PRGM, SGS and calibration

Uncertainty convention 2

Internal NMI service identifier: NPL/15
Mechanisms for measurement service delivery: CRMs

### Biological fluids and materials, Blood serum
United States, NIST (National Institute of Standards and Technology)
Complete CMCs in Amount of Substance for Biological fluids and materials for United States (.pdf file)

<table>
<thead>
<tr>
<th>Matrix or material</th>
<th>Analyte or component</th>
<th>Dissemination range of measurement capability</th>
<th>Range of certified values in reference materials</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Amount-of-substance concentration in mmol/l</td>
<td>Amount-of-substance concentration in mmol/l</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Relative expanded uncertainty in %</td>
<td>Relative expanded uncertainty in %</td>
</tr>
<tr>
<td>human serum</td>
<td>cholesterol</td>
<td>3 to 10</td>
<td>3.453 to 8.61</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.2 to 1.5</td>
<td>0.20 to 1.3</td>
</tr>
</tbody>
</table>

**Mechanism(s) for measurement service delivery:** SRM 1589a, SRM 1951a, SRM 1952a, SRM 909b, SRM 968c

Uncertainty convention 1. The expanded uncertainty for certified values in reference materials is given at a 95% level of confidence, but the coverage factor is not explicitly equal to 2.

**Internal NMI service identifier:** NIST/8392169

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### High purity chemicals, Organic compounds
United States, NIST (National Institute of Standards and Technology)
Complete CMCs in Amount of Substance for High purity chemicals for United States (.pdf file)

<table>
<thead>
<tr>
<th>Matrix or material</th>
<th>Analyte or component</th>
<th>Dissemination range of measurement capability</th>
<th>Range of certified values in reference materials</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Mass fraction in %</td>
<td>Relative expanded uncertainty in %</td>
</tr>
<tr>
<td>high purity cholesterol</td>
<td>cholesterol</td>
<td>95 to 100</td>
<td>0.2 to 0.1</td>
</tr>
</tbody>
</table>

**Mechanism(s) for measurement service delivery:** SRM 911c

Approved on 24 June 2008.

Uncertainty convention 2

**Internal NMI service identifier:** NIST/8392005
A sound **measurement system** is fundamental in fields of science, production of goods and services, health, commerce, communications,…It creates the **framework** in which suppliers of products and services can demonstrate **compliance with specifications** within an internationally standardized system.

**Quality Chain, the importance of reliable measurements**

MSTQ is essential for strengthening export and quality of life.
Joint Committee on Traceability in Laboratory Medicine - JCTLM

Principal promotors
- CIPM/BIPM
- IFCC
- ILAC

Supported by
- WHO
- Regulators (FDA, EC, Japan)
- CRM producers (NIST, IRMM, a.o.)
- Reference laboratories (CDC, DGKS, etc.)
- PT and QA organisations (CAP, EQA, etc)
- Written Standards (NCCLS, JCCLS, ISO)
- IVD industry (ADVAMED, EDMA, JARC)

JCTLM triggered by EC IVD Directive
- Implementation of
  - EC-IVD Directive (98/79/EC)
  - prEN ISO 17511
- EC-IVD Directive Annex 1
  - Essential requirements A 3

'...The traceability of values assigned to calibrators and/or control materials must be assured through available reference measurement procedures and/or available reference materials of a higher order.'
### JCTLM WG 1 Measurand/Analyte-Based Review Teams

Co-chaired: K. Phinney (NIST) an H. Schimmel (IRMM)

<table>
<thead>
<tr>
<th>Measurand/Analyte</th>
<th>Leader</th>
<th>Affiliation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood cell counting</td>
<td>Lili Wang</td>
<td>NIST, United States</td>
</tr>
<tr>
<td>Blood Groupings</td>
<td>Susan Thorpe</td>
<td>NIBSC, United Kingdom</td>
</tr>
<tr>
<td>Coagulation Factors</td>
<td>Elaine Gray</td>
<td>NIBSC, United Kingdom</td>
</tr>
<tr>
<td>Drugs</td>
<td>Andre Henrion</td>
<td>PTB, Germany</td>
</tr>
<tr>
<td>Electrolytes/Blood Gases</td>
<td>Brigitte Toussaint</td>
<td>IRMM, European Union</td>
</tr>
<tr>
<td>Enzymes</td>
<td>Mauro Panteghini</td>
<td>University of Milan, Italy</td>
</tr>
<tr>
<td>Metabolites/Substrates</td>
<td>Xu Bei</td>
<td>NIM, China</td>
</tr>
<tr>
<td>Microbial Serology</td>
<td>Claude Giroud</td>
<td>Bio-Rad,</td>
</tr>
<tr>
<td>Non-electrolyte Metals</td>
<td>Lee Yu</td>
<td>NIST, United States</td>
</tr>
<tr>
<td>Non-Peptide Hormones</td>
<td>Heinz Schimmel</td>
<td>IRMM, European Union</td>
</tr>
<tr>
<td>Nucleic Acids</td>
<td>Helen Parkes</td>
<td>LGC, United Kingdom</td>
</tr>
<tr>
<td>Proteins</td>
<td>David Bunk</td>
<td>NIST, United States</td>
</tr>
<tr>
<td>Vitamins</td>
<td>Donald Wiebe</td>
<td>Univ. of Wisconsin, United States</td>
</tr>
</tbody>
</table>

**Quality System**

<table>
<thead>
<tr>
<th>Leader</th>
<th>Affiliation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Robert Wielgosz</td>
<td>BIPM</td>
</tr>
</tbody>
</table>

*Review Teams established with worldwide representation from Laboratory Accreditation Organizations, National Metrology Institutes, Professional Societies, and IVD Industry in order to facilitate a fair and transparent review process.*
Glucose in Blood, Serum, Urine, CSF
SI-Unit: mmol/l

**Section 1** – External to manufacturer, credentialing of the Certified Reference Material

- **Primary calibrator**
  - SRM917b
  - Weighed amount

- **Secondary calibrator**
  - Human Patient Specimens, e.g. Blood, Serum, Urine, CSF

- **Manufacturer's working calibrator**
  - Manufacturer's Master Calibrator, Master Lot of Product Calibrator

- **Product Calibrator**
  - New Lot Commercial Product Calibrator

**JCTLM ACTIVITIES**
ISO15193, ISO15194, ISO15195

- **SRM917b**
  - NIST certification of SRM917b (purity)
  - Weighing procedure
  - Higher Order Reference Procedure – e.g. Isotope Dilution - Mass Spectrometry or Procedure of Similar Trueness and Precision
  - Reference Procedure traceable to higher order reference procedure - e.g. Hexokinase/glucose-6-phosphate Dehydrogenase Procedure

- **Routine Sample – Human Patient Specimens, e.g. Blood, Serum, Urine or CSF**
  - Commercially available system including product reagent and calibrator lots

**Combined standard uncertainty (%)**

- 0.1%
- 0.87%
- 1.21%
- 1.49%

**ISO 15189**
Comparison of Capabilities and Certified Reference Materials for Creatinine in Human Serum

Documented degree of equivalence of measurement capabilities

Comparison of value-assigned CRMs for Creatinine in Serum
Comparability of Cholesterol in Serum
CRMs on JCTLM LIST

The measured/certified ratios for this set of CRMs are:
- ~ normally distributed
- with a standard deviation of ~0.7%
JCTLM Database of Reference Materials for IVD measurements

www.bipm.org
<table>
<thead>
<tr>
<th>Analyte</th>
<th>Matrix</th>
<th>Material Name and/or ID #</th>
<th>Estimated Availability (months, as of Jan 2004)</th>
<th>Contact Information</th>
<th>Reference Materials</th>
</tr>
</thead>
<tbody>
<tr>
<td>cholesterol</td>
<td>cholesterol</td>
<td>GBW09203b</td>
<td>60</td>
<td>NRCCRM, China</td>
<td>Primary calibrator for higher order reference methods</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Tel: 086-10-64221811</td>
<td>Email: <a href="mailto:crmservice@nrccrm.com.cn">crmservice@nrccrm.com.cn</a></td>
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<td>Fax: 086-10-64213149</td>
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<td>DGKC definitive Method for Serum Cholesterol</td>
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<td>ID/GC/MS</td>
<td>Siekmann et al., Z. anal. Chem. 279, 145-146 (1976)</td>
<td>PTB - National Key Comparison for Accreditation</td>
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</table>

**UGent, Belgium**

Phone: +32 (0)9 264 81 04  
Fax: +32 (0)9 264 81 98  

**Contact person:** Prof. Dr. L. Thienpont  
**Email:** linda.thienpont@Ugent.be

| Analyte | glucose |
| Material or matrix | blood serum, blood plasma |
| Quantity | Amount-of-substance concentration |
| Service measurement range | 1 mmol/L to 25 mmol/L |
| Expanded uncertainty (level of confidence 95%) | 1.5% |

The expanded uncertainty is calculated for measurement protocol n = 8

**Interlaboratory comparison results**  

**Measurement principle**  
Isotope dilution gas chromatography mass spectrometry (ID/GC/MS)

**JCTLM reference measurement method/procedure**  
University of Ghent reference method for glucose
CCQM charged with establishing the system for global comparability of bio and chemical measurement results through traceability to the SI, or if not (yet) possible, to other internationally agreed references, by that being the basis for international recognition and acceptance of your bio and chemical measurement and test results, taking away Technical Barriers to Trade and contributing to a sustainable economy and competitiveness, innovation and a better environment and quality of life.

Thank you!

Questions?