Consultative Committee for Amount of Substance: Metrology in Chemistry and Biology (CCQM)

Dr Willie E. May

25th meeting of the CGPM
Paris, April 2014

President: Willie E. May, CIPM, NIST
Executive Secretary: Robert Wielgosz, BIPM
Immediate Past President: Robert Kaarls
The CCQM is responsible for developing, improving and documenting the equivalence of national reference systems for chemical and biological measurements.

It advises the CIPM on matters related to chemical and biological measurements including advice on the BIPM scientific program activities.

CCQM’s specific responsibilities are:

a. to establish global comparability of measurements through promoting traceability to the SI, and where traceability to the SI is not yet feasible, to other internationally agreed references;

b. to contribute to the establishment of a globally recognized system of national measurement standards, methods and facilities for chemical and biological measurements;

c. to contribute to the implementation and maintenance of the CIPM MRA with respect to chemical and biological measurements;

d. to review and advise the CIPM on the uncertainties of the BIPM's calibration and measurements services as published on the BIPM website;

e. to act as a forum for the exchange of information about the research and measurement service delivery programs and other technical activities of the CC members and observers, thereby creating new opportunities for collaboration.
Consultative Committee for Metrology in Chemistry and Biology (CCQM)

- Established by the CIPM in 1993
- 40 Official member (28) and observer (12) organizations
- 8 Standing Working Groups and 3 ad hoc Working Groups
  - 6 Standing Technical Working Groups that meet twice a year
    - Attended by ~ 200+ experts from NMI’s and other expert institutes
- Yearly meetings of CCQM plenary, attended by ~70 representatives from Member and Observer Institutes, stakeholder organizations and Guests

Working Groups are responsible for:

- Over 5700 CMCs are currently published in the KCDB in Chem/Bio service area
  - Sep 2011 to Jul 2014: 877 CMCs added to KCDB
  - 830 different analytes (3050 different analyte-matrix combinations)
    - Number of analyte matrix combinations increasing at a rate of about 250 per year.
- 365 comparisons (187 Key and 178 Pilot) have been conducted
  - Sep 2011 to Jul 2014: Results of 29 KCs and 6 stand-alone PS published
- 25 additional comparisons are currently underway Including the first 2 comparisons on Microbial Identity and Cell Counting
Current CCQM Organization

- **President:** W. E. May, CIPM, NIST
- **Executive Secretary:** R. Wielgosz, BIPM

### 8 permanent working groups, chairs, and deputy chairs
- **Bioanalysis (BAWG)**
  - Chair: H. Parkes, LGC
  - Deputy Chair: S-R Park, KRISS
  - Members: S-R Park, KRISS

- **Electrochemical Analysis (EAWG)**
  - Chair: M. Mariassy, SMU
  - Deputy Chair: S. Seitz, PTB
  - Members: S. Seitz, PTB

- **Gas Analysis (GAWG)**
  - Chair: J.S. Kim, KRISS
  - Deputy Chair: P. Brewer, NPL
  - Members: P. Brewer, NPL

- **Inorganic Analysis (IAWG)**
  - Chair: M. Sargent, LGC
  - Deputy Chair: P. Fisicaro, LNE
  - Members: P. Fisicaro, LNE

- **Organic Analysis (OAWG)**
  - Chair: L. Mackay, NMIA
  - Deputy Chair: A. Windust, NRCC
  - Members: A. Windust, NRCC

- **Surface Analysis (SAWG)**
  - Chair: W. Unger, BAM
  - Deputy Chair: T. Fujimoto, NMIJ
  - Members: T. Fujimoto, NMIJ

- **Key Comparison & CMC Quality (KCWG)**
  - Chair: W.M. (Della) Sin, GLHK
  - Deputy Chair: A. Botha, NMISA
  - Members: A. Botha, NMISA

- **Strategic Planning (SPWG)**
  - Chair: W. E. May, NIST

### 3 current ad hoc groups:
- **ad hoc working group on the mole**
  - Chair: B. Guettler, PTB

- **ad hoc steering group on microbial measurements (MBSG)**
  - Chair: J. Morrow, NIST

- **ad hoc working group on CMC generation, formatting, and presentation**
A Context for the Importance and Complexity of Chemical Measurements

- According to a study released by the Council for Chemical Research, chemistry is core or important to virtually all industrial sectors and technology areas: “Measuring Up: Chemical R&D Counts for Everyone”, CCR, 2006

- For metrology in chemistry the task is to determine the quantity of a specific chemical entity in a given matrix and not merely "amount of substance" (i.e., requires confirmation of identity as well as amount)

- Chemical measurements are multidimensional
  - a large number of chemical entities (>10^5)
  - in a broad range of matrices (10^7)
  - and mass fractions ranging from <10^{-12} to 1
Regulated Classes of Chemicals in Foods
(there are multiple measurands within each class)

Nominal Concentrations of Measurands in Foods

- 1 g/g: proximates, dietary fiber, minerals, GMOs
- 1 mg/g: trans fatty acids, caffeine, nitrates
- 1 μg/g: vitamins, allergens, toxic elements (lead, mercury)
- 1 ng/g: pesticides, marine biotoxins (okadaic acid, yessotoxins), veterinary drug residues
- 1 pg/g: PAHs, mycotoxins (aflatoxin, ochratoxin), dioxins and dioxin-like PCBs

- 50 to 60 elemental species of importance
- $>10^5$ organic species in a wide variety of sample types
- covering 12 orders of magnitude in concentration.

All of these measurements are impacted by legislation.
## NMIs Deliver Chemical Measurement Services in Several Areas

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| 12 | Fuels                | 12.1| Coal and Coke             |
|    |                      | 12.2| Petroleum Products        |
|    |                      | 12.3| Bio-mass                  |
|    |                      | 12.4| Other                     |

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Addressing Metrological Issues in the “Biosciences” is Hard

Life processes are very complex and the information space is very vast

Understanding life processes requires more than physical and chemical measurements

**Physical:** What’s the mass of Willie? 90 kg

**Chemical:** How much cholesterol is there in Willie’s blood? 150 mg/dL

**Biological:** Which cholesterol-lowering drug would be best for Willie in terms of both efficacy and potential side effects? Trial and Error
WG's Conduct Key Comparisons that Interrogate Measurement Competencies across a Broad Range of Critical 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
Examples of Impact
in three Grand Challenge Areas

• Health

• Climate Assessment

• Food Safety and Nutrition
Healthcare reform is a major issue throughout the world

- The rising cost of healthcare and increased prevalence of chronic diseases is having a devastating affect on economic security and quality of life in all parts of the world.

- In 2013 in the U.S. alone, ~$2.8 trillion spent on healthcare of which 10% - 15% was based on measurements
  - 70% of healthcare decisions are based on results from clinical laboratory measurements
    - Measurements need to be comparable over space and time
    - Standards exists for only ~10% of the 700 diagnostic markers routinely measured
    - Several NMIs have begun developing CRMs to address this lack of standards
    - Standards within and among NMIs need to be comparable
Comparisons have assisted in establishing and or validating NMI capabilities for establishing primary references for organic molecules with molecular weight less than 500 Da. Standard uncertainties are less than 1 mg/g for purities greater than 950 mg/g.
Comparison of degrees of equivalence of measurement capabilities for Creatinine in Human Serum

Documented degree of equivalence of measurement capabilities

Comparison of value-assigned CRMs for Creatinine in Serum
Measurement Science Advancing Measurable, Reportable, and Verifiable (MRV) Greenhouse Gas Mitigation Activities

- Measurable & reportable emissions form the basis for a country’s GHG Inventory (Bali Action Plan, UNFCCC Conference of the Parties, 2007 (COP 13))

- Transparent verifications of inventories and mitigation activity using measurements independent of the reporting entity are essential for international acceptance of these reports

- Metrological advances based on sound scientific principals are needed for these measurements and for verification of measurement results
Ten fold improvement in equivalence of standards between 2003 and 2013. Target uncertainty is 0.5 nmol/mol for standards to have negligible impact on global monitoring of methane in air.
The on-going (every two years since 2008) key comparison BIPM.QM-K1:

- evaluates the level of comparability of ozone reference standards that are maintained as national standards, or as primary standards within international networks for ambient ozone measurements.

- applies to ozone standards based on the UV photometry principle as per protocol. Other types of instruments can participate in the key comparison, but with a modified version of the protocol.
Background

VOCs (simple hydrocarbons) are precursors for formation of ozone ($O_3$)
- contributes to photochemical smog

WMO/GAW obtaining atmospheric measurements of VOCs
- bias between current sources of standards; need for one central source

WMO requested that CCQM NMIs develop standards to underpin their atmospheric measurements for VOCs
- request for ppb (nmol/mol) level standards for groups of HC’s, terpenes, and oxygenates (they dilute to measure ppt (pmol/mol) levels)

Approach

NMIs have formed a Central Calibration Laboratory (CCL)
- NIST USA
- NPL the UK
- NMi the Netherlands
- KRISS Korea

A 27 component HC standard at nominal 2 ppb has been supplied to WMO/GAW
- confirmed by all 4 NMIs of the CCL through EURAMET 886 comparison
Measurement Challenges for Enforcement of Food Regulations: Four Key Areas

1) Incurred residues and contaminants in food

- Hormones
  - Natural and synthetic
- Antibiotic
  - Chloramphenicol, sulphonamides, penicillin, in milk, tissue linking rapid tests to reference methods,
  - Chloramphenicol in milk + others
- Biogenic amines in fish
  - Histamine, putrescine, cadaverine, tyramine
- 3-MCPD Soya sauce and vegetable hydrosolates,
- PAHs, dioxins and dioxin like PCBs in a suitable matrix
- Nitrates in lettuce, spinach, Nitrites/Nitrites in cured meat
- Heavy metals and trace elements Hg, Cd, Pb, Cu, Fe
- Tin in canned food
- Nitrates in lettuce and inorganic

2) Labeling and nutritional legislation

- Vitamins, A, D, E, C, B vitamins
- Amino acids
- Vitamin A or D in a milk powder or processed food
- SO₂, sorbic or benzoic acid
- Other, caffeine in soft drinks
- Sulphur dioxide in processed food
- Sorbic or benzoic acid
- Protein, fat, ash, etc.
- Butter fat in spreads
- GMO presence in seeds, maize or processed food
- Fat in a milk product or other matrix
- GMO

3) Indigenous contaminants

- Mycotoxins
  - Aflatoxins nuts/milk, infant formula, Ochratoxins in coffee, cereals, beer, Patulin in apple juice
  - Fusarium mycotoxins in cereals
  - Aflatoxin M1 in milk
  - Shell fish toxins
    - Mouse bioassay (reference method)
    - Okadaic acid

4) Tariff classification

- Butterfat (methyl ester of butyric acid), Individual sugars,
- Caffeine or theobromine, chocolate
- Fat in milk powder
- Protein in meat
- Butterfat (butyric acid methyl ester) in mixed spread, chocolate or cream liqueur
- Caffeine/theobromine in chocolate (i...
CCQM-K45: Tin in Tomato Paste

MEASURAND: Mass fraction of Tin in tomato paste
NOMINAL VALUE: ~230 mg/kg

Degrees of equivalence, $D_i$ and expanded uncertainty $U_i$ ($k = 2$), expressed in mg/kg

$x_R = 227.1$ mg/kg and $u_R = 1.2$ mg/kg
Food Analysis Performance Assessment Scheme (FAPAS®)
Proficiency Test 0754 Results (>70 food testing laboratories)
Tin in a frozen tomato paste

Traceable Reference Value Assigned by LGC = 224.6 mg/kg
Consensus value (as used in FAPAS PT evaluation) = 206 mg/kg

Changes in ratings of laboratories PT performance if use reference value instead of consensus value

<table>
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<th>Effect on Rating</th>
<th>Number of Labs.</th>
<th>Percent</th>
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Major Issues

• Exponential increase in interest/needs for Comparisons and studies

• Steady Increase in number of CMCs to review
  – Continuing with the current approach at the same level of effort is not sustainable !!!

• Organizational Structure

Planned Actions

• Establishing a Strategic Planning Framework for Key Comparisons
  – defining a finite number of comparisons that test not the techniques -- but rather the institutional knowledge and core competencies required to deliver services recognized under CIPM MRA

• Examining basis and structure for CMCs
• Combining Inorganic and Electrochemical WGs; subdividing Bio WG
Established in 1993:

CCQM Activities have -- without question –

• enabled NMIs to identify “spikes” of excellence within the chem/bio world that have led to establishment of strategic collaborations for both research and standards development purposes

• Improved the quality of chemical and biological measurements within the worldwide NMI community
  • Which has led to better (more and higher quality) services for end user customers
Session I

• The Importance and Role of the Mole and the Kilogram in Chemical and Biological Measurements

• CIPM Activities to Redefine the Mole and Kilogram

Session II

• The CCQM and its Activities to Assess and Improve the Equivalence of National Standards for Chemical and Biological Measurements
19th meeting of the CCQM Plenary
Paris, April 2013

Bio, Organic, Inorganic and Gas Working Groups, Pretoria, SA
November, 2013